**Scientific Plenary I: Snap, Crackle, PARP**

**Saturday, March 16, 2019**

Moderators: John K. Chan, MD, California Pacific & Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA
Barbara Norquist, MD, University of Washington Medical Center, Seattle, WA, USA

1 - Scientific Plenary

**Time without symptoms or toxicity in patients with recurrent ovarian cancer receiving niraparib maintenance treatment versus placebo: A TWiST analysis of the ENGOT24-OV16/NOVA trial**


**aDana-Farber Cancer Institute, Boston, MA, USA, bFIECON Ltd, St Albans, United Kingdom, cRigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, dBritish Colombia Cancer Agency, Vancouver, BC, Canada, eArbeitsgemeinschaft Gynaekologische Onkologie (AGO) Study Group and Department of Obstetrics and Gynecology, University Hospital, Ludwig-Maximilians, University of Munich, Munich, Germany, fInstitut Català d’Oncologia-IDIBELL, L’Hospitalet-Barcelona, Barcelona, Spain, gGroupe d'Investigateurs Nationaux pour l’Etude des Cancers Ovariens (GINECO) and Institut du Cancer de Montpellier, Montpellier, France, hThe Royal Marsden NHS Foundation Trust, London, United Kingdom, iThe Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, United Kingdom, jH. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA, kHaukeland University Hospital, Bergen, Norway, lMcGill University Health Centre, Montreal, QC, Canada, mArbeitsgemeinschaft Gynaekologische Onkologie (AGO) Study Group and Department of Gynecologic Oncology, Kliniken Essen Mitte, Essen, Germany, nHospital Universitario San Carlos, Madrid, Spain, oGroupe d’Investigateurs Nationaux pour l’Étude des Cancers Ovariens (GINECO) and Centre Antoine Lacassagne, Nice, France, pUniversity College London, London, United Kingdom, qCentre Hospitalier Régional de la Citadelle, Liège, Belgium, rCannizzaro Hospital, Catania, Italy, sThe Nordic Society of Gynecological Oncology (NSGO) and Aalborg University, Aalborg University, Aalborg, Denmark, tThe Nordic Society of Gynecological Oncology (NSGO) and Lund University Hospital, Lund, Sweden, uThe Nordic Society of Gynecological Oncology (NSGO) and Rigshospitalet-Copenhagen University Hospital, Copenhagen, Denmark

**Objective:** Results from the ENGOT-OV16/NOVA study demonstrated that women with recurrent ovarian cancer who receive niraparib, a poly(ADP-ribose) polymerase inhibitor, as maintenance therapy after platinum treatment had significantly longer PFS compared to those on placebo. In addition, quality of life (QOL) data from the trial support the finding that women on niraparib had comparable QOL to those on placebo. Here we look further into QOL and estimate the time without symptoms or toxicity (TWiST) in women receiving niraparib maintenance compared with women receiving placebo.

**Method:** Mean PFS was estimated for niraparib and placebo using parametric survival curves based on 553 patients enrolled in the ENGOT-OV16/NOVA phase III trial. A restricted mean time with toxicity was estimated based on Kaplan-Meier curves for adverse events (AEs) using patient level data. Symptomatic AEs included were grade ≥2 fatigue, nausea, and vomiting. Toxicity time was calculated as the number of days a patient experienced an AE after randomization and prior to disease progression. TWiST was then estimated as the difference between mean PFS and mean toxicity time between niraparib and placebo. Uncertainty was explored using alternative survival models for estimating mean PFS.

**Results:** Treatment with niraparib resulted in a mean PFS benefit of 3.23 years and a mean toxicity time of 0.28 years compared with placebo in the gBRCAmut cohort. Treatment with niraparib resulted in a mean PFS benefit of 1.44 years and a mean toxicity time of 0.10 years compared with placebo in the non-gBRCAmut cohort. Hence, treatment with niraparib compared with placebo in the gBRCAmut and non-gBRCAmut cohorts resulted in a mean TWiST benefit of 2.95 and 1.34 years, respectively. When using alternative survival models to estimate PFS, the mean TWiST benefit of niraparib compared with placebo was 1.62, 1.64, 2.66, and 3.65 years, and 0.63, 0.73, 1.23, and 0.94 years using the lognormal, log-logistic, normal $k = 1$, and odds $k = 3$ distributions in the gBRCAmut and non-gBRCAmut cohorts, respectively.

**Conclusion:** Patients treated with niraparib experienced increased mean TWiST compared with placebo. Thus, patients treated with niraparib in the ENGOT-OV16/NOVA trial experienced more time without symptoms or toxicities compared with control.
2 - Scientific Plenary
Baseline platelet count and body weight as predictors of early dose modification in the quadra trial of niraparib monotherapy for the treatment of heavily pretreated (≥4th line), advanced, recurrent high-grade serous ovarian cancer


Objective: A previous analysis from the NOVA phase 3 study of patients receiving niraparib maintenance in the recurrent setting identified baseline platelet count (PC) < 150,000/μL and baseline body weight (BW) < 77 kg as predictive factors for early thrombocytopenia. Based on this analysis, a 200-mg starting dose for patients with BW < 77 kg or PC < 150,000/μL has been suggested to improve tolerability without compromising efficacy. A post hoc analysis of the phase 2, single-arm QUADRA trial (NCT02354586) was performed to determine whether baseline PC and BW were predictors of early niraparib dose modification in heavily pretreated ovarian cancer patients and whether early dose modifications had an impact on treatment efficacy.

Method: A total of 463 patients were included in the safety population. Starting dose of niraparib was 300 mg daily, and treatment-emergent adverse events (TEAEs) were managed with dose interruptions and reductions to 200 or 100 mg. Incidence of TEAEs was assessed based on baseline PC and BW. A post hoc analysis compared efficacy outcomes between patients receiving ≤200 mg versus >200 mg mean niraparib dose during the first 2 months of therapy.

Results: Of the 463 patients, 316 (68%) had PC < 150,000/μL or BW < 77 kg. Patients with either low baseline PC or BW compared with the remaining patients experienced more AEIs, more grade ≥3 and serious TEAEs, including grade 3/4 hematologic AEs: thrombocytopenia (30% vs 14%, P < 0.0001), neutropenia (12% vs 5%, P = 0.03), and anemia (9% vs 3%, P = 0.003). Among these patients who, based on NOVA analysis, would be suitable for a starting dose of 200 mg, objective response rate (ORR), disease control rate (DCR) and clinical benefit rate at 24 weeks (CBR24) were 8%, 58%, and 19%, respectively, for those who received a mean daily dose of ≤200 mg versus 7%, 39%, and 15%, respectively, for patients who received a mean dose >200 mg. Among the remaining patients with PC ≥ 150,000/μL and BW ≥ 77 kg, ORR, DCR, and CBR24 were 9%, 59%, and 21%, respectively, for those who received a mean dose of ≤200 mg vs 11%, 57%, and 23%, respectively, for patients who received a mean dose >200 mg. Overall survival among patient subgroups determined based on mean niraparib dose, PC, and BW is depicted in Figure 1.
Conclusion: Consistent with the NOVA trial results, our findings suggest that baseline PC and BW can be used to determine optimal niraparib dosing. In this difficult-to-treat patient population, efficacy was preserved despite dose adjustments.

3 - Scientific Plenary
A prospective evaluation of tolerability of niraparib dosing based upon baseline body weight and platelet count:
Blinded pooled interim safety data from the ENGOT-OV26/PRIMA study
*Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Phoenix Creighton University School of Medicine at St. Joseph’s Hospital, Phoenix, AZ, USA, #The Nordic Society of Gynecological Oncology (NSGO) and Rigshospitalet-Copenhagen University Hospital, Copenhagen, Denmark, †Belgian Gynecologic Oncology Group (BGOG) and University of Leuven, Leuven Cancer Institute, Leuven, Belgium, TESARO, Inc., Waltham, MA, USA, Medical University of South Carolina, Charleston, SC, USA, NYU Langone Medical Center, New York, NY, USA, Grupo Español de Investigación en Cáncer de Ovario (GEICO) y Clínica Universidad de Navarra, Madrid, Spain

Objective: Niraparib (ZEJULA®) is a selective inhibitor of PARP1/2 approved for maintenance treatment of recurrent ovarian cancer (OC) patients who are in complete or partial response to platinum therapy regardless of BRCA or homologous recombination deficiency status, based on the pivotal phase III ENGOT-OV16/NOVA trial (*N Engl J Med*. 2016 375:2154-2164). In NOVA, dose adjustments due to adverse events (AEs) occurred in 69% of patients and tended to occur early, with most patients reaching their individualized dose within 3 months. A retrospective analysis of NOVA showed that patients with body weight <77 kg or platelet count <150 K/µL were more likely to be dose-reduced due to hematologic AEs; importantly, efficacy was not compromised in those patients. The PRIMA study evaluates niraparib versus placebo as maintenance therapy in high-risk stage III/IV OC patients after frontline platinum therapy. Regular and independent safety data reviews have not identified any new safety issues in the trial. The study was prospectively amended to evaluate the safety and efficacy of a new dosing paradigm.

Method: Patients were initially randomized 2:1 to start at niraparib 300 mg QD or placebo. The protocol was amended to modify the starting dose to 200 mg QD in patients with baseline weight < 77 kg or platelet count <150 K/µL and 300 mg in all other patients. The trial remains blinded for efficacy and safety. The safety analyses were conducted to compare the AEs in patients who started the study with 300 mg prior to the amendment compared with those who started at 200 or 300 mg after the protocol was amended.

Results: Based on the data cutoff on August 15, 2018, 733 patients were randomized, and 727 patients were dosed. Of those dosed, ≈34% (n = 247 patients) were dosed based on weight and platelet count. Blinded data were pooled from niraparib and placebo. There were no major differences in key patient demographics or disease characteristics. Relevant safety data are presented in Table 1.

Conclusion: These interim safety data prospectively confirm that niraparib tolerability is improved with the starting dose of 200 and 300 mg when dosing is based upon body weight and platelet count.

Table 1: Overall Survival and Progression Free Survival by Subgroups; All Randomized Patients
4 - Scientific Plenary
The effect of age on efficacy and safety outcomes with rucaparib: A post hoc exploratory analysis of ARIEL3, a phase III, randomized, placebo-controlled maintenance study in patients with recurrent ovarian carcinoma


UCL Cancer Institute and UCL Hospitals, London, United Kingdom, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, Fondazione IRCCS Istituto Nazionale dei Tumori and MITO, Milan, Italy, Memorial Sloan Kettering Cancer Center, New York, NY, USA, Vall d’Hebrón University Hospital, Vall d’Hebrón Institute of Oncology (VHIO), Barcelona, Spain, St John of God Subiaco Hospital, Subiaco, Australia, European Institute of Oncology and University of Milan-Bicocca, Milan, Italy, Ottawa Hospital Research Institute, Ottawa, ON, Canada, The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom, Policlinico Universitario A. Gemelli IRCCS Università Cattolica del Sacro Cuore Roma, Rome, Italy, Gustave Roussy Cancer Center, INSERM U981, and Groupe d’Investigateurs Nationaux pour l’Etude des Cancers Ovariens (GINECO), Villejuif, France, Florida Hospital Cancer Institute, Orlando, FL, USA, Oncology Center of Galicia, La Coruña, Spain, Auckland City Hospital, Grafton, New Zealand, Royal Brisbane and Women’s Hospital, Herston, QLD, Australia, University of Queensland, St Lucia, QLD, Australia, The Ohio State University, James Cancer Center, Columbus, OH, USA, The Royal Marsden NHS Foundation Trust, London, United Kingdom, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, United Kingdom, Clovis Oncology Inc., Boulder, CO, USA, Clovis Oncology, Inc., Boulder, CO, USA, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Initial results from ARIEL3 were reported previously (Coleman et al. Lancet. 2017;390:1949-61). We investigated the efficacy and safety of rucaparib maintenance treatment in three age-based subgroups from ARIEL3 in a post hoc exploratory analysis.

Method: In ARIEL3, patients were randomized 2:1 to oral rucaparib (600 mg BID) or placebo. Analysis subgroups were based on patient age at baseline: <65, 65–74, or ≥75 years. Investigator-assessed progression-free survival (PFS) and safety were analyzed in the intent-to-treat (ITT) population (i.e., all randomized patients) for each subgroup.

Results: The visit cutoff dates for efficacy and safety were April 15, 2017, and August 15, 2017, respectively. More patients aged <65 years had a deleterious germline or somatic BRCA mutation (rucaparib, n = 96 [40.5%]; placebo, n = 49 [41.9%]) than patients aged 65–74 years (rucaparib, n = 29 [25.7%]; placebo, n = 15 [23.4%]) or patients aged ≥75 years (rucaparib, n = 5 [20.0%]; placebo, n = 2 [25.0%]). In the ITT population, investigator-assessed median PFS for patients aged <65 years was 11.1 months (n = 237) in the rucaparib arm versus 5.4 months (n = 117) in the placebo arm (HR = 0.33; 95% CI 0.25–0.43); for patients aged 65–74 years, median PFS was 8.3 months (n = 113) versus 5.3 months (n = 64; HR = 0.43; 95% CI 0.29–0.64); and for patients aged ≥75 years, median PFS was 9.2 months (n = 25) versus 5.5 months (n = 8; HR = 0.47; 95% CI 0.16–1.35). The most common (≥35%) treatment-emergent adverse events (TEAEs) (any grade and grade ≥3), dose modifications (i.e., treatment interruptions and/or dose reductions), and treatment discontinuations by age group are shown in Figure 1. The most common nonhematologic TEAEs in the rucaparib arm included nausea, asthenia, and vomiting; the most common hematologic TEAEs in the rucaparib arm included anemia and thrombocytopenia.

Conclusion: Maintenance treatment with rucaparib improved median PFS and reduced the risk of progression versus placebo regardless of age subgroup. In general, the safety profile of rucaparib was consistent across the three age subgroups. Although there was no clear trend, rates of dose modifications and treatment discontinuations varied by age subgroup in the rucaparib and placebo arms.
**5 - Scientific Plenary**

**Costs and benefits of tumor testing for BRCA mutations in high-grade serous ovarian cancer as a triage for confirmatory genetic testing**

*University of British Columbia, Vancouver, BC, Canada, British Columbia Cancer Agency, Vancouver, BC, Canada, BC Cancer, Vancouver, BC, Canada*

**Objective:** Women with high-grade serous ovarian carcinoma (HGSC) have a 1 in 5 chance of carrying a BRCA mutation and are eligible for genetic testing. Costs are incurred to the health care system for genetic testing, regardless of the testing result. Testing HGSC tissue for BRCA mutations (tumor testing) could improve genetic testing efficiency by referring only those with BRCA mutations in the tumor, rather than all HGSC patients. The objective was to conduct a cost-effectiveness analysis to compare universal genetic (germline) testing to tumor testing as a triage for germline testing in HGSC patients.

**Method:** The Markov Monte Carlo simulation model was used to compare the costs and benefits of these two strategies. Primary outcomes included the number of BRCA mutation carriers identified from index cases and first-degree relatives (FDR), ovarian and breast cancer cases averted in FDR, and costs associated with each strategy. Tumor-testing performance measures were derived from published literature. Costs (U.S. dollars) were estimated from Medicare claims. Sensitivity analyses accounted for uncertainty around various parameters. Time horizon was 50 years.

**Results:** Germline testing identifies more BRCA mutation carriers but is more costly than tumor testing. Assuming 10,000 newly diagnosed women in the United States with HGSC every year, the model predicts that germline and tumor testing will identify 1,759 and 1,672 BRCA mutation carriers, respectively. Average lifetime costs were $7,237 and $6,660, and life expectancy gains were 22.41 and 22.40 years for FDR, yielding an incremental cost-effectiveness ratio of $76,624. Tumor testing becomes cost-effective if its sensitivity exceeds 97%, and costs are below one-third of germline testing costs.

**Conclusion:** Germline testing is more effective in identifying BRCA mutation carriers, but tumor testing is less costly by triaging women with HGSC to BRCA mutation testing. Tumor testing may become the preferred strategy given improved sensitivity and further reduction in costs.

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**6 - Scientific Plenary**

**Simultaneous clinical testing for germline and somatic mutations in ovarian carcinoma (OC): Mutation rate and impact on therapeutic decisions**

Objective: Germline genetic testing is recommended for all patients diagnosed with ovarian carcinoma (OC). The presence of somatic BRCA1 and BRCA2 (BRCA) mutations predicts response to PARP inhibitors, occurs in 6% of cases, and is not routinely identified at diagnosis. Our goal was to report our experience with simultaneous clinical testing for both germline and somatic mutations in OC cases and identify the frequency with which such testing had a impact on clinical decision making.

Method: Between July 2017 and July 2018, 69 cancer susceptibility genes in DNA from paired peripheral blood (germline) and OC specimens (somatic) were sequenced using targeted sequencing with the BROCA test whenever clinicians ordered simultaneous clinical genetic testing. We retrospectively reviewed each patient’s medical record to extract demographic and clinical information, and calculated descriptive statistics.

Results: Clinicians ordered simultaneous testing for 36 women with newly diagnosed OC and 7 women with recurrent OC. Average age at diagnosis was 60 years (range 27–83 years). The majority of patients were white (31, 72.1%) and had high-grade serous OC (28, 65.1%) and stage III disease (22, 51.2%). Neoplastic samples came from surgical specimens in 31 cases (72.1%), from biopsy in 11 cases (25.6%), and from cytology in 1 case (2.3%). Figure 1 shows the distribution of germline and somatic mutations identified through testing. In 18 cases (41.9%), somatic testing provided additional information on actionable mutations when germline testing was negative or inconclusive. With a median follow-up of 8.5 months (IQR 16–68.4 months), treating providers documented reviewing the results of genetic testing in 34 (79%) of cases. Genetic testing had an impact on clinical decision making in 10 cases (23.3%); 7 based on somatic mutations (3 BRCA1, 2 BRCA2, 1 RAD51B, 1 BRIPI) and 3 on germline mutations (1 BRCA1, 1 BRCA2, 1 PMS2). In response to genetic test results, patients were referred to cancer screening programs, enrolled in clinical trials of maintenance PARP inhibitors after response to upfront treatment, and started on maintenance PARP inhibitors after a recurrence.

Conclusion: Simultaneous germline and somatic mutation testing is an efficient way to provide enhanced information to guide the clinical care of patients with OC. This strategy may prove increasingly valuable as more targeted therapies become available for the upfront treatment of OC.

Fig. 1. Results of germline and somatic sequencing. Negative = neither germline nor somatic mutation identified. Germline = germline mutation identified with corresponding somatic mutation. Somatic = somatic mutation identified but no germline mutation. (N = 43, 100%)
Scientific Plenary II: Challenges in Cancer Care Delivery
Saturday, March 16, 2019
Moderators: Kemi M. Doll, MD, MSc, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
Christine Fisher, MD, University of Colorado Hospital, dept OBGYN, Aurora, CO, USA

8 - Scientific Plenary
The cost of treatment: Financial toxicity and opportunity costs among gynecologic cancer patients starting a new line of treatment

Objective: Our objective was to evaluate the frequency of financial toxicity and opportunity costs experienced by gynecologic cancer patients receiving systemic therapy.

Method: A cross-sectional survey of gynecologic cancer patients starting a new line of systemic therapy within the previous 8 weeks was conducted over the phone or in-person at a tertiary-care referral center. Comprehensive Score for Financial Toxicity (COST) <26 was used as a threshold for financial toxicity, and severity was graded on a scale of 1–3. Opportunity costs were defined and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Results: Twenty-one patients were identified. For initial PARPi (PARPi1), 12 patients (57.1%) received veliparib; 6 patients (28.6%) olaparib; and 3 patients (14.3%) rucaparib, resulting in 10 complete responses (CR), 3 partial responses (PR), 4 stable disease (SD), and 2 progressive disease (PD). PARPi1 was used as maintenance in 2 patients. PARPi1 was discontinued because the planned number of cycles was reached (n = 10), progression (n = 7), toxicity (n = 2), adverse effects of other chemotherapy (n = 1), and patient choice (n = 1). For second PARPi (PARPi2), 9 patients (42.9%) received niraparib; 6 patients (28.6%) olaparib; and 6 patients (28.6%) rucaparib, resulting in 3 PR, 13 SD, and 2 PD. PARPi2 was used as maintenance in 3 patients. Notably, the 3 patients who experienced a PR to PARPi2 had a BRCA mutation and had all experienced a CR to PARPi1. PARPi2 was discontinued because of progression (n = 12), toxicity (n = 6), financial reasons (n = 1), or provider choice (n = 1). One patient currently remains on therapy with PARPi2. One patient (5.0%) experienced grade 3/4 anemia; 5 patients (25.0%) grade 3/4 thrombocytopenia; and 1 patient (5.0%) grade 3/4 neutropenia. In this small cohort of patients, overall response to initial PARPi did not predict overall response to second PARPi (P > 0.05). Toxicity after initial PARPi was not significantly associated with toxicity following second PARPi (P > 0.05).

Conclusion: In this multiinstitutional study, PARPi2 demonstrated activity in patients with recurrent EOC but only in those with excellent responses to PARPi1 and a BRCA mutation. Prior PARPi did not predict response or toxicity to second PARPi. Now that there are three FDA-approved PARPi for different indications, repeat use of PARPi may become more common. More data are needed regarding the efficacy and safety of this approach.
Conclusion: Financial toxicity is common, affecting 60% of gynecologic cancer patients starting a new line of treatment. The money and time spent on health care have a significant and likely under-recognized impact on patients’ employment and spending behaviors.

9 - Scientific Plenary
Impact of financial assistance programs on time to completion of therapy in women receiving chemoradiation for cervical cancer
J. Gillena, S. Grimesb, K.G. Essela, G. Duinincka, D. Zhaoa, J.S. Thompsonb and D.L. Richardsonc. aThe University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, bThe University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK, USA, cThe University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK, USA

Objective: The aim of this study was to evaluate how social services programs improve outcomes among patients with cervical cancer undergoing chemoradiation.

Method: This is a single-institution, retrospective analysis of all patients receiving chemoradiation for squamous cell, adenocarcinoma, or adenosquamous cancer of the cervix from January 1, 2015, to July 31, 2018. Demographic, clinical, and social services utilization data were collected. Descriptive statistics and univariate and multivariate analyses were performed. Kaplan-Meier curves were used to estimate PFS and OS.

Results: Of the 116 patients who met inclusion criteria, 106 (91.45%) completed therapy in ≤63 days. The median household income among patients was $45,782 ($19,771–$96,222). Patients, on average, used 1.24 services, including registration for disability and Medicaid, assistance with medication costs, financial assistance, access to emergency funds, access to low-cost or free lodging, and transportation. Only disability registration was associated with improved time to completion of therapy ($P < 0.001$); however, registration for federally funded breast and cervical cancer Medicaid demonstrated a trend toward ability to complete therapy in ≤63 days ($P = 0.06$). When compared to high-income patients who did not require assistance, low-income patients (those whose household income was less than the median) who received assistance from the cancer center did not experience a significantly different median PFS or median OS (11.2 vs 12.1 months, $P = 0.495$ and 16.2 vs 15.3 months, $P = 0.098$). Low-income patients receiving assistance were also able to complete therapy in a similar timeframe as their high-income counterparts (56.5 vs 50 days, $P = 0.11$).

Conclusion: In a rural state with a single academic cancer center, our data demonstrate that we may be able to overcome barriers to care with social and financial assistance programs. Identifying individual patients’ needs prior to therapy may allow for continued improvement in therapy compliance and patient outcomes.

10 - Scientific Plenary
Better late than never: Brachytherapy is more important than timeframe in cervical cancer outcomes
T.R.K. Korenaga, W. Piersonb, M. Swansonb, J.S. Chapmanc and L.M. Chenb. aUniversity of California, San Francisco, San Francisco, CA, USA, bUCSF School of Medicine, San Francisco, CA, USA, cUCSF Helen Diller Comprehensive Cancer Center, San Francisco, CA, USA

Objective: Prolonged treatment of chemoradiation therapy has been shown to have worse outcomes in patients with locally advanced cervical cancer. Our objective is to evaluate the utilization of standard-of-care (SOC) treatment of external beam radiation therapy (EBRT) with brachytherapy and concurrent chemotherapy within the recommended 8 weeks, evaluate its effect on survival, and identify possible disparities in health care delivery.

Method: The National Cancer Data Base (NCDB) was queried to identify stage II-IVA cervical cancer patients diagnosed in the United States between 2004 and 2015 and receiving EBRT with concurrent chemotherapy as primary treatment. We identified whether patients received brachytherapy boost and whether patients completed treatment within the recommended 8 weeks. The primary outcome was OS; survival curves were adjusted for a fitted Cox model with a conditional approach. We evaluated the effect of sociodemographic and clinical variables on receiving SOC treatment. Differences in demographic distribution compared to the referent group were determined with $\chi^2$ tests.

Results: We identified 10,598 women with locally advanced cervical cancer primarily treated with chemotherapy and concurrent EBRT. Of those women, 7,786 (73.5%) had brachytherapy boost, and 3,882 (36.6%) received brachytherapy boost within the recommended 8 weeks (SOC). Women who received SOC had significantly superior median OS (121.3 months)
when compared to all other groups. Those who had EBRT plus brachytherapy >8 weeks (93.6 months) still had a survival advantage compared to those who had EBRT only <8 weeks (45.3 months), or EBRT only >8 weeks (51 months). Women were less likely to receive SOC within 8 weeks if they were non-Hispanic black, low income, on government insurance or uninsured, higher stage, or treated at more than one location for their radiation. See Figure 1.

**Conclusion**: Completing SOC concurrent chemoradiation therapy in the recommended 8 weeks shows a superior overall survival. Patients who received brachytherapy boost show superior survival to patients receiving EBRT alone, regardless of treatment duration. Disparities in care for vulnerable populations highlight the importance of programs that facilitate timely care coordination for patients with cervical cancer.

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**11 - Scientific Plenary**

**Disparities in utilization and timing of brachytherapy for patients with locally advanced cervical cancer: A National Cancer Database study**

S. Alimena, D. Yang, A. Melamed, L. Lee, M.J. Worley Jr, K.M. Elias, P. Oriole, and M. King. Brigham and Women’s Hospital/Harvard Medical School, Boston, MA, USA, Massachusetts General Hospital, Boston, MA, USA, Harvard Medical School, Boston, MA, USA, Dana-Farber Cancer Institute, Boston, MA, USA

**Objective**: African-American, Hispanic, and American Indian women have the highest incidence of cervical cancer in the U.S., and mortality is worse for black patients with cervical cancer. Treatment of locally advanced cervical cancer consists of external beam radiation therapy (EBRT) and chemotherapy, followed by brachytherapy (BT). This study sought to evaluate racial disparities in BT use in patients with stage IB2–IVA cervical cancer treated in the last 10 years using the National Cancer Data Base.

**Method**: A retrospective cohort study was performed using 15,411 eligible women. Women were excluded if they did not receive EBRT or had unknown survival data. Multivariate logistic regression was used to evaluate factors associated with BT boost. Kaplan-Meier analysis and a propensity score adjusted model with inverse probability treatment weighting were used evaluate racial differences in survival.

**Results**: Black women were significantly less likely to receive BT (OR 0.86, 95% CI 0.77-0.95, p=0.003) and had the worst all-cause mortality (median survival 52.5 months [95% CI 46.3-58.6] versus 65.3 months [95% CI 61.5-69.1] for non-blacks, p<0.001). In the propensity score adjusted model, blacks had an increased risk of death compared to non-blacks (AHR 1.11, 95% CI 1.02-1.21, p=0.013) among women who did not receive BT. However, there was no significant difference in survival between blacks and non-blacks among women who received BT (AHR 1.01, 95% CI 0.92-1.11, p=0.83, p-interaction=0.043). Other factors associated with a lower likelihood of receiving BT beside race included age >70, uninsured or publicly insured, residents of the South and West of the U.S., and Charlson/Deyo comorbidity score of 2 or more. See Table 1.

**Conclusions**: Black women with locally advanced cervical cancer are less likely to receive BT compared to non-black women, which mediates survival differences by race. Improving access to BT for black women may improve overall survival.

**Table 1.** Results of multivariate logistic regression for factors associated with brachytherapy use.
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<td>1.06</td>
<td>0.93-1.19</td>
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<td>$63,000+</td>
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<td>0.95-1.28</td>
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<tr>
<td>II</td>
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<td>0.76-1.04</td>
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<td>III</td>
<td>0.47</td>
<td>0.41-0.56</td>
<td>&lt;0.001*</td>
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<tr>
<td>IVA</td>
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<td>0.16-0.24</td>
<td>&lt;0.001*</td>
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<tr>
<td>Non-squamous cell</td>
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<td>0.86-1.00</td>
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<td>Moderately differentiated</td>
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<td>Poorly differentiated / Undifferentiated</td>
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<td>Unknown</td>
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<td>Comprehensive Community Cancer Program</td>
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<td>0.70-0.82</td>
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<td>Community Cancer Program</td>
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<td>0.48-0.66</td>
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<td>Integrated Network Cancer Program</td>
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<td>Midwest</td>
<td>0.96</td>
<td>0.85-1.08</td>
<td>0.46</td>
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<td>South</td>
<td>0.67</td>
<td>0.60-0.75</td>
<td>&lt;0.001*</td>
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<tr>
<td>West</td>
<td>0.86</td>
<td>0.76-0.97</td>
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<td>≤ 5 miles</td>
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<td>5.1 - 10 miles</td>
<td>1.04</td>
<td>0.93-1.15</td>
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<td>10.1 - 30 miles</td>
<td>1.08</td>
<td>0.98-1.20</td>
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<tr>
<td>&gt;30 miles</td>
<td>1.33</td>
<td>1.17-1.51</td>
<td>&lt;0.001*</td>
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<table>
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<th>Education (%) who did not graduate high school</th>
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<th></th>
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<tr>
<td>≥ 21%</td>
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<td>13-20.9%</td>
<td>1.03</td>
<td>0.93-1.14</td>
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<tr>
<td>7-12.9%</td>
<td>1.08</td>
<td>0.96-1.22</td>
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<tr>
<td>&lt; 7%</td>
<td>1.02</td>
<td>0.87-1.20</td>
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<tr>
<th>Urban or Rural</th>
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<tr>
<td>Metropolitan</td>
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<td>Reference</td>
<td></td>
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<tr>
<td>Urban</td>
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<tr>
<td>Rural</td>
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<td>0.61-1.08</td>
<td>0.15</td>
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<tr>
<td>Other/missing</td>
<td>1.56</td>
<td>1.19-2.05</td>
<td>0.001*</td>
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<tr>
<td>Charlson/Deyo Score</td>
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<tr>
<td>0</td>
<td>1.0</td>
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<tr>
<td>1</td>
<td>1.04</td>
<td>0.93-1.16</td>
<td>0.50</td>
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<tr>
<td>2 or more</td>
<td>0.73</td>
<td>0.60-0.89</td>
<td>0.001*</td>
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</table>

| Nodal Status | | | |
| Negative | 1.0 | Reference | |
| Positive | 0.97 | 0.75-1.24 | 0.79 |

| Year of Diagnosis | | | |
| 2004-2009 | 1.0 | Reference | |
| 2010-2014 | 1.29 | 1.20-1.39 | <0.001 |

OR = odds ratios. CI = confidence interval.

12 - Scientific Plenary
Epidemiologic profile of type specific human papillomavirus (HPV) infection after initiation of HPV vaccination in Japanese girls
M. Sekine1, M. Yamaguchi3, R. Kudo1, S. Adachi2, Y. Ueda5, S.J.B. Hanley3 and T. Enomoto5. 1Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, 2Niigata University Graduate School of Medicine, Niigata, Japan, 3Osaka University Graduate School of Medicine, Osaka, Japan, 4Hokkaido University Graduate School of Medicine, Sapporo, Japan

Objective: Organized human papillomavirus vaccination (OHPV) in Japan was introduced in 2010 for girls aged 12–16 years who were born in 1994 or later. The rate of OHPV coverage was 70%–80% in girls born in from 1994 to 1998. However, after suspension of the governmental recommendation in June 2013, vaccination coverage dramatically decreased. In this study, we aim to investigate the change in prevalence of HPV infection after initiation of HPV vaccination in Japanese girls.

Method: We recruited 20- to 21-year-old females attending for public cervical cancer screening in Niigata from fiscal year 2014 to 2017. Residual Pap test specimens were collected for HPV screening and type-specific HPV testing. The previous HPV immunization was examined from a questionnaire to the participants. We compared the prevalence of HPV type-specific infection between women registered in 2014 (born 1993–1994) and registered in 2015–2017 (born in 1994–1997: post OHPV generation).

Results: We collected 2,493 specimens. The rates of vaccination coverage were 28.6%, 74.8%, 76.7%, and 80.0% (P < 0.01) from 2014 to 2017, respectively. The prevalence of HPV16/18 infection was significantly decreased from 1.3% in 2014 to 0.5% in 2015, 0.4% in 2016, and 0% in 2017 (P = 0.02). The 3 most prevalent types were HPV52, 16 and 56 in 2014, and HPV52, 51 and 58 in 2017. See Figure 1.

Conclusion: Our study demonstrates that the profile of type-specific HPV infection was changed after initiation of HPV vaccination in Japan.

Fig. 1. Prevalence of vaccine types HPV16/18 infection.

13 - Scientific Plenary
HPV vaccination uptake associated with HPV-related cancer incidence but not rurality in the Deep South: Does perceived risk outweigh access concerns?
J.Y. Pierce, M.J. Vickers, C. Green, J.M. Scalici and C.L. Daniel. Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA
Objective: In the United States, rurality is associated with lower human papilloma virus (HPV) vaccination rates, and uptake in the Deep South continues to lag behind national rates. We sought to understand factors associated with HPV vaccination uptake across counties by overlapping HPV-related cancer risk and epidemiologic factors associated with access to vaccination services.

Method: A secondary analysis was conducted utilizing epidemiologic data to map rates of HPV cancers, HPV vaccination, and associated variables by county in Alabama. HPV vaccine uptake of adolescents aged 13–17 was determined using the state immunization registry (ImmPRINT). Data from the U.S. Census, county health rankings for Alabama, Alabama state cancer registry, and other relevant sources were used for analysis. Frequencies were compared for descriptive data, and Pearson correlation coefficients were calculated.

Results: HPV vaccination rates (≥1 dose) in Alabama’s 67 counties ranged from 33% to 66% (median 44.5%). A total of 32 counties (47.8%) are rural (RUCC code ≥6), and 40 counties (59.7%) have a percentage of poverty above the state average of 18.4%. Mean HPV vaccination uptake was not significantly different among adolescents in metro versus nonmetro counties (44.5% vs 45.9%, \( P = 0.91 \)) and impoverished versus affluent counties (46.9% vs 42.9%, \( P = 0.75 \)). All seven highest performing counties are rural counties with above average poverty rates. There was a significant positive association between HPV vaccine uptake and the percentage of residents with public insurance (\( r = 0.47, P < 0.0001 \)). HPV vaccine uptake was also significantly correlated with poverty rate (\( r = 0.39, P = 0.0011 \)), HPV-related cancer in males (\( r = 0.48, P = 0.0008 \)), and cervical cancer incidence (\( r = 0.48, P = 0.0128 \)). Of note, county cervical cancer incidence was associated with increased HPV vaccine uptake among both adolescent males (\( r = 0.46, P = 0.0170 \)) and females (\( r = 0.49, P = 0.0110 \)) (Figure 1). HPV vaccine uptake was not associated with the number of primary care providers or pediatricians in the county.

Conclusion: Efforts to increase HPV vaccine uptake should consider a focus on perceived risk of HPV-related cancer as this appears to overcome more traditional health disparities resulting in higher vaccination in rural counties and adolescents with public insurance compared to their more affluent peers.

Fig. 1.
**Method:** A cross-sectional analysis was conducted via electronic survey among all gynecologic oncology trainees enrolled in an Accreditation Council for Graduate Medical Education-accredited fellowship in spring 2018. Burnout was measured using the Maslach Burnout Inventory. The AUDIT-C tool was used to assess alcohol use patterns, and depression screening was conducted via PHQ-2 questionnaire. Sociodemographic variables, program attributes, and well-being parameters were also evaluated. The survey was anonymous, and no incentive was provided.

**Results:** Of the 183 invited participants, 61 trainees (33.3%) responded. Overall rate of burnout for responding trainees was 87.5%. High emotional exhaustion scores were met in 85.7% of respondents, while 57.4% scored high for depersonalization. Positive depression screens and hazardous alcohol use patterns were identified in 76.7% and 85.7% of respondents, respectively. History of suicidal ideation was reported by 17.8%. High sense of personal satisfaction was noted among 83.9% of trainees; however, individuals with self-described idealist beliefs were more likely to use alcohol excessively ($P = 0.018$). Marital status, fewer duty hours, or advancing year in training were not protective against provider burnout. Twenty-five percent of respondents had not received formal training in burnout and physician wellness as part of their fellowship curriculum and were more likely to report high depersonalization scores ($P = 0.015$).

**Conclusion:** The current generations of gynecologic oncology fellowship trainees demonstrate higher than anticipated rates of burnout in comparison to SGO members, emphasizing a need to redouble efforts for wellness and burnout prevention strategies to protect patients, young physicians, and the future of the specialty.

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**15 – Wellness Session**

**The Society of Gynecologic Oncology wellness curriculum pilot: A groundbreaking initiative for fellowship training**


St. Luke’s Mountain States Tumor Institute, Boise, ID, USA, University of Wisconsin, Madison, WI, USA, New York University School of Medicine, New York, NY, USA, Society of Gynecologic Oncology, Chicago, IL, USA, Icahn School of Medicine at Mount Sinai, New York, NY, USA, The Ohio State University, Columbus, OH, USA, University of Alabama at Birmingham, Birmingham, AL, USA

**Objective:** Trainee well-being is a core component of Accreditation Council for Graduate Medical Education (ACGME) program requirements, and the Society of Gynecology Oncology (SGO) has recognized the high incidence of burnout and its negative impact. To foster a culture of wellness throughout the SGO community, we sought to engage current fellows along with the fellowship directors in wellness initiatives. We evaluated the feasibility of a pilot curriculum designed to teach skills that promote wellness and prevent burnout.

**Method:** The SGO Wellness Task Force developed a curriculum with topics based on established wellness concepts as well as specialty specific stressors such as end-of-life discussions. Faculty leaders from 15 beta-sites attended a full-day training course and then taught 4 modules over 4 months. Modules included guided discussion, multimedia presentations, and journaling. Fellows were surveyed using the perceived stress scale pre- and post-implementation. Faculty surveys focused on attitudes toward the curriculum as well as trainee responses during and after implementation.

**Results:** Ninety-five percent and 70% of fellows responded to the pre- and post-surveys, respectively. At the pre-survey, 35% of respondents did not have any wellness programs at their institution, and 60% did not utilize any wellness programming even if available. Eighty percent of fellows showed above average stress levels compared to 74% post-intervention. After the curriculum, the percentage of fellows comfortable discussing wellness topics increased from 63% to 74%. Prior to the curriculum, 75% felt they could identify symptoms of burnout or psychosocial distress. This increased to 90% post-intervention. Ninety-two percent of fellowship leaders reported their fellows were receptive to the curriculum; 73% felt that their fellows were using the techniques and tools from the curriculum. The modules were well received by fellows, and the time spent addressing wellness was widely appreciated.

**Conclusion:** The pilot wellness curriculum was well received, addresses ACGME requirements regarding trainee well-being, and could be implemented nationwide. The impact of a shift in work culture to one that openly discusses wellness and burnout was not measured but may be the more significant outcome of a gynecology oncology fellowship wellness program. Further longitudinal studies will be necessary to understand the natural course of burnout and the impact of structured wellness programming.

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#MeToo in Medicine: Understanding Sexual Harassment  

**Sunday, March 17, 2019**
**Moderator:** Michael Carney, MD, *University of Hawaii Women’s Cancer Center, Honolulu, HI*

**16 - #METOO Session**

**Workplace and sexual harassment and discrimination in gynecology**

L. Browna, L.K. Drurya, K.M. Rauba, B. Levyb, P. Brantnerc, T.C. Krivakd and R.W. Naumann. aLevine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA, bThe American College of Obstetricians and Gynecologists, Washington, DC, USA, cPB Work Solutions, Washington, DC, USA, dWestern Pennsylvania Hospital, Pittsburgh, PA, USA

**Objective:** To define and characterize the presence of workplace and sexual harassment and discrimination among physicians in gynecology.

**Method:** A beta-tested survey was distributed by email to all members of an international gynecologic society using the REDCap platform. Questions included demographics, attitudes, experiences, and sequelae regarding harassment and discrimination. All responses were anonymous. Frequency distributions and nonparametric tests were performed.

**Results:** A total of 907 physicians responded, including 604 (66.6%) United States-based gynecologists, reported here. Of U.S. respondents, 60.3% identified as female and 37.9% as male. Female respondents were younger, with 78.7% of them <50 years old compared with 45.7% of male respondents (*P < 0.05*). Trainees represented 16.5% of respondents and were more often female than male (*P < 0.006*). Females were more likely than males to think the #MeToo movement was justified and overdue (*P < 0.05*), independent of age or trainee status. More females (69.5%) than males (44.9%) felt discriminated against in the workplace (*P < 0.05*), but gender was the most common form of discrimination identified by both males (77.2%) and females (95.6%). As a result, females reported decreased self-confidence (55.6%) and lower salary (43.5%), while males reported fewer employment opportunities (53.9%) and lower patient volume (51%). Harassment was perceived to be more prevalent by females and younger males (*P < 0.05*). Of all females, 58% reported sexual or nonsexual harassment in the workplace compared with 19.7% of males (*P < 0.05*). Of female trainees 47.2% and of male trainees 16% reported harassment (*P = 0.006*). For respondents reporting harassment, 22.8% reported nonsexual harassment; 36.7% reported sexual harassment; and 39.8% reported both. Females were more likely than males to report sexual harassment (45.2% compared with 14.5%, *P < 0.05*). Most harassed respondents felt the offender was in a position of power and did not report the incident, often because of fear of reprisal. The most common sequela after an incident was loss of self-confidence, but some respondents required counseling or had relationship issues. Multiple women reported workplace-related sexual assault.

**Conclusion:** Workplace harassment, including sexual harassment, is commonly experienced by female and male gynecologists and is usually related to a power differential. Substantial improvements must be made in the workplace environment to achieve equity and a safe workplace free of harassment and discrimination.

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**Scientific Plenary III: The Elephant in the Room: MIS & Cervical Cancer**

**Monday, March 18, 2019**

**Moderators:** Robert T. Morris, MD, Barbara Ann Karmanos Cancer Institute Wayne State University School of Medicine, Detroit, MI, USA

Emma L. Barber, MD, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

**17 - Scientific Plenary**

**Minimally invasive surgery versus laparotomic surgery as a primary treatment for patients with stage IA1-IIA2 cervical cancer**

S.I. Kim3, M. Lee3, H.S. Kimb, N.H. Parka and J.W. Kimb,c. aSeoul National University Hospital, Seoul, South Korea, bSeoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea, cKorean Gynecologic Oncology Group (KGO), Seoul, South Korea

**Objective:** We sought to compare survival outcomes between minimally invasive surgery (MIS) and laparotomic surgery (LS) as a primary treatment for patients with cervical cancer (CC) in Korea.

**Method:** We reviewed medical records of patients diagnosed with FIGO stage IA1-IIA2 CC and treated at Seoul National University Hospital between 2000 and 2017. Women who received hysterectomy by LS or MIS were included, whereas those who received chemotherapy or radiation prior to surgery and fertility-sparing surgery were excluded in this study. PFS and OS were compared between the LS and MIS groups. Clinicopathologic characteristics and surgical factors associated with survival outcome were also investigated.
Results: In total, 752 patients with CC were enrolled; 543 (72.2%), 191 (25.4%), and 18 (2.4%) received LS, laparoscopic surgery, and robotic surgery (MIS group), respectively. The median length of observation was 65.3 months, during which 91 patients (12.1%) experienced disease recurrence. The proportion of stage IB1-2A2 was less frequent in the MIS group than in the LS group (82.3% vs 96.9%). However, the MIS group showed significantly poorer PFS compared to the LS group (3-year PFS rate, 90.0% vs 91.8%, and 5-year PFS rate, 80.2% vs 84.9%; \( P = 0.002 \)), while similar OS was observed between the two groups (5-year OS rate, 98.0% vs 98.1%, \( P = 0.721 \)). Multivariate analyses adjusting stage, histology, size of tumor, radicality, and pelvic lymph node dissection identified MIS as an independent poor prognostic factor for PFS (adjusted HR = 2.160, 95% CI 1.371–3.404, \( P = 0.001 \)). Similar results were also found in patients with stage IB. Confined to the patients who had bulky tumor (>2 cm) in the MIS group, intracorporeal colpotomy was associated with a decrease in PFS (\( P = 0.024 \)).

Conclusion: In this retrospective study with a relatively long observation period, MIS was associated with higher recurrence rates compared with LS in women with stage IA1-IIA2 cervical cancer.

Scientific Plenary IV: Coming Attractions: Clinical Trials
Monday, March 18, 2019
Moderators: Mark Shahram Shahin, MD, Abington Memorial Hospital, Abington, PA, USA
Katherine Fuh, MD, Washington University, School of Medicine, St. Louis, MO.

18 - Scientific Plenary
Neratinib in patients with HER2-mutant, metastatic cervical cancer: findings from the phase 2 SUMMIT ‘basket’ trial
A. D’Souzaa, L.D. Romanb, C. Saurac, I. Brañac, G.I. Shapiro, R. Passalacquac, S. Piha-Paul, R.E. Cutler, S. Shahin, L.D. Elia, F. Xu, M. Dujka, A.S. Lalani, R. Bryce, F. Meric-Bernstam, D.B. Solit, and D.M. Hyman. aUSC Norris Cancer Hospital, Los Angeles, CA, USA, bUSC Norris Comprehensive Cancer Hospital, Los Angeles, CA, USA, cVall d’Hebron University Hospital, cVall d’Hebron Institute of Oncology, VHI, Barcelona, dDana-Farber Cancer Institute, Boston, MA, USA, eIstituti Ospitalieri di Cremona, Cremona, Italy, fThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, gPuma Biotechnology Inc., South San Francisco, CA, USA, hPuma Biotechnology Inc., Los Angeles, CA, USA, iMemorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: Somatic \( \text{HER2} \) (\( \text{ERBB2} \)) mutations are observed in approximately 5% of metastatic cervical cancers (MCC), are oncogenic, and are associated with poor prognosis (Xiang et al. 2018; Ojesina et al. 2014). Neratinib is an irreversible pan-\( \text{HER2} \) tyrosine kinase inhibitor that has single-agent clinical activity in multiple \( \text{HER2} \)-mutant cancers (Hyman et al. Nature 2018). Here we describe updated interim efficacy results from the \( \text{HER2} \)-mutant MCC cohort treated with neratinib in the ongoing phase 2 SUMMIT ‘basket’ trial (Clinicaltrials.gov: NCT01953926).

Method: MCC patients with \( \text{HER2} \) mutations documented by local testing were eligible to receive oral neratinib 240 mg once daily. High-dose loperamide prophylaxis was mandatory during cycle 1. Key objectives were safety and efficacy with response assessed by RECIST 1.1 and/or PET response criteria. Genomic profiling from fresh or archival tumor tissues and/or plasma cfDNA was performed retrospectively by next-generation sequencing (MSK-IMPACT).

Results: As of August 17, 2018, nine \( \text{HER2} \)-mutant MCC patients are evaluable for efficacy. \( \text{HER2} \) mutations were S310F/Y (\( n = 6 \)); G776V (\( n = 1 \)); R678Q (\( n = 1 \)); and D769N (\( n = 1 \)). Of all patients, 89% had adenocarcinoma and 11% squamous cell carcinoma. Six of nine patients were initially diagnosed with locoregional disease—all received definitive radiotherapy and platinum. Across all nine patients at the time of enrollment, the median number of total prior regimens was two (range 1–4). All patients had prior treatment with a platinum-based chemotherapy, and 56% had prior bevacizumab. Efficacy results are shown in Table 1. Four patients had objective responses (\( \text{ORR} = 44\% \), 95% CI 14–79). and an additional two patients had SD lasting ≥16 weeks (clinical benefit rate 67%, 95% CI 30–93). Median PFS was 8 months (IQR 6–20 months). Diarrhea was the most commonly reported adverse event (11% grade 3; no grade 4). There were no treatment discontinuations due to diarrhea.

Conclusion: \( \text{HER2} \) mutations are a newly identified class of oncogenic drivers in cervical cancer, most particularly adenocarcinoma, and appear to be sensitive to \( \text{HER2} \) inhibition with neratinib. No new safety signals were identified. Neratinib use in this cohort led to durable responses and disease control in heavily pretreated metastatic patients with \( \text{HER2} \)-mutant cervical cancer.
Table 1.

<table>
<thead>
<tr>
<th>Response</th>
<th>All patients (N=9)</th>
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<tbody>
<tr>
<td>Confirmed overall objective response, n (%)</td>
<td>4 (44)</td>
</tr>
<tr>
<td>Complete response</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Partial response</td>
<td>3 (33)</td>
</tr>
<tr>
<td>Overall objective response rate, % (95% CI)</td>
<td>44 (14–79)</td>
</tr>
<tr>
<td>Clinical benefit, n (%)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Complete response</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Partial response</td>
<td>3 (33)</td>
</tr>
<tr>
<td>Stable disease ≥16 weeks</td>
<td>2 (22)</td>
</tr>
<tr>
<td>Clinical benefit rate, % (95% CI)</td>
<td>67 (30–93)</td>
</tr>
<tr>
<td>Median progression-free survival, months (IQR)</td>
<td>8 (6–20)</td>
</tr>
</tbody>
</table>

19 - Scientific Plenary

Tisotumab vedotin (TV) in patients with previously treated recurrent or metastatic cervical cancer: Updated safety and efficacy results from the full cervical cohort of the phase II innova TV 201 study (NCT02001623)

D.S. Honga, H.T. Arkenaub, J. de Bonoc, U.N. Lassen4, Y. Drew5, B.M. Slomovitz6, S. Ghattas, K. Windfeldh, R.A. Rangwalag and N. Concini. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bSarah Cannon Research Institute, London, United Kingdom, cCancer Research/Royal Marsden, London, United Kingdom, dRigshospitalet, Copenhagen, Denmark, eNewcastle University, Northern Institute for Cancer Research, Newcastle-upon-Tyne, United Kingdom, fUniversity of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, gGenmab US, Inc., Princeton, NJ, USA, hGenmab, Copenhagen, Denmark, iBGOG and University of Leuven, Leuven Cancer Institute, Leuven, Belgium

Objective: Expression of tissue factor (TF) in solid tumors has been associated with poor prognosis, and gynecological cancers have been described to abundantly express TF. Tisotumab vedotin (TV) is a novel antibody-drug conjugate comprising a human monoclonal antibody specific for TF conjugated to the microtubule disrupting agent monomethyl auristatin E (MMAE) via a protease cleavable linker. The ongoing phase I–IIa dose escalation and expansion Innova TV 201 study evaluated TV in pretreated, recurrent, or advanced/metastatic solid tumors. In the first 34 patients TV demonstrated encouraging activity in patients with recurrent/metastatic cervical cancer with an overall response rate (ORR) of 32% (95% CI 17%–51%). Here we present updated follow-up from the full cervical cohort (n = 55).

Method: Eligible patients had recurrent or metastatic cervical cancer that progressed on standard therapy (including GOG240 regimen) and Eastern Cooperative Oncology Group (ECOG) performance status 0–1. Patients received TV 2 mg/kg every 3 weeks until disease progression, toxicity, or withdrawal. Safety was assessed per Common Terminology Criteria for Adverse Events (CTCAE) version 4.03, and antitumor activity was assessed per Response Evaluation Criteria In Solid Tumor (RECIST) version1.1. Complete or partial responses were confirmed by a subsequent repeat CT scan performed at least 4 weeks after initial response.

Results: At the time of data cutoff (May 2018) among the first 34 enrolled patients, the most common all-grade adverse events (AEs) were conjunctivitis, epistaxis, fatigue, alopecia, and nausea. Investigator (INV)-assessed overall response was 32% (95% CI 17%–51%). Median duration of response in confirmed responders was 5.5 months (95% CI 3.0–9.6). Confirmed ORR was concordant between INV and independent imaging review (IIR) (26% and 24%). Concordance between INV and IIR for ORR in the full cohort will be presented. Responses were observed in heavily pretreated (≥3 prior lines of therapy) and refractory patients; select cases will be presented in detail. Updated safety and efficacy data from the full cervical cancer cohort (n = 55) will be presented.

Conclusion: TV has shown encouraging activity with a tolerable safety profile in heavily pretreated recurrent or metastatic cervical cancer, supporting the continued investigation of TV in this population.
A randomized, open-label study comparing trabectedin and pegylated liposomal doxorubicin with pegylated liposomal doxorubicin alone for the treatment of advanced-relapsed epithelial ovarian, primary peritoneal, or fallopian tube cancer (ET743-OVC-3006)


Arizona Oncology (US Oncology Network); University of Arizona; Creighton University, Phoenix, AZ, USA; University of Cincinnati Cancer Institute, University of Cincinnati, Cincinnati, OH, USA; Janssen Research & Development, Titusville, NJ, USA; Janssen Scientific Affairs, LLC, Horsham, PA, USA; The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Objective:** The aim of this study was to compare OS with trabectedin (T) + pegylated doxorubicin (PLD) with PLD monotherapy in patients with relapsed epithelial ovarian, primary peritoneal, or fallopian tube cancer (collectively “ovarian cancer”) who have received two previous lines of platinum-based therapy.

**Method:** Women with advanced-relapsed epithelial ovarian cancer responding to two lines of platinum-based therapy were enrolled. Patients were randomly assigned 1:1 to T+PLD (T, 1.1 mg/m², IV over 3 hours; PLD, 30 mg/m², IV over 90 min, Q3 weeks) or PLD (PLD, 50 mg/m², IV over 90 minutes, Q4 weeks). The primary endpoint was OS. Secondary endpoints included progression-free survival (PFS). Prespecified analyses included OS/PFS in patients by stratification variables: gBRCA1/2 mutation status and platinum-free interval (PFI).

**Results:** Because of an interim analysis exceeding the futility threshold for OS and observed higher toxicity in the T plus PLD group, the study was discontinued on January 18, 2018, per the IDMC’s recommendation. A total of 576 patients were randomized (T plus PLD, n = 289; PLD, n = 287). In patients with a gBRCA1/2 mutation, the median OS was 34.2 months (T plus PLD) versus 20.9 months (PLD) (HR = 0.542, 95% CI 0.380–0.901, P = 0.0165) (Table 1), corresponding to a median survival benefit of 13.3 months. In patients with both a BRCA mutation and a PFI of 6–12 months, the median OS in T plus PLD versus PLD was 31.5 months versus 14.9 months, respectively (HR = 0.37, 95% CI 0.17–0.82, P = 0.011). Significant findings in PFS and trends in OS were also observed based on PFI. Although in all treated subjects both groups had similar rates of all-grade adverse events (AEs), grade 3–4 AE rates were higher in T plus PLD (79%) versus PLD alone (54%). Drug-related AEs leading to treatment discontinuation were higher in T plus PLD (22%) versus PLD (6%). There were no drug-related AEs leading to death in either treatment group.

**Conclusion:** The addition of T to PLD did not prolong OS compared to PLD alone in unselected patients with advanced-relapsed epithelial ovarian cancer. However, in a prespecified subgroup analysis, a significant OS and PFS benefit was identified in patients with gBRCA mutations and/or a PFI of 6–12 months. Results of this phase 3 subanalysis are consistent with previous observations showing that T alone or T plus PLD displays selective antitumor activity in BRCA mutations. No new safety signals were identified.

**Table 1. Overall Survival and Progression Free Survival by Subgroups; All Randomized Patients**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median, months (Trabectedin + PLD/PLD)</th>
<th>Hazard Ratio</th>
<th>95% CI of HR</th>
<th>p-value (log-rank test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gBRCA mutation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>421</td>
<td>21.5/22.2</td>
<td>1.127</td>
<td>(0.856, 1.485)</td>
<td>0.3933</td>
</tr>
<tr>
<td>Yes</td>
<td>155</td>
<td>34.2/20.9</td>
<td>0.542</td>
<td>(0.327, 0.901)</td>
<td>0.0165</td>
</tr>
<tr>
<td><strong>PFI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 - 12 months</td>
<td>224</td>
<td>24.8/17.4</td>
<td>0.694</td>
<td>(0.476, 1.012)</td>
<td>0.0565</td>
</tr>
<tr>
<td>12 - 24 months</td>
<td>210</td>
<td>21.7/20.4</td>
<td>1.027</td>
<td>(0.685, 1.338)</td>
<td>0.8975</td>
</tr>
<tr>
<td>≥24 months</td>
<td>142</td>
<td>23.9/27.9</td>
<td>1.263</td>
<td>(0.763, 2.090)</td>
<td>0.3630</td>
</tr>
</tbody>
</table>
### Table

<table>
<thead>
<tr>
<th>gBRCA mutation and PFI = 6 - 12 months</th>
<th>60</th>
<th>31.5/14.9</th>
<th>0.374</th>
<th>(0.171, 0.819)</th>
<th>0.0108</th>
</tr>
</thead>
</table>

#### Progression Free Survival

<table>
<thead>
<tr>
<th>gBRCA mutation</th>
<th>No</th>
<th>421</th>
<th>7.1/7.1</th>
<th>1.014</th>
<th>(0.799, 1.287)</th>
<th>0.9081</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>155</td>
<td></td>
<td>10.1/7.6</td>
<td>0.722</td>
<td>(0.484, 1.078)</td>
<td>0.1080</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>PFI 6 - 12 months</th>
<th>224</th>
<th>7.5/5.5</th>
<th>0.715</th>
<th>(0.519, 0.986)</th>
<th>0.0388</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 - 24 months</td>
<td>210</td>
<td>7.4/7.6</td>
<td>1.172</td>
<td>(0.822, 1.670)</td>
<td>0.3794</td>
</tr>
<tr>
<td>≥ 24 months</td>
<td>142</td>
<td>9.9/8.0</td>
<td>0.964</td>
<td>(0.640, 1.451)</td>
<td>0.8598</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>gBRCA mutation and PFI = 6 - 12 months</th>
<th>60</th>
<th>10.1/6.1</th>
<th>0.472</th>
<th>(0.255, 0.875)</th>
<th>0.0143</th>
</tr>
</thead>
</table>

**Note:** Hazard ratio is estimated using Cox proportional hazards model with treatment group as the only covariate for each subgroup.

**Note:** Hazard ratio is calculated as the hazard in trabectedin+PLD treatment group divided by the hazard in PLD treatment group.

### 21 - Scientific Plenary

**Molecular determinants of immune response in ovarian cancer racial disparity: Can selective immunotherapy optimize therapy and close the disparity gap?**

**L. Madeira da Silva**, **D. Starenki**, **J.M. Scalici** and **R.P. Rocconi**. **Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA; Genetics/Genomics, Huntsville, AL, USA**

**Objective:** Molecular determinants of ovarian cancer (OC) racial disparity have been under investigation in order to find avenues for improved targeted therapeutics. Our objective was to evaluate and compare the immunologic landscape of primary ovarian cancer stratified by race.

**Method:** Self-reported black and white patients with OC were matched for age, stage, and survival. A full genome RNAseq library was constructed and sequenced on an Illumina HiSeq instrument with differentially expressed genes inferred using DESeq2 software. Candidate gene sets of significantly regulated genes were used for functional and pathway enrichment analyses. Using a global 700-gene panel for immune-oncology, a validated tumor inflammation signature (TIS) algorithm was used to determine the presence of a pre-existing adaptive immune response of "hot" versus "cold" tumors.

**Results:** OC tissue samples from 94 patients with primary advanced-stage OC were identified and matched by survival and platinum sensitivity. Self-reported patients were 55% white (n = 52) and 45% (n = 42) black. Groups were similar in age, BMI, histology, and grade. A total of 4,392 genes demonstrated significant differential expression when races were compared. Subsequent pathway analyses revealed significant upregulation of five genes associated with indoleamine 2,3-dioxygenase (IDO) pathway in black patients (WARS, IDO1, IDO2, AFMID, GCDH, p < 0.01). When compared to IDO<sub>low</sub>, progression-free survival (PFS) was shown to be worse in IDO<sub>high</sub> cancers, 18 versus 12 months (P = 0.03). Global immune-oncology gene signature panel showed IDO<sub>high</sub> cancers exhibited escape from immune control via adaptive resistance by overexpression of T cells and IFN-gamma and enhanced resistance to apoptosis. IDO<sub>high</sub> cancers served as a surrogate marker for global immune escape with significant correlation to elevated TIS (P = 0.008).
Conclusion: In a well-matched cohort, OC from black patients demonstrated higher proportion IDO pathway expression that correlated to worse survivals. Genetic mapping revealed a global immune escape by an adaptive resistance mediated by T-cell secretion of IFN-gamma. These findings support an opportunity to selectively utilize immunotherapy for “hot” tumors preferentially found in black patients and offers the potential to close the disparity gap.

22 - Scientific Plenary
Minority participation in phase I gynecologic clinical trials: Three decades of inequity
E. Awad, M.L. Mattei, N.L. Jones, J.Y. Pierce, J.M. Scalici and R.P. Rocconi, Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA

Objective: One theory of cancer health disparities revolves around the lack of minority participation in early-phase trials. In the age of targeted therapy, underrepresentation of minorities results in selection of agents that work in majority populations at the onset of trial pipeline. Paramount to creating equity in cancer health care is the development of therapeutic agents that specifically are effective in minority populations. Our objective is to evaluate minority participation in phase I gynecologic oncology clinical trials.

Method: Publications of phase I gynecologic oncology clinical trials from years 1985 to 2018 were reviewed. Data abstracted included racial breakdown, tumor type, and year published. Minority enrollment was stratified by tumor site (ovary, endometrial, and cervix) and year published. Based on CDC age-adjusted incidence for race, expected and observed ratios of racial participation were calculated.

Results: A total of 357 phase I publications involving 9,492 patients were reviewed. Racial breakdown was provided in 83 studies (23%) for a total of 2,483 patients: 79% Caucasian (n = 1,950); 5% African-American (n = 130), and 16% other (n = 403). The majority of studies were ovarian (n = 213). When enrollment was evaluated by 5-year increments, a 1.8-fold lower proportion of African-Americans was seen in 2015 to 2018 (6.2%), compared to 1995–1999 (11.4%) (P < 0.025). In addition, “other” races exceeded African-American enrollment in 46 of 83 trials (55%) that listed race. Utilizing CDC age-adjusted incidence, observed enrollment of African-American patients into phase I trials was significantly less than expected if accrual rates were equal across all races. Observed African-American enrollment was 19-fold lower than expected for ovarian trials, 4.6-fold lower for endometrial, and 7.1-fold lower for cervix (each P < 0.001). Individually, none of the phase I studies met expected enrollment for African-American patients by these methods.

Conclusion: A significant racial disparity in phase I gynecologic oncology clinical trials has existed for nearly three decades. Based on this study, significant attention should be directed toward strategies to enhance equity of African-American patient enrollment onto phase I gynecologic oncology clinical trials.

Education Forum XI: Surgical and Cancer Pain Management During Our Opioid Crisis
Monday, March 18, 2019
Moderator: Carolyn Lefkowits, MD, University of Colorado Denver, Aurora, CO, USA

27 - Education Forum
How much is too much? Ending excessive opioid prescribing after major gynecologic oncology procedures

Objective: To demonstrate that after hospital discharge, postsurgical acute pain can be effectively managed with a radically reduced number of opioid doses in patients undergoing major gynecologic oncology procedures.

Method: A survey of the members of the Society of Gynecologic Oncology was conducted to map national opioid-prescribing practices among gynecologic oncologists. In parallel a retrospective-control (n = 626 controls) and prospective-case cohort (n = 604 cases) study was implemented for 12 months (June 2017–June 2018) for all gynecologic oncology patients undergoing surgery at a tertiary-care Comprehensive Cancer Center using an ultrarestrictive opioid-prescribing protocol (UROPP) for pain management at the time of hospital discharge to determine whether radical opioid sparing is feasible in this patient population. Postoperative complications, pain scores, and all pre- and postoperative opioid refills were tracked using the state monitoring system. ANOVA was used for continuous variables and χ² or Fisher’s exact tests for categorical variables.
**Results:** We demonstrate that in opioid-naïve patients, using UROPP at the time of discharge led to a 73% reduction in dispensed opioids in standard laparotomy cases (11.9 vs 44.7 tablets in the past, \( P < 0.001 \)), 75% reduction in debulking cases (10.2 vs 41.9 tablets, \( P < 0.001 \)), and 97% reduction in minimally invasive cases (1.2 vs 38.3 tablets, \( P < 0.001 \)). Using UROPP for postoperative pain management was feasible in the chronic opioid users with a similar magnitude in opioid reduction (standard laparotomy 16.1 vs 40.4 tablets, debulking cases 6 vs 42 tablets, minimally invasive cases 2.7 vs 39.3 tablets). The significant reduction in dispensed opioids did not increase refill requests, postoperative visit pain scores, and complications. Based on these results, at least 79% of the responding gynecologic oncologists largely overprescribe opioids to postoperative patients after a major surgery, while 40% of the respondents stated that they fear patient satisfaction would decrease if fewer opiates were prescribed.

**Conclusion:** Opioids are prescribed far in excess following major open and minimally invasive gynecologic oncology procedures. Implementation of an UROPP led to an average 81% reduction in dispensed opioids without increased morbidity or increase in opioid refills.

**Scientific Plenary V: Operations Matter, Improving Efficiency**
**Tuesday, March 19, 2019**
Moderator: Cyril Otis Spann, MD, Emory University School of Medicine, Decatur, GA, USA
Monique A. Spillman, MD, PhD, Baylor University Medical Center, Dallas, TX, USA

28 - Scientific Plenary
Discrepancies created by surgeon self-reported operative time and its impact on procedural relative value units (RVUs) and reimbursement

University of Michigan Health Systems, Ann Arbor, MI, USA,
Northwestern University Feinberg School of Medicine, Chicago, IL, USA,
University of Michigan, Ann Arbor, MI, USA,
University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

**Objective:** The aim of this study was to demonstrate discrepancies between operative times in the National Surgical Quality Improvement Project (NSQIP) and self-reported operative time from the American Medical Association (AMA) Relative Value Units (RVU) surveys and the effect of these discrepancies on RVU assignments and reimbursements.

**Method:** Using the Centers for Medicare and Medicaid Services (CMS) methodology, we calculated total relative value units (totRVU) for surgeries in the 2016 NSQIP dataset. We divided the totRVU by the NSQIP operative time to calculate RVU per hour. We obtained the self-reported operative times from the CMS physician time file, which are based on the specialty society surveys conducted by the AMA’s RVS Update Committee (RUC). We compared the self-reported operative times from the CMS physician time file to the recorded operative times in NSQIP for procedures in which only one CPT procedure code was submitted. The excess self-reported time was called “overreported time.” We then compared and analyzed the estimated RVU/hour for each surgical specialty after adjusting for patient morbidity, age, length of stay, and NSQIP-provided mortality and morbidity probabilities to ensure that discrepancies in RVU/hour were not due to differences in high-risk patients.

**Results:** We analyzed 904,424 surgeries and found a wide variation in median RVU/hour for the 11 surgical specialties. Orthopedics (16), neurosurgery (15.2), and urology (14.7) had the highest RVU/hour, whereas gynecology (GYN) had the third lowest (12.1) \( P < 0.001 \) for all comparisons. These results remained unchanged on multivariate regression analysis. GYN had the lowest average overreporting (5 minutes/case), whereas general surgery (27 minutes/case) and neurosurgery (23 minutes/case) had the highest (Figure 1). Overreporting of operative time strongly correlated to higher RVU/hour payments to surgeons \( r = 0.87, \ P = 0.002 \). On multivariate analysis, the RVU/hour remained highly discrepant between surgical specialties.

**Conclusion:** Despite reliable electronic records, the AMA continues to use self-reported surveys for operative times. Self-reported times are inaccurate, and overreporting results in discrepancies in RVU/hour and reimbursement across specialties. This leads to a disparity in the reimbursement for GYN surgeries. RVU levels should be based on available objective data to eliminate these disparities.
Objective: Fragmentation of care, wherein a patient is discharged from an index hospital and undergoes an unexpected readmission to a nonindex hospital, is associated with increased risk of adverse outcomes. This trend is not well characterized in the gynecologic oncology literature. The objective of this study was to assess risk factors and outcomes associated with fragmentation of care among women with ovarian cancer treated surgically.

Method: The Nationwide Readmission Database was used to identify all-cause 30-day and 90-day postoperative readmissions following surgical management of ovarian cancer between 2010 and 2014. Postoperative fragmentation was defined as readmission to a hospital other than that of the index hospital of primary surgery. Univariable analyses were conducted to assess the difference between readmission length of stay (LOS), charges, and mortality rates, stratifying for fragmentation. Multivariable regression analyses were used to identify predictors of fragmentation in both 30-day and 90-day readmissions. Models were adjusted for patient, hospital, and clinical factors.

Results: A total of 10,445 30-day readmissions and 16,656 90-day readmissions in women with ovarian cancer surgery were identified. Of these, there was a 20.8% and 25.4% rate of postoperative care fragmentation for 30-day and 90-day readmissions, respectively. Readmission mortality rates were higher among fragmented readmissions (30 days, 4.7% vs 3.1%, P < 0.01; 90 days, 4.3% vs 2.8%, P < 0.01). Independent risk factors associated with fragmented postoperative care included Medicare insurance, lower income quartiles, and discharge to a nursing facility. Factors associated with decreased risk of fragmentation included operation at a metropolitan teaching hospital, presence of extended procedures, lymphadenectomy, or
postoperative blood transfusion. Readmission LOS and charges did not differ statistically between the two groups. See Table 1.

**Conclusion:** One in 5 postoperative readmissions experience fragmented care with higher rates and risk of mortality. Risk factors include patients with Medicare insurance status, lower income, and discharge to skilled nursing facilities, which represent a high-risk cohort. With the increasing use of regionalized surgical cancer care, optimization of short- and long-term postoperative follow-up to decrease fragmentation of care in these vulnerable cohorts may be important in reducing mortality.

### Table 1. Multivariable logistic regression for factors associated with 30- and 90-day fragmentation of care.

<table>
<thead>
<tr>
<th>Variable</th>
<th>30-day readmission</th>
<th>P value</th>
<th>90-day readmission</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td></td>
<td>Odds ratio (95% CI)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years old)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>0.96 (0.78-1.18)</td>
<td>0.07</td>
<td>0.92 (0.79-1.07)</td>
<td>0.26</td>
</tr>
<tr>
<td>50-59</td>
<td>1.13 (0.94-1.36)</td>
<td>0.20</td>
<td>0.97 (0.8-1.106)</td>
<td>0.24</td>
</tr>
<tr>
<td>60-69</td>
<td>1.03 (0.88-1.38)</td>
<td>0.75</td>
<td>0.90 (0.78-1.03)</td>
<td>0.14</td>
</tr>
<tr>
<td>70-79</td>
<td>1.11 (0.88-1.38)</td>
<td>0.38</td>
<td>0.99 (0.84-1.16)</td>
<td>0.87</td>
</tr>
<tr>
<td>≥ 80</td>
<td>1.33 (1.04-1.70)</td>
<td>0.02</td>
<td>1.03 (0.86-1.24)</td>
<td>0.76</td>
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<tr>
<td><strong>Comorbidity conditions</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(number)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.96 (0.87-1.11)</td>
<td>0.59</td>
<td>1.03 (0.93-1.14)</td>
<td>0.61</td>
</tr>
<tr>
<td>≥ 2</td>
<td>0.98 (0.87-1.11)</td>
<td>0.80</td>
<td>1.08 (0.98-1.19)</td>
<td>0.11</td>
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<td><strong>Insurance status</strong></td>
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<tr>
<td>Medicare</td>
<td>1.17 (1.02-1.34)</td>
<td>0.02</td>
<td>1.15 (1.04-1.28)</td>
<td>0.01</td>
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<tr>
<td>Medicaid</td>
<td>1.04 (0.89-1.22)</td>
<td>0.60</td>
<td>0.97 (0.85-1.1)</td>
<td>0.63</td>
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<tr>
<td>Self-pay</td>
<td>1.12 (0.85-1.47)</td>
<td>0.43</td>
<td>1.05 (0.85-1.28)</td>
<td>0.67</td>
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<tr>
<td>No Charge</td>
<td>0.84 (0.34-2.11)</td>
<td>0.72</td>
<td>0.97 (0.52-1.81)</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Income Quartile</strong></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>0-25%</td>
<td>1.19 (1.04-1.35)</td>
<td>&lt;0.01</td>
<td>1.16 (1.05-1.28)</td>
<td>0.01</td>
</tr>
<tr>
<td>26-50% (median)</td>
<td>1.29 (1.13-1.46)</td>
<td>&lt;0.01</td>
<td>1.24 (1.13-1.37)</td>
<td>&lt;0.01</td>
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<tr>
<td>51-75%</td>
<td>1.28 (1.13-1.45)</td>
<td>&lt;0.01</td>
<td>1.18 (1.07-1.3)</td>
<td>&lt;0.01</td>
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<tr>
<td><strong>Hospital bed size</strong></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Medium</td>
<td>1.1 (0.93-1.3)</td>
<td>0.29</td>
<td>0.99 (0.86-1.13)</td>
<td>0.89</td>
</tr>
<tr>
<td>Large</td>
<td>0.67 (0.58-0.79)</td>
<td>&lt;0.01</td>
<td>0.71 (0.63-0.8)</td>
<td>&lt;0.01</td>
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<tr>
<td><strong>Hospital type</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metro teaching</td>
<td>0.87 (0.78-0.97)</td>
<td>0.01</td>
<td>0.84 (0.77-0.91)</td>
<td>&lt;0.01</td>
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<tr>
<td>Non-metro</td>
<td>1.18 (0.87-1.6)</td>
<td>0.3</td>
<td>1.04 (0.81-1.32)</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>Discharge status</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Short-term hospital</td>
<td>1.41 (0.72-2.74)</td>
<td>0.32</td>
<td>0.88 (0.5-1.57)</td>
<td>0.67</td>
</tr>
<tr>
<td>SNF, ICF, other</td>
<td>1.32 (1.15-1.51)</td>
<td>&lt;0.01</td>
<td>1.04 (0.93-1.17)</td>
<td>0.47</td>
</tr>
<tr>
<td>Home health care</td>
<td>0.96 (0.86-1.08)</td>
<td>0.52</td>
<td>0.92 (0.84-1.01)</td>
<td>0.07</td>
</tr>
<tr>
<td>AMA</td>
<td>2.35 (1.22-4.52)</td>
<td>0.01</td>
<td>2.38 (1.38-4.11)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Surgical complexity</strong></td>
<td></td>
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</tr>
<tr>
<td>Extended procedure</td>
<td>0.81 (0.73-0.89)</td>
<td>&lt;0.01</td>
<td>0.81 (0.75-0.87)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lymphadenectomy</td>
<td>0.9 (0.83-0.99)</td>
<td>0.03</td>
<td>0.89 (0.84-0.96)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Postoperative complication</td>
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</table>
Objective: To assess outcomes in women with morbidly adherent placenta (MAP) treated with a multidisciplinary algorithm.

Method: In 2005 our program initiated a prospective multidisciplinary algorithm including interventional radiology (IR) and obstetrical anesthesia consultation for women with MAP. Women treated from January 2005 to August 2018 were reviewed, including those enrolled prospectively and a retrospective cohort treated during the same interval. Only viable pregnancies with final pathology confirming MAP were included. Patients were stratified based on pathologic subtype (accreta, increta, or percreta) and hysterectomy timing (cesarean hysterectomy [CHYS] or delayed hysterectomy [DH]). The primary outcome was unit of RBCs transfused. Secondary outcomes included EBL, bowel and unintentional genitourinary (GU) injuries, venous thromboembolism (VTE), readmission, and infection. Data were obtained via chart abstraction, and statistical analysis was performed using the Student t and Fisher exact tests.

Results: A total of 99 subjects were identified: 14 percreta, 39 increta, 36 accreta, and 10 microinvasive accreta; 55 underwent CHYS, while 24 had DH. Forty-one subjects (41%) were treated per algorithm. Average unit pRBCs transfused for all subtypes treated per algorithm was 1.5 versus 3.8 off-algorithm ($P = 0.0003, 95\% \text{CI} 0.8–3.8$), and EBL (cc) was 1,682 versus 2,571 ($P = 0.0005, 95\% \text{CI} 282–1,497$). When stratified based on subtype, pRBC transfused for accreta was 2.7 versus 3.8 ($P = 0.46, 95\% \text{CI} –2.1–4.4$) and for increta, 1.1 versus 5.6 ($P = 0.02, 95\% \text{CI} 0.8–8.1$). Average EBL for accreta managed per algorithm was 2,575 versus 2,733 ($P = 0.85, 95\% \text{CI} –1,802–2,119$) and for increta, 1,397 versus 3,340 ($P = 0.002, 95\% \text{CI} 824–3,061$). Average pRBC transfused for percreta was 1.7 units, with EBL 1,779; comparative data were unavailable, as all but two cases were managed per algorithm. Surgical complications were similar between the two cohorts, including bowel injury, unintentional GU injury, VTE, and readmission. There were no maternal deaths.

Conclusion: A multidisciplinary algorithm, including use of IR and DH, represents a feasible approach in women with MAP. Transfusion rates and blood loss were lower in the patients treated per algorithm, and this was most pronounced for increta. Further study is warranted to assess the value of the algorithm’s subinterventions.
urogynecologist and offered all treatment options, including concomitant surgery. QOL was assessed at baseline and 6 weeks and 6 months postoperatively using the Functional Assessment of Cancer Therapy—Endometrial (FACT-EN). Multivariate linear regression with generalized estimating equations was used to examine the relationship between SUI treatment group and cubic transformed FACT-EN. Adjusted mean differences were reported after cubic root back-transformation.

**Results:** Of the 1,322 women screened, 702 (53.1%) screened positive for SUI. A total of 88 women declined participation; 58 were ineligible. A total of 556 women were enrolled; 17 were ineligible or withdrew; and 30 were missing baseline data, leaving 509 evaluable subjects. Of these 509, 107 (21%) women chose concomitant cancer and SUI surgery; 96 (19%) chose nonsurgical SUI treatment with cancer surgery; and 306 (60%) chose cancer surgery alone. A total of 110 (21.6%) women had EIN; 396 (77.8%) had clinical stage I; and 3 (0.6%) had clinical stage II endometrial cancer. A total of 316 had grade I/II endometrioid adenocarcinoma, and 83 had high grade or mixed histology types. Adjusting for demographics, clinical measures, and baseline SUI severity, QOL increased for all groups from baseline and 6 weeks and 6 months postsurgery ($P < 0.0001$ overall). Concomitant surgery was associated with higher QOL compared to cancer surgery alone (mean difference = $4.60, P = 0.008$) and compared to nonsurgical SUI treatment (mean difference = $3.81, P = 0.065$). See Figure 1.

**Conclusion:** Concomitant SUI and cancer surgery improves QOL at 6 months compared to cancer surgery alone in women with EIN or clinical stage I–II cancer. These potential benefits should be discussed, and patient preferences should guide treatment management.

![Figure 1](image.png)

**Scientific Plenary VI: Immunotherapy: Treatment, Trials, Toxicity**

**Tuesday, March 19, 2019**

**Moderators:** Marilyn Huang, MD, University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA
Alessandro D Santin, MD, Yale University School of Medicine, New Haven, CT, USA

**32 - Scientific Plenary**

**Phase II trial of pembrolizumab with cisplatin and gemcitabine in women with recurrent platinum-resistant ovarian cancer**

C. Walsh, M. Kamrava, A. Rogatko, A.J. Li, I. Cass, B.Y. Karlan and B.J. Rimel. Cedars-Sinai Medical Center, Los Angeles, CA, USA
Objective: To evaluate the combination of pembrolizumab with cisplatin and gemcitabine chemotherapy in patients with recurrent platinum-resistant epithelial ovarian cancer.

Method: Patients received six cycles of chemotherapy with gemcitabine 750 mg/m² and cisplatin 30 mg/m² on day 1 and day 8 of a 21-day treatment cycle. Pembrolizumab 200 mg IV was administered on day 1 of each cycle with chemotherapy (cycles 3–6) and as a single-agent maintenance therapy (cycle 7–34). Palliative radiation to a nontarget symptomatic lesion was allowed during trial treatment. Response was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 criteria with imaging scheduled after cycle 2, 4, 6, and 9 and every 3 cycles thereafter. The primary endpoint was overall response rate (ORR), defined as complete response (CR) plus partial response (PR). Clinical benefit rate (CBR) is defined as CR plus PR plus stable disease (SD). Duration of response (DOR) is defined as time from response to progressive disease (PD). We used a two-stage design with interim analysis for futility of 18 evaluable patients and total sample size of 25 patients.

Results: A total of 26 patients were consented and screened; 19 were eligible and started protocol treatment; and 14 are currently evaluable for RECIST response. Best response was 1 CR (7%), 7 PR (50%), 4 SD (29%), and 2 PD (14%) (ORR = 57%; CBR = 86%). Median PFS was 5.35 months (range 1.2–17.3). Median DOR was 3.5 months (range 0.6–6.6). In all patients, CA125 levels dropped with response and rose with progression. Among four patients who received palliative radiation, one patient with recurrent ovarian clear cell carcinoma had reversal and normalization of CA125 trend, RECIST response improved from SD to PR, and response appears to be durable (currently on cycle 24 of treatment). There have been no new safety signals with the combination of pembrolizumab with cisplatin and gemcitabine.

Conclusion: The combination of cisplatin, gemcitabine, and pembrolizumab is well-tolerated and has activity in recurrent platinum-resistant ovarian cancer. One patient with recurrent OCCC appears to be experiencing a durable abscopal response (shrinkage of tumors outside a localized treatment field) after receiving palliative radiation to a symptomatic nontarget lesion during the maintenance phase with single-agent pembrolizumab.

33 - Scientific Plenary
Preliminary safety, efficacy, and pharmacokinetic/pharmacodynamic characterization from GARNET, a phase I/II clinical trial of the anti–PD-1 monoclonal antibody, TSR-042, in patients with recurrent or advanced MSI-h and MSS endometrial cancer

A. Oaknin, L.R. Duska, R.J. Sullivan, B. Pothuri, S.L. Ellard, C.A. Leath III, V. Moreno, R.S. Kristeleith, W. Guo, H. Danaei, E. Im and L. Gilbert. #Vall d’Hebron University Hospital, #Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain, #Emily Couric Clinical Cancer Center, University of Virginia, Charlottesville, VA, USA, †Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA, ‡New York University, New York, NY, USA, §British Columbia Cancer Agency and University of British Columbia, Vancouver, BC, Canada, ‖University of Alabama at Birmingham, Birmingham, AL, USA, #START MADRID-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain, ″University College London UCL Cancer Institute, London, United Kingdom, #TESARO, Inc., Waltham, MA, USA, /McGill University, McGill University Health Centre, Montreal, QC, Canada

Objective: TSR-042 is an investigational humanized antiprogrammed death (PD)–1 monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks interaction with the ligands PD-L1 and PD-L2. TSR-042 is being evaluated in patients with advanced solid tumors in the ongoing phase I/II GARNET trial (NCT02715284) (Sachdev JC et al. Ann Oncol. 2017(suppl 5):28:420;1185P). Here we present safety and efficacy data from the previously treated recurrent or advanced endometrial cancer (EC) cohorts, along with pharmacokinetics (PK) and receptor occupancy (RO) findings at the recommended phase II dose (RP2D).

Method: Patients with previously treated recurrent or advanced EC were evaluated. Patients received the RP2D of TSR-042: 500 mg Q3 weeks for the first 4 cycles and 1,000 mg Q6 weeks thereafter. Antitumor activity was assessed by investigators per immune related (ir) RECIST. Serum and peripheral blood mononuclear cells were collected for PK and RO measurements, respectively.

Results: A total of 110 EC patients received at least 1 dose of TSR-042 at the RP2D. The median age was 66.0 years. The median number of prior lines of therapy for advanced or metastatic disease was 1 (range 0–3). Overall, 94 patients had at least 1 tumor assessment (n = 79) or discontinued treatment prior to week 12 (n = 15); the overall response rate (including confirmed and unconfirmed responses per irRECIST) among these patients was 27.7% (50.0% in microsatellite instability-high [MSI-H] patients; 19.1% in microsatellite stable [MSS] patients). The disease control rate among these patients was 48.9%. At the time of data cutoff, responses were ongoing in 88.4% of responders. Detailed efficacy results based on microsatellite status will be presented at the meeting. Sixty-eight EC patients (61.8%) had at least 1 treatment-related adverse
Conclusion: TSR-042 demonstrated robust clinical activity in patients with previously treated recurrent or advanced EC in both MSI-H and MSS subgroups and a safety profile similar to approved anti-PD-1 therapies.
Objective: DCVAC/OvCa may induce a delayed immunotherapeutic effect, and despite insignificant difference in PFS, it may still prolong OS. Therefore, we aimed to collect additional OS data and analyze long-term survival in this study (NCT02107950).

Method: Eligible women had serous, endometrioid, or mucinous ovarian carcinoma, ECOG performance status 0–2, complete response after first-line platinum-based chemotherapy that lasted more than 6 months, and at least one measurable lesion per RECIST 1.1. Patients were randomized into arm A (DCVAC/OvCa concomitantly with chemotherapy) and arm B (chemotherapy alone). Stratification factors were previous bevacizumab use (yes or no) and duration of remission (6–12 or >12 months). A combination of carboplatin and gemcitabine was administered as standard-of-care chemotherapy for 6–10 cycles. From the second chemotherapy cycle, patients in A received 5 induction doses of DCVAC/OvCa every 3 weeks, and 5 maintenance doses afterward every 6 weeks. The primary endpoint was PFS. Main secondary endpoint was OS. Final data cutoff was planned when approximately 32 OS events had occurred (50% maturity).

Results: Between November 2013 and May 2015, 71 patients were randomized from 15 centers in Europe (A, 39; B, 32). Median age was 58.5 years in A and 60.5 years in B; other baseline characteristics were comparable. After patients who failed leukapheresis were excluded, the intention-to-treat population included 32 patients in each arm. With a median follow-up of 36.6 months, 36 patients have died. No significant difference was observed in median PFS (11.3 months in A and 10.1 months in B; HR = 0.77, 95% CI 0.44–1.35, P = 0.35). On the contrary, survival curves showed a significant difference in favor of DCVAC/OvCa with chemotherapy (HR = 0.38, 95% CI 0.20–0.74, P = 0.0032), corresponding to 2-year survival of 72.4% and 40.9% in A and B, respectively (difference 31.5%, 95% CI 5.3–57.7%). Median OS reached 35.5 months in A and 22.1 months in B (Figure 1).

Conclusion: Addition of DCVAC/OvCa to chemotherapy significantly prolonged OS in a randomized phase 2 trial. We hypothesize that the effect on OS but not PFS is due to the induction of long-lasting antitumor immunity by DCVAC/OvCa.
Scientific Plenary VII: Navigating Life Challenges After Cancer
Tuesday, March 19, 2019
Moderators: Min Kyu Kim, MD, SungKyunKwan University of Medicine, Changwon-si, Korea, Republic of (South)
Leslie H. Clark, MD, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

36 - Scientific Plenary
National patterns of care and fertility outcomes for reproductive-aged women with endometrial cancer or hyperplasia with atypia, 1999-2014
The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: While uncommon, the incidence of endometrial cancer or hyperplasia with atypia (EC/CAH) among women of childbearing age is increasing. We aim to describe the patterns of care and fertility outcomes of young women with EC/CAH.

Method: Women 45 years and younger diagnosed between 1999 and 2014 with EC/CAH were identified in Truven Health Marketscan, a national claims database (Table 1). Women were categorized as receiving fertility-sparing progestin-based hormonal therapy (HT), HT followed by hysterectomy, or surgical management with hysterectomy. Pregnancy events and receipt of fertility treatments were identified by diagnosis/billing codes.

Results: A total of 5,190 women 45 years and younger diagnosed with EC/CAH were identified. The majority of these women (4,212, 81%) received surgical management. Of the 978 women (18.8%) treated initially with HT, 45.3% (443/978) subsequently underwent hysterectomy, whereas 54.7% (535/978) did not. Patients treated with progestin-based HT therapy had a lower median age than those who received surgical management (median age 36 vs 41 years, P < 0.001). The proportion of patients receiving HT increased over the study period with 27.1% treated at least initially with progestin-based HT in 2014 (P < 0.001). Multivariate analysis showed that younger age, a diagnosis of CAH, and diagnosis later in the study period were associated with an increased likelihood of receiving HT (P < 0.0001). Levonorgestrel-releasing IUD was used only in 20.6% of those who received HT. Among those patients who received fertility-sparing treatment, 102 (19.1%, 102/535) had 142 pregnancies including 54 births for a live birth rate of 10.1%. Among those treated with HT followed by hysterectomy, 25 patients (5.6%, 25/443) had 34 pregnancies with 13 live births. Among the 61 women who received fertility-sparing treatment for EC/CAH and had a live birth, 41% utilized some form of assisted reproductive treatment.

Conclusion: Fertility-sparing treatment for EC/CAH is becoming more common, but the live birth rate among these women is relatively small (10.1%). Notably, assisted reproductive treatment was utilized by many of the individuals who went on to have a live birth.

Table 1. Cohort selection

<table>
<thead>
<tr>
<th>Selection Criteria</th>
<th>Included / Remaining</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Patients with ≥2 diagnosis-associated insurance claims ≥ 30 days apart for</td>
<td>112771</td>
<td>-</td>
</tr>
<tr>
<td>endometrial cancer / endometrial hyperplasia with atypia, 1999-2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 2: Age ≤ 45</td>
<td>12788</td>
<td>99983</td>
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<td>Step 3: Adequate follow-up for analysis with continuous insurance coverage for</td>
<td>5847</td>
<td>6941</td>
</tr>
<tr>
<td>24 months following diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 4: 1-year washout time window to exclude prevalent cases</td>
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<td>724</td>
</tr>
<tr>
<td>Step 5: Exclude patients with unavailable treatment information¹</td>
<td>4007</td>
<td>1116</td>
</tr>
<tr>
<td>Final Cohort</td>
<td>4007</td>
<td></td>
</tr>
</tbody>
</table>

¹ patients were excluded if no data was available regarding receipt of hysterectomy or hormone therapy

37 - Scientific Plenary
Abuse history and sexual function among female cancer survivors attending a specialized sexual health clinic
The University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, University of Wisconsin Hospital and Clinics- Madison, Madison, WI, USA, The University of Chicago Medicine, Chicago, IL, USA.
Objective: The aim of this study was to determine the prevalence of abuse and describe its relationship to sexual function among women with cancer seeking care for sexual function problems.

Method: Patients at the University of Wisconsin Women's Integrative Sexual Health (WISH) and University of Chicago Program in Integrative Sexual Medicine (PRISM) clinics were enrolled to a REDCap registry (WISH, January 2014–December 12, 2017; PRISM, July 2008–July 2018). The full registry was queried for registrants with cancer. Abuse prevalence was calculated from both the registry (WISH, PRISM) and medical record abstraction (WISH). Sexual function in eight domains was assessed using Sexual Function Questionnaire (SFQ-28) cut points. Distress was assessed using the 13-item Female Sexual Distress Scale-Revised (FSDS-R) (range 0–52, score ≥11 classified as distress).

Results: The study analyzed data for 86 WISH (age 28–76 years) and 193 PRISM (age 24–85 years) registrants. Most had breast (WISH, 52%; PRISM, 52%) or gynecologic (WISH, 32%; PRISM, 27%) cancer types. Abuse prevalence was higher among WISH (38%) than PRISM (19%) patients. Among women with abuse history, types included emotional (WISH, 21%; PRISM, 41%), physical (WISH, 17%; PRISM, 24%) and sexual (WISH, 20%; PRISM, 52%). Thirty-three percent of WISH and 23% of PRISM patients with an abuse history reported 32 abuse types. The most prevalent sexual dysfunction types were arousal-lubrication (68% WISH; 51% PRISM), desire (65% WISH; 67% PRISM), and arousal-sensation (56% WISH; 48% PRISM). No significant association was found between abuse history and sexual dysfunction type at either clinic. Among women with an abuse history, nearly all screened positive for sexual distress; these rates were not significantly higher than those for women without abuse history (WISH, 100% vs 88%, P = 0.08; PRISM, 96% vs 90%, P = 0.45).

Conclusion: Abuse was prevalent among women with cancer seeking care for sexual function concerns. Sexual dysfunction types were similar among women with and without an abuse history. Sexual distress rates were high overall, but nearly ubiquitous among women with an abuse history. This two-site study highlights the need to better understand the relationship between abuse and sexual function in cancer patients. Clinicians caring for this population should be capable of identifying abuse history and responding therapeutically.

38 - Scientific Plenary
Opportunities to improve sexual health and quality of life in endometrial cancer survivors
G.E. Glaesera, K. Millerb, K.S. Bevisc, C. Howeb, K. Wohlrabd, V. Sungb, H. Richtere, E. Lokichd, C.K. McCourtd, A.K. Brownf, S. Wethingtoni, M.J. Carlssonh, P.A. DiSilvestrod, J.L. Lowderi, D.D. Rahnb, J.A. Occhinoi, G. Dunivanb, E. Tunitskyf, G. Chenl, C. Luisd, C. Rakerf, M. Clark and K.M. Robisong, aMayo Clinic, Rochester, MN, USA, bWomen & Infants Hospital, Brown University, Providence, RI, USA, cUniversity of Alabama at Birmingham, Birmingham, AL, USA, dWomen & Infants Hospital, Brown University, Providence, RI, USA, eUniversity of Alabama Health Services Foundation, Birmingham, AL, USA, fHartford Hospital, Hartford, CT, USA, gMemorial Sloan Kettering Cancer Center, New York, NY, USA, hThe University of Texas Southwestern Medical Center, Dallas, TX, USA, iWashington University School of Medicine in St. Louis, St. Louis, MO, USA, jThe Mayo Clinic, Rochester, MN, USA, kUniversity of New Mexico Health Sciences Center, Albuquerque, NM, USA, lJohns Hopkins School of Medicine, Baltimore, MD, USA, mBrown University, Providence, RI, USA

Objective: The aim of this study was to determine characteristics associated with sexual dysfunction among women with endometrial intraepithelial neoplasia (EIN) or clinical stage I–II endometrial cancer and stress urinary incontinence (SUI).

Method: A multicenter, prospective cohort study was conducted across eight sites. Women diagnosed with presumed stage I–II endometrial cancer (including EIN) and SUI were eligible. This secondary analysis describes sexual dysfunction in this cohort. Prior to surgical treatment, baseline sexual function data were collected using the female sexual function index (FSFI Form F). Sexual dysfunction, demographics, quality of life, SUI symptom severity, life orientation and clinical measures were analyzed using χ² or Fisher exact tests or t tests.

Results: A total of 556 women were enrolled, and of those, 498 were evaluable for these analyses. Of these patients, 158 (31.7%) were not sexually active, and 189 (38%) had an incomplete FSFI. One hundred and fifty-one (30.3%) women completed the FSFI and were sexually active. Of these, 61.6% reported sexual dysfunction prior to surgery (score ≤ 26.6).

Women with sexual dysfunction had significantly lower quality of life scores (FACT-EN, P < 0.0001), including physical (P = 0.0017) and functional (P = 0.0012) well-being, as well as lower optimism scores (Life Orientation Test, Form D, P = 0.027) and higher SUI severity scores (Sandvik's Severity Index Form B, P = 0.049). There were no differences in age, marital status, race, education level, body mass index, medical comorbid conditions, or Eastern Cooperative Oncology Group performance status between women with and without sexual dysfunction.
**Conclusion:** Over 60% of sexually active women with presumed stage I–II endometrial cancer and SUI have significant sexual dysfunction. This sexual dysfunction was positively associated with poorer quality of life, which is important, as most patients in this group will have good oncologic outcomes and thus long survivorships. Results of this study may help to inform possible interventions for the improvement of sexual health in women with both endometrial cancer and SUI.

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**39 - Scientific Plenary**

**The impact of obesity and physical activity on inflammation and cancer mortality in women**

J.K. Chan, A.K. Mann, A. Koh-Bell, D.S. Kapp and J.E. Chan. *California Pacific and Palo Alto Medical Foundation/Sutter Health Institute, San Francisco, CA, USA, bPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, cCalifornia Pacific Medical Center, San Francisco, CA, USA, dStanford University, Stanford, CA, USA, eCalifornia Pacific and Palo Alto Medical Foundation/Sutter Research Institute, San Francisco, CA, USA*

**Objective:** The aim of this study was to evaluate the impact of physical activity and obesity on inflammation and cancer mortality in women.

**Method:** Data were extracted from the Third U.S. National Health and Nutrition Examination Survey (NHANES III) on all respondents from 1988 to 1994. \( \chi^2 \), multivariable Cox regression, and Kaplan-Meier estimates were employed for statistical analyses. Obese patients were defined as BMI \( \geq 30 \) kg/m\(^2\). Physical activity was previously defined as less active, about the same, and more active compared to their peers.

**Results:** Of 3,380 women (median age 55 years, range 40–89 years), 87% were white, 10% were black, and the remainder were other race. Of these, 27% were obese (BMI \( \geq 30 \) kg/m\(^2\)), while 73% were nonobese (BMI <30.0 kg/m\(^2\)). Physical activity relative to peers was divided, with 21% being less active, 45% about the same, and 34% relatively more active. Using C-reactive protein (CRP) (mean 0.52 mg/dL) and fibrinogen (mean 309 mg/dL) as inflammatory biomarkers, obese women had higher mean levels of C-reactive protein (0.76 mg/dL vs 0.43 mg/dL, \( P < 0.001 \)) and fibrinogen (332.16 mg/dL vs 300.31 mg/dL, \( P < 0.001 \)) than nonobese women. Those with higher physical activity had lower levels of C-reactive protein (0.42 mg/dL vs 0.66 mg/dL, \( P < 0.001 \)) and fibrinogen (300.44 mg/dL vs 325.61 mg/dL, \( P = 0.001 \)) than less physically active individuals. Obesity and lower physical activity were both correlated with increased cancer mortality. On multivariate analysis, both obesity (HR = 1.58, 95% CI 1.06–2.34, \( P = 0.024 \)) and lower physical activity (HR = 1.67, 95% CI 1.03–2.70, \( P = 0.038 \)) were found to be independent predictors for increased cancer mortality. In a subset analysis of the obese patients, increase in physical activity did not lower the risk of cancer mortality (\( P = 0.21 \)); however, in the nonobese patients, increase in physical activity significantly decreased the risk of cancer death (\( P = 0.01 \)).

**Conclusion:** Our data suggest that obesity and lower physical activity are correlated with increased inflammation as well as higher risk for cancer mortality. Increased physical activity decreased the risk of cancer mortality only in the nonobese patients.

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**40 - Scientific Plenary**

**Behavioral weight loss interventions are insufficient to address the obesity crisis in endometrial cancer survivors: Results of a randomized, controlled trial**


**Objective:** Obesity is a major risk factor for endometrial cancer (EC) and increases risk for all-cause mortality in women diagnosed and treated for EC. We aimed to scale up a previously tested weight-loss intervention for survivors of EC with obesity and assess its reach in an office-based academic gynecologic oncology setting.

**Method:** We screened all clinic visits during May–December 2017 for obese EC survivors with a BMI \( \geq 30 \) kg/m\(^2\), requesting providers to recruit eligible patients. A total of 80 obese EC survivors were randomly assigned to either a text-messaging, tailored goal-based intervention (text) or enhanced usual care (EUC, a less intensive control intervention) and observed for 6 months. Primary outcome was percentage weight loss at 6 months; secondary outcomes included quality of life (QOL) measures, assessment of patient-identified barriers to weight loss, and engagement data with text messaging.

**Results:** Screening identified 580 eligible obese EC survivors, and 80 participants (15%) with a mean BMI of 41 kg/m\(^2\) (range, 30–74 kg/m\(^2\)) went on to enroll and be randomized. Participants had a mean age of 59 ± 9.8 years and primarily stage I
disease (75%), and were predominantly Caucasian (62%) and African-American (15%). Sixty-five percent indicated awareness of obesity's association with EC, but 64% did not know whether obesity would have an impact on their overall survival. At 6 months, with 80% completing follow-up, weight change from baseline was not significant, nor was it different between intervention groups (EUC −0.29 lb ± 8.5; text −1.0 lb ± 11.5; \( P = 0.8 \)). Four patients (12.1%) in the text group compared to 2 (6.5%) in EUC lost ≥5% of their initial body weight (IBW) (\( P = 0.6 \)), while 14 (22%) of the total participants lost at least 2.5% IBW. Of all participants, 30 (47%) gained weight. There was no significant change in QOL measures from baseline to 6 months in either group.

**Conclusion:** Awareness of obesity-associated mortality continues to be low among women with EC. Behavioral weight-loss interventions in EC survivors are feasible in the gynecologic oncology clinic, but participation rates among eligible patients are low, and percentage weight change is insufficient to significantly change long-term outcomes. Further study in this challenging but increasing population of EC survivors should focus on strategies other than behavioral interventions alone.

**41 - Scientific Plenary**

Endometrial cancer survivors one decade post-exercise intervention: Happier and healthier?

S. Armbruster, C.C.L. Sun, J. Song, L. Gatus, K.H. Lu and K.M. Basen-Engquist. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Objective:** Exercise interventions improve the short-term health and quality of life (QOL) of endometrial cancer survivors (ECS). However, the sustainability of these results remains unknown. Thus, our objective was to examine outcomes 7–10 years post-exercise intervention.

**Method:** From 2007 to 2010, post-treatment stage I-IIIa sedentary ECS completed a prospective 6-month single-arm, home-based physical activity (PA) intervention employing telephone counseling, printed material, and pedometers. At baseline and 6-month (post-intervention) time points, anthropometrics, physical activity (Community Healthy Activities Model Program for Seniors), QOL (SF-36), and exercise self-efficacy questionnaires were collected. In May 2017, surveys including these metrics and an investigator-derived questionnaire were sent to all participants via email or mail.

**Results:** Thirty of 93 survivors completed surveys. In 2017, the median age was 70 years (range 42–85 years). Since our intervention, 50% of survivors participated in exercise/diet programs: 1 program (\( n = 8 \)), 2 programs (\( n = 5 \)), and 3 programs (\( n = 2 \)). Two participants were diagnosed with an obesity-associated cancer. From 6 months to 2017, minutes of total and moderate PA /week (\( P = 0.629 \); \( P = 0.811 \)) remained similar, including participants who increased their PA during the intervention. Exercise self-efficacy and frequency per week of total PA were higher at 6 months than in 2017 (\( P < 0.001 \), \( P = 0.02 \), respectively). Since study completion, survivors' physical and mental QOL (\( P = 0.14 \); \( P = 0.75 \)) has not changed. In survivors who lost at least 3% of their body weight during the intervention, their 2017 BMIs were significantly lower than those who did not (\( P = 0.020 \)). A decrease in minutes of activity per day from 6 months to 2017 was associated with higher BMIs in 2017 (41.9 kg/m\(^2\) and 29.1 kg/m\(^2\), respectively, \( P = 0.019 \)).

**Conclusion:** Post-intervention, 50% of participants remained motivated to improve their health. In 2017, increased PA was sustained for women who increased PA during the study. Survivors with higher BMIs exercised less post-intervention. Participants who lost weight during the intervention were more likely to weigh less in 2017. QOL remained stable since study completion. These findings support further investigation of interventions to increase exercise and weight loss in ECS, while highlighting challenges faced by survivors with higher BMIs.

**Featured Poster Session: Health Outcomes and Disparities**

Sunday, March 17, 2019

Moderators: Rahel Ghebre, MD, University of Minnesota, Minneapolis, MN, USA
Diana English, MBBS, Stanford University School of Medicine, Stanford, CA, USA

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Factors to explain racial disparity in survival for women with uterine cancer: Further investigations by histologic subtype

C.L. Prestia\(^a\), C. Tian\(^b\), K.E. Oliver\(^c\), N.W. Bateman\(^b,d\), T.P. Conrad\(^b,d,e\), C.A. Hamilton\(^a,b,d,e\), Y. Casablanca\(^b,d\), G.L. Maxwell\(^a,b,d,e\) and K.M. Darcy\(^b,d\).

\(^a\)Inova Fairfax Hospital, Falls Church, VA, USA, \(^b\)Gynecologic Cancer Center of Excellence, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, \(^c\)Women’s Health Department,
Objective: Our prior study demonstrated that histology explained 53% of racial disparity in survival between non-Hispanic black and non-Hispanic white women with uterine cancer. The objective of this study was to determine whether the explained and unexplained contributors of racial disparity in survival between non-Hispanic black and non-Hispanic white women varied by histology.

Method: Propensity score analysis using inverse probability treatment weighting was applied to non-Hispanic black and non-Hispanic white women diagnosed with a first primary stage I–IV uterine endometrioid (UEC), serous (USC), clear cell (UCC), or mixed epithelial (UMC) carcinoma between 2004 and 2014 in the National Cancer Data Base to sequentially balance the population by demographics, neighborhood income, insurance, comorbidity score, grade, stage, and treatment within these four histologic subtypes. Hazard ratio (HR) and 95% CI were calculated from weighted Cox modeling, and excess relative risk (ERR) of death was expressed as a percentage of the individual contribution of each factor.

Results: Racial disparity in survival was evident in all four histologic subtypes (Figures 1A–1D). After sequential balancing of the seven sets of explanatory variables, the HR dropped from 1.8 to 1.2 for UEC, 1.3 to 1.1 for USC, 1.4 to 1.2 for UCC, and 1.9 to 1.2 for UMC. The individual contribution to the ERR of death in non-Hispanic black versus non-Hispanic white women varied by histology (Figures 1E–1H). The largest contributors to racial disparity in survival were grade (29%), income (23%), and unexplained factors (21%) for UEC compared with unexplained factors (43%), stage (16%), treatment (16%), and income (14%) for USC. Unexplained factors, stage, and treatment accounted for 61%, 14%, and 13% of the ERR of death in UCC, whereas grade, unexplained factors, stage, and income, accounted for 31%, 27%, 16%, and 15% of racial disparity in survival in UMC, respectively.

Conclusion: Neighborhood income and insurance represent potentially actionable factors to mitigate survival disparities between non-Hispanic black and non-Hispanic white women through policy changes to expand equitable pay and equal access to care. Histology and unexplained factors combine to provide the largest explanation for the observed racial disparity prompting additional research including investigations of racial admixture, molecular alterations, and social determinants of health.
**Fig. 1.** Racial disparity in survival between non-Hispanic Black (NHB) and non-Hispanic White (NHW) women with endometrioid carcinoma (A), serous carcinoma (B), clear cell carcinoma (C) or mixed epithelial carcinoma (D) with hazard ratio (HR) and 95% confidence interval (CI) from the unadjusted population inserted into the underlying table. The pie chart displays the individual contribution to the ERR (%) for NHB versus NHW women with endometrioid carcinoma (E), serious carcinoma (F), clear cell carcinoma (G) or mixed epithelial carcinoma (H). Grade was included in the analysis of women with endometrioid or mixed epithelial, but not serous or clear cell carcinoma.

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**Utilizing the health leads screening toolkit: A quality improvement initiative to detect and address essential and social resource needs in gynecologic oncology clinic patients**


aJohns Hopkins Hospital, Baltimore, MD, USA, bJohns Hopkins School of Medicine, Baltimore, MD, USA, cJohns Hopkins Hospital, The Kelly Gynecologic Oncology Service, Baltimore, MD, USA, dJohns Hopkins University, Baltimore, MD, USA

**Objective:** Health care disparities are attributed to the social determinants of health, but screening is often not part of routine outpatient cancer care. Health Leads is a social enterprise that addresses basic resource needs as part of routine health care. We incorporated a resource screening tool and referral mechanism in an ambulatory gynecologic oncology clinic as a quality improvement initiative to address patients’ basic resource needs.

**Method:** A basic resource screening tool adapted from the Health Leads Social Needs Screening Toolkit was given to patients at a gynecologic oncology clinic at an urban academic center from July 2017 to May 2018. Patients were screened for five essential needs—food insecurity, house insecurity, utilities, financial strain, and transportation—and three social needs—child care, assistance in reading hospital materials, and basic household items. Frequency of needs was calculated, and multivariate Poisson regression was used to determine patient characteristics associated with the presence of any need. Proportion of patients eligible for and referred to Health Leads was reported.

**Results:** In total, 500 women were screened; 57% were white, and 30% were black. More than half had a history of invasive cancer, and 21% were undergoing treatment. Of all the women, 36% (n = 179) lacked at least 1 need (mean number of needs = 1, range 0–7); of those, 11% reported speaking with their provider and 17% reported speaking to a social worker about these needs previously. The most common needs were financial strain (23%), transportation (13%), needing assistance in reading hospital materials (7%), housing insecurity (4%), food insecurity (3%), child care issues (3%), needing household items (3%), and utility needs (1%). Being single (RR = 1.49, 95% CI 1.13–1.96), black race (RR = 1.72, 95% CI 1.32–2.23), current smoker (RR = 2.14, 95% CI 1.53–3.00), and having nonprivate insurance (RR = 1.62, 1.24–2.01) were associated with having 1 or more needs. Twenty percent (n = 34) of patients with any need met eligibility for referral to the Health Leads program; of these, 59% (n = 20) were successfully enrolled and received at least one resource.

**Conclusion:** Essential and social resource needs are prevalent in an urban gynecologic oncology population, most commonly in non-white, publicly insured women, but patients rarely report these needs to their providers. Resource screening tools can help identify women who have basic resource needs and could be included as part of comprehensive cancer care.

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**An economic analysis: Examining the cost-effectiveness of bevacizumab and olaparib as upfront maintenance treatment of advanced ovarian cancer**


aUC Irvine Medical Center, Orange, CA, USA, bPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, cUniversity of California Irvine Medical Center, Orange, CA, USA, dUCSD Rebecca and John Moores Cancer Center, La Jolla, CA, USA, eStanford University School of Medicine, Stanford, CA, USA, fCalifornia Pacific Medical Center, San Francisco, CA, USA

**Objective:** We evaluated the cost-effectiveness of bevacizumab in comparison to olaparib in an economic model for upfront maintenance treatment for advanced ovarian cancer.

**Method:** Using TreeAge Pro, a Markov model was assembled allowing patients to flow through response, complications, and on to progression. Data were extracted from GOG 218, a study evaluating the addition of bevacizumab to standard chemotherapy followed by maintenance bevacizumab, and for SOLO1, a study evaluating olaparib as first-line maintenance
monotherapy in mBRCA patients, for which we modeled three different potential PFS values. Costs of medications, toxicity management, pretreatment/testing, infusion administration, and supportive care were estimated using Medicare data. Incremental cost-effectiveness ratios (ICERs) were estimated, and survival was reported in progression-free life-year saved (PF-LYS).

Results: The estimated cost of standard chemotherapy is $535 per cycle; chemotherapy plus bevacizumab is $10,092 per cycle for the first 6 cycles and $9,557 per cycle for 14 (median) maintenance bevacizumab cycles. After estimating a cost prior to progression with the Markov model, with an estimated 6-month improvement in PFS, the ICER of bevacizumab was $416,051 PF-LYS. Based on data from Norquist et al., considering only mBRCA patients with an expected 20-month median PFS and similar PFS improvement, the ICER of bevacizumab would be $565,362 PF-LYS. The estimated drug cost of maintenance olaparib is $16,178 per cycle. Based on the SOLO1 trial, the three probable models we included were an estimated 6-, 10-, and 14-month improvement in PFS, which showed that the ICER of olaparib would be $697,136, $495,938, and $409,710 PF-LYS, respectively.

Conclusion: Our economic model suggests that with a biomarker-driven approach in the use of upfront maintenance treatment for mBRCA patients, olaparib may contribute less of a financial burden on the health care system.

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Patient decision making regarding maintenance therapy for ovarian cancer: A qualitative exploration
L.A. Meyer, C.C.L. Sun, K. Savelieva, V. Leal, L. Crocker, E. Molina, S.N. Westin, R.L. Coleman, R.J. Volk and L.M. Lowenstein. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: To identify ovarian cancer patients’ decision-making factors regarding maintenance therapy (MT).

Method: We used purposive sampling to recruit patients for semistructured interviews. Interviewers queried patients’ preferences for MT versus routine surveillance (RS) for two scenarios: (1) after first-line therapy and (2) after platinum-sensitive recurrence with complete response. A third scenario explored MT after recurrence with low-volume stable disease. Interviews were audio-recorded and transcribed verbatim. Framework analyses guided the content analysis using ATLAS.ti V8. All interviews were independently coded by at least three investigators and consensus obtained.

Results: The sample included 39 patients (20 primary treatment, 19 recurrent treatment) with a median age of 60 years (range 37–77 years). Of the patients, 85% were stage III/IV, 77% had high-grade serous histology, and 28% reported children at home. Table 1 outlines the preference results for the scenarios. The overarching decision-making factor, regardless of preference, was their physician’s opinion. Other dominant themes were possible MT side effects and impact on daily life. Patients who preferred MT expressed a strong desire to proactively manage their cancer, delay recurrence, and improve chances at survival, thereby maintaining a sense of hope. One patient chose MT because “the increased peace of mind ... would be worth more ... than any physical side effects that I may experience... ” Patients who preferred RS expressed a desire to be free from medications, wanted time off from oncologic therapy, and had a desire for a higher quality of life. A recurrent patient explained, “It’s going to recur anyway ... any break that you have in it that you can give yourself time ... for your life to be normal and do things before you have to start taking more drugs would be good ... I mean, ... it’s recurred once, it’s going to recur so I don’t know that ... maintenance would really have an effect in delaying it.” The patients described the tension between quantity and quality of life, but this tension was more apparent in those who chose RS or shifted their choices. One patient who initially chose RS stated later she would choose MT because you “grasp any straw you can for life and you do it.”

Conclusion: Patients heavily rely on the expert opinion of their physicians. While more patients preferred MT, many experience internal conflict and may benefit from formal decision support to make treatment decisions in the maintenance setting.

Table 1. Patients’ stated choice for 3 clinical scenarios of maintenance therapy (MT) versus routine surveillance (RS) or additional chemotherapy
Impact of surgical approach on survival outcomes in women undergoing radical hysterectomy for cervical cancer: A population-based cohort study


Objective: To determine whether cervical cancer patients undergoing minimally invasive radical hysterectomy (MH) are at increased risk of all-cause and cancer-specific mortality compared to those undergoing open radical hysterectomy (OH).

Method: We performed a population-based matched cohort study of cervical cancer patients from the Ontario Cancer Registry undergoing primary radical hysterectomy in Ontario, Canada, between 2002 and 2016. Patients undergoing MH and OH were matched 1:1 on stage and histology. Patient- and surgeon-level covariates, mortality, and cause of death were obtained by record linkage to provincial administrative health databases and vital statistics registries. Overall survival (OS) was compared between groups with a marginal Cox proportional hazards model, and cervical cancer-specific survival (CS) was compared between groups with a cause-specific hazards model taking death from other causes as a competing event. Both models used robust sandwich variance estimators to account for the matched pairs, and adjusted for patient age, comorbid conditions, socioeconomic status, fiscal year of surgery, and surgeon volume of minimally invasive (MIS) hysterectomy in the preceding year.

Results: We identified 1,345 patients (MH 513, OH 789), and 1,000 were matched (MH 500, OH 500, mean age 45 years). Of MH cases, 96.3% were done laparoscopically and 3.7% robotically. There were 92 deaths (MH 45, OH 47) by March 31, 2018. The 5-year cumulative incidence of all-cause death for MH and OH was 9.0% (95% CI 6.6–12.3) and 6.0% (95% CI 4.1–8.6), respectively. The 5-year cumulative incidence of cervical cancer death for MH and OH was 8.6% (95% CI 5.6–12.4) and 3.9% (95% CI 2.2–6.4), respectively. Over a median follow-up of 7 years (IQR 4–10), patients undergoing MH had similar OS (HR = 1.23, 95% CI 0.78–1.93) and trended toward worse CS (HR = 1.49, 95% CI 0.80–2.76) compared to patients undergoing OH. Surgeon volume of MIS hysterectomy had no significant impact on OS or CS.

Conclusion: There were no statistically significant differences in OS and CS between cervical cancer patients undergoing MH and OH. However, both all-cause and cervical cancer-specific deaths were uncommon. While potentially limited by unmeasured confounding, the hazards associated with MH in this retrospective population-based study were far lower than those observed in the locoregionally advanced cervical cancer (LACC) trial.
There may be an increased recurrence risk with MIS for stage IB cases, but this did not translate into a worsened DSS. MIS does not compromise outcome in stage IA disease or in cases without residual in the hysterectomy specimen.

**Conclusion**

We identified 660 cases for analysis: 438 MIS (369 robotic [84%]) and 222 OPEN. The OPEN cohort had more tumors >2 cm in size, more occurrences of residual disease in the hysterectomy specimen, and more use of adjuvant therapy. Median follow-up was 32 months (range 0–129 months) for MIS, and 53 months (range 0–136 months) for OPEN. Forty-five (10.3%) of 436 MIS and 18 (8.2%) of 219 OPEN cases recurred ($P = 0.4$). The 3-year PFS rates were 88.9% (standard error [SE] = 1.8%) and 93.6% (SE = 1.8%), respectively ($P = 0.08$). The 3-year disease-specific survival (DSS) rates were 97% (SE = 1.0%) and 99.4% (SE = 0.6%), respectively ($P = 0.14$). In cases with no residual disease in the hysterectomy specimen, the 3-year PFS rates were 96% (SE = 2.1%) for the MIS and 100% for the OPEN groups ($P = 0.2$). The 3-year DSS rates were 99.2% (SE = 0.8%) and 100%, respectively ($P = 0.6$). The 3-year PFS and OS rates were 100% for all stage IA cases regardless of surgical approach. In stage IB1 cases, the 3-year PFS rates were 85.5% (SE = 2.3%) for the MIS and 92.8% (SE = 2.0%) for the OPEN groups ($P = 0.03$). The 3-year DSS rates were 96% (SE = 1.3%) and 99.3% (SE = 0.7%), respectively ($P = 0.08$).

**Conclusion:** This preliminary multiinstitutional analysis provides additional insight regarding the role of MIS in cervical cancer. MIS does not compromise outcome in stage IA disease or in cases without residual in the hysterectomy specimen. There may be an increased recurrence risk with MIS for stage IB cases, but this did not translate into a worsened DSS.

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**The impact of surgeon learning curve and hospital volume on the survival of stage IB cervical cancer patients after minimally invasive surgery**

S. Chow\(^a\), C. Liao\(^b\), D.S. Kapp\(^c\), A.K. Mann\(^d\) and J.K. Chan\(^e\), \(^a\)Kaiser Permanente Santa Clara, Santa Clara, CA, USA, \(^b\)Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan, \(^c\)Stanford University School of Medicine, Stanford, CA, USA, \(^d\)Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, \(^e\)California Pacific Medical Center, San Francisco, CA, USA

**Objective:** To determine the trends and survival of stage IB1 cervical cancer patients after open (OH), laparoscopic (LH), and robotic (RH) radical hysterectomies.

**Method:** Data were extracted from the National Cancer Data Base from 2010 to 2015. $\chi^2$ tests and Cox regression were used for statistical analyses.

**Results:** Of 2,771 stage IB1 cervical cancer patients, 47.2%, 9.9%, and 42.8% had open (OH), laparoscopic (LH), and robotic (RH) radical hysterectomies, respectively. Over the study period, the proportion of patients undergoing OH decreased from 69.4% to 30.0%; LH increased from 5.2% to 11.7%; and RH increased from 25.4% to 58.3% ($P < 0.001$). Of OH, LH, and RH patients, the percentage with positive margins were 3.2%, 3.3%, and 2.0% ($P = 0.212$); positive pelvic nodes were 8.0%, 6.3% and 5.5% ($P = 0.06$); positive paraaortic nodes were 0.8%, 0.6%, and 0.5% ($P = 0.728$); use of adjuvant radiation was 24.0%, 19.6%, and 22.0% ($P = 0.438$); and use of adjuvant chemotherapy was 15.6%, 14.2%, and 13.9% ($P = 0.761$), respectively. We defined high-volume hospitals as those with case numbers greater than the 75th percentile, or ≥12 cases for RH over 6 years. The overall survival (OS) in high- and low-volume facilities for RS was 91.9% and 93.6% ($P = 0.53$), respectively. From 2010 to 2012, we divided the study period by year and found OS improved from 86.9% to 92.6% to 95.2% ($P = 0.178$) with RH at high-volume hospitals. On subgroup analysis of tumor size >2 cm, OS with RH at high-volume facilities also improved each year from 69.7% to 86.7% to 97.5% ($P = 0.017$). After 2012, the OS of those who underwent RH were comparable to that of OH (OS 95.7%, $P = 0.119$).
Conclusion: In patients with stage IB1 cervical cancer, there has been an increasing trend in the use of minimally invasive surgery. Overall survival of patients is better in high-volume institutions with survival in robotic surgery improving over time, equaling open surgery after the year 2012.

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Patterns of recurrence and survival of node-positive cervical cancer after open versus laparoscopic radical surgery
Y.J. Young Jae, D.Y. Kim, S.W. Lee, D.S. Suh, Y.M. Kim, and J.H. Nam. University of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea, ASAN Medical Center, Seoul, Korea, Republic of (South), University of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea, University of Ulsan College of Medicine, ASAN Medical Center, Seoul, Korea, Republic of (South)

Objectives: To compare patterns of disease recurrence and survival in node-positive cervical cancer patients who underwent open (RH) versus laparoscopic radical hysterectomy (LRH) including pelvic lymph node dissection (PLND).

Methods: From a total of 1,714 consecutive radical surgery cases at Asan Medical Center for stage IA2 to IIB cervical cancer from February 2001 to December 2012, 298 node-positive cases (17.4%) were identified. In all, 72 (24.1%) patients underwent PLND only and 226 (75.9%) patients underwent PLND with para-aortic lymph node sampling or dissection. The clinicopathologic data of all node-positive patients were retrospectively analyzed.

Results: Among the 298 study patients, 181 underwent RH and 117 underwent LRH. The mean number of positive lymph nodes was 4.46 (range 1–57), and the mean size of largest LN metastasis was 11.1 mm (range 1–40 mm). Of the 293 patients (98.3%) who received adjuvant therapy, 174 (58.2%) received concurrent chemoradiation therapy with weekly cisplatin and 22 (7.4%) received systemic chemotherapy. Recurrence occurred in 95 patients (31.9%); 57 cases (31.5%) occurred in the RH group and 38 cases (32.4%) occurred in the LRH group. Extrapelvic recurrence occurred in 47 cases (26.0%) in the RH group and 28 cases (23.9%) in the LRH group. LN recurrence rates of each group were 16.6% (30 of 181) and 16.2% (19 of 117), and extrapelvic LN recurrence rates were 13.8% (25 of 181) and 14.5% (17 of 117), respectively. Progression-free survival (PFS) and 5-year overall survival (OS) were 69.1% and 70.7% in RH group and 69.2% and 74.3% in LRH group, respectively. No significant differences were found regarding recurrence rates, site of recurrence, PFS, and OS between the RH and LRH groups by multivariable analysis.

Conclusions: This study found that LRH does not affect recurrence rates, recurrence patterns, or survival rate when compared with RH even in the case of postoperative lymph node metastasis in cervical cancer.

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Surgical site infection rates in vulvar surgery: Evidence-based approach to optimal wound classification
I. Mert, B.A. Cliby, K.A. Bews, E.B. Habermann and S.C. Dowdy. Mayo Clinic, Rochester, MN, USA

Objective: Surgical wounds are classified into four categories based on the risk of surgical site infection (SSI), with most pelvic procedures being classified as clean or clean-contaminated. However, correct classification for vulvar procedures (VP) is ambiguous according to current definitions, and infection rates are poorly described. In this study, we aimed to analyze the rate of SSI in women who underwent vulvar surgery and, as a reference, compared results to women undergoing abdominal hysterectomy (TAH) to determine the most appropriate wound classification.

Method: This is a retrospective study utilizing the National Surgical Quality Improvement Program database (NSQIP). Patients who underwent vulvar resections for dysplasia or carcinoma were included. SSI rates of vulvar cases were compared to patients undergoing TAH. Surgical wound classification, introduced by the National Academy of Sciences in 1964, was utilized to define SSI risk. Descriptive analyses of categorical variables were performed.

Results: Between 2008 and 2016, 2,116 and 31,506 patients underwent a VP and TAH, respectively. Among VP, 1,345 (63.6%), 364 (17.2%), and 407 (19.2%) women underwent simple, radical, or radical vulvectomy with lymphadenectomy, respectively. The overall rate of SSI occurrence was 5.6%. Interestingly, the rate of SSI for VP was higher than that for TAH (3.0% simple VP, 10.1% radical VP, vs 3.8% TAH; P < 0.0001). Furthermore, while patients undergoing TAH displayed a corresponding increase in the rate of SSI with wound type (type I, 3.4%; type II, 3.8%; type III, 6.8%; type IV, 10.6%; P <
0.001), no such correlation was observed for simple VP (type I, 3.3%; type II, 3.0%; type III, 3.2%; type IV, 0%; $P = 0.80$). A nonsignificant correlation was observed for radical VP (type I, 4%; type II, 10.1%; type III, 14.3%; type IV, 20%; $P = 0.17$). Patients undergoing VP for invasive cancer had a higher rate of SSI (8.9%) compared to patients undergoing VP for dysplasia (2.1%, $P < 0.0001$).

**Conclusion:** VPs are at high risk of infection and should not be classified as type I wounds. Patients with invasive cancer, particularly those who undergo inguinal lymphadenectomy, are at very high risk of infection, in excess of rates for women undergoing TAH with type III/IV incisions, suggesting the need to adopt new strategies for reducing vulvar SSI.

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**Outcomes associated with chemoradiation versus radiation alone in squamous cell carcinoma of the vulva**  
T. Castellano$^a$, D. Brinkman$^b$, K. Ding$^c$ and C.C. Gunderson$^d$. $^a$The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, $^b$The University of Oklahoma, Norman, OK, USA, $^c$The University of Oklahoma, Oklahoma City, OK, USA

**Objective:** To evaluate the impact of chemoradiation (CRT) versus radiation therapy (RT) alone in the adjuvant treatment of squamous cell carcinoma (SCC) of the vulva.

**Method:** A multiinstitutional retrospective cohort study of women with at least IB SCC of the vulva from 1995 to 2015 was performed. Differences in clinicopathologic characteristics of women receiving either adjuvant CRT versus RT alone were assessed, including age, BMI, stage, nodal positivity, tumor size, and margin status. Outcomes of primary interest include risk of recurrence, progression-free survival (PFS), and overall survival (OS). In addition, a subset of women with at least one positive inguino-femoral lymph node (IFLN) was evaluated for significant differences in outcomes and baseline characteristics according to treatment approach.

**Results:** Fifty-seven patients received adjuvant therapy; 47% had RT alone and 53% had CRT. The median age was 63 years (range 25–87 years); the majority (79%) were Caucasian; mean BMI was 31.9 kg/m$^2$; and mean width of primary lesion was 3.9 cm. Twenty-nine women had at least one positive IFLN, and there were 26 recurrences with median time to recurrence of 15.9 months (range 1.7–65.8 months) during a median follow-up of 16.7 months (range 1–197 months). Women undergoing CRT were significantly younger than those who received RT alone (median age 63 versus 67 years, $P < 0.05$). There were no significant differences in BMI, stage, nodal status, or tumor size. HR for recurrence in CRT patients was 1.10 (95% CI 0.65–1.86, $P = 0.715$). No difference in OS between the treatment groups was found ($P = 0.77$). After controlling for age, OS was also similar between groups ($P = 0.59$). Median PFS for CRT was 57.3 months versus 21.7 months for RT alone; thus, there was a nonsignificant trend of longer PFS with CRT ($P = 0.08$). After controlling for age, PFS appears more similar between RT and CRT patients ($P = 0.20$). When comparing patients with at least one lymph node, there were no significant differences in race ($P = 0.66$), BMI ($P = 0.86$), size of primary lesion ($P = 0.20$), margin status ($P = 0.30$), PFS ($P = 0.337$), or OS ($P = 0.997$). See Figure 1.

**Conclusion:** As improved RT modalities are increasingly used, we show that, contrary to older similar studies, the addition of chemotherapy to adjuvant RT of SCC vulvar cancer does not appear to improve outcomes. CRT may increase risk of toxicity and thus should be reserved for younger women.
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**Oncological results and recurrent risk factors following abdominal radical trachelectomy (ART): An updated series of 333 patients**

X. Wu and X. Li. Fudan University Shanghai Cancer Center, Shanghai, China

**Objective:** To update the oncological results and identify recurrent risk factors in young patients with early-stage cervical cancers following abdominal radical trachelectomy (ART) at our institution.

**Method:** We conducted a retrospective analysis from a prospectively maintained database of patients undergoing ART from April 2004 to December 2017. Clinicopathological factors related to recurrences were evaluated.

**Results:** Among 333 patients studied, 271 had squamous carcinomas (SCC), 51 pure adenocarcinomas (AC), and 11 adenosquamous carcinomas (AS). One hundred thirty-two women (39.6%) had tumors ≥2 cm. With a median follow-up of 56 months (range, 6–169 months), 11 patients (3.3%) had recurrence, and 5 patients (1.5%) died. The cumulative 5-year recurrence-free survival and overall survival rates were 96.3% and 98.6%, respectively. The recurrence rate in women with tumors ≥2 cm was comparable to that in patients with tumors <2 cm (5.3% vs 2.0%, respectively, \( P = \text{NS} \)). However, the recurrence rate was significantly higher in patients with AS histology than in those with AC and SCC histology (18.2%, 3.9%, 2.6%, respectively, \( P < 0.05 \)). All the recurrent patients with AS histology had tumors ≥2 cm. Multivariate analysis showed that only histology type was an independent risk factor for recurrence.

**Conclusion:** This updated series showed a favorable survival rate following ART. These results further support that ART is a safe option for well-selected patients with stage IB1 cervical cancers ≥2 cm. However, if patients with tumors ≥2 cm had AS histology, they should be advised with great caution when contemplating ART.

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**Impact of carboplatin hypersensitivity and desensitization on overall survival in patients with recurrent ovarian cancer**

G. Altwerger, C. Han, B. Zeybek, K. Haines, G.M. Gressel, G.S. Huang, B. Litkouhi, M. Azodi, D.A. Silasi, A.D. Santin, P.E. Schwartz and E.S. Ratner. *Yale University School of Medicine, New Haven, CT, USA, Montefiore Medical Center, Bronx, NY, USA, Smilow Cancer Hospital at Yale and Yale University, New Haven, CT, USA*

**Objective:** Carboplatin desensitization protocols aim to maximize the administration of carboplatin to ovarian cancer patients with hypersensitivity reactions (HSRs). The precise impact of a desensitization protocol on overall survival (OS) remains unknown. This study aims to compare OS in patients with HSRs undergoing desensitization to patients without HSRs. New risk factors for developing carboplatin HSRs were also identified.

**Method:** This was a retrospective study in patients with recurrent ovarian cancer who received more than six infusions of carboplatin from 2005 to 2016. Two-sided Fischer exact test, Gehan-Breslow-Wilcoxon test, and univariate and multivariate analyses were used.

**Results:** Ninety-one patients met inclusion; all were tested for germline (g) BRCA1/2 deficiencies. Importantly, hypersensitive patients who underwent carboplatin desensitization had a 48-month longer OS than patients without hypersensitivity (\( P = 0.0094 \)); this was independent of age, BMI, stage, cytoreduction, total chemotherapy regimens, or total carboplatin cycles by Cox regression analysis (Figure 1A). Furthermore, a subgroup analysis indicated that gBRCA1/2 proficient hypersensitive patients undergoing carboplatin desensitization had a 43-month longer OS than gBRCA1/2 proficient patients without HSRs (\( P = 0.035 \)) (Figure 1B). No difference in OS was seen in the gBRCA1/2-deficient patients (Figure 1C). Last, patients with recurrent advanced-stage (III–IV) ovarian cancer had a higher likelihood of developing HSRs with a HR of 4.783 (1.008–22.689) by logistic regression analysis, while age, BMI, early stage, number of carboplatin cycles, degree of cytoreduction, or NACT were not independent prognostic factors for developing carboplatin HSRs (Table 1). Cox regression showed that age, BMI, chemotherapy regimens, number of carboplatin cycles, or degree of cytoreduction were not independent prognostic factors for OS (Tables 2 and 3).
Conclusion: Hypersensitive patients receiving desensitization have improved OS when compared to nonhypersensitive patients, independent of gBRCA1/2 status. Furthermore, advanced-stage ovarian cancer is an independent prognostic factor for the development of carboplatin hypersensitivity. These findings identify a new risk factor and support the continued use of desensitization protocols in patients with HSRs.
Does the fallopian tube influence the metastatic potential of uterine serous and clear cell carcinoma?

**Objective:** Uterine serous (USC) and clear cell (CCC) carcinomas are aggressive endometrial cancers with poor outcome. The fallopian tube may be an important route for extraterine metastasis. The objective of this study was to determine whether women diagnosed with USC and CCC who have had a tubal sterilization (TS) are diagnosed at an earlier stage and have lower mortality, compared to those without TS.

**Method:** A population-based retrospective cohort of women with pathology-confirmed USC and CCC from 2000 to 2015 was identified through the British Columbia Cancer Registry. Chart reviews provided demographic, clinical, pathological, and outcome data. Multivariable logistic and Cox regression analyses evaluated the association between TS and stage at diagnosis and overall survival.

**Results:** There were 283, 73, and 157 women with USC, CCC, and mixed USC/CCC, respectively, and 18%, 10%, and 19% of these women had previous TS, respectively. The majority of TSs were tubal ligation (91%) versus salpingectomy (9%). Average age at diagnosis was 68.7 years. Median follow-up was 33 months (range 0–176 months). A higher proportion of those with TS had stage I/II disease (78%) compared to those without (63%) ($P = 0.0061$). TS was significantly associated with decreased likelihood of stage III/IV disease after multivariable adjustment for age, BMI, diabetes, region of residence, and personal and family history of breast cancer (OR = 0.37, 95% CI 0.18–0.79). TS was also marginally associated with better survival after multivariable adjustment (HR = 0.69, 95% CI 0.47–1.01).

**Conclusion:** Tubal sterilization (TS) is associated with decreased extraterine metastases of USC and CCC and reduced mortality from these cancers. The metastatic potential of these cancers appears to be influenced by occlusion or removal of the fallopian tubes; this provides additional justification for the British Columbia-led opportunistic salpingectomy campaign to reduce the mortality associated with gynecologic cancers.

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Rate of venous thromboembolism during neoadjuvant chemotherapy for advanced ovarian cancer

**Objective:** Neoadjuvant chemotherapy (NACT) may be offered to women with ovarian cancer (OC) who have poor performance status or a disease burden not amenable to optimal primary debulking surgery. Indications for NACT overlap with well-established risk factors for venous thromboembolism (VTE), including extent of malignancy and impaired mobility. The objective of this study was to determine the rate of VTE among women receiving NACT for advanced OC.

**Method:** This was a cohort study of patients receiving NACT for primary ovarian, fallopian tube, or peritoneal cancer from January 2000 to June 2018 at two academic institutions. Institutional Review Board approval was obtained at both institutions. The primary outcome was the incidence of VTE during NACT. Binomial logistic regression was used to evaluate associations between patient characteristics and the occurrence of VTE during NACT. Secondary outcomes included rates of VTE at diagnosis, following interval debulking surgery (prior to restarting chemotherapy), during adjuvant therapy and during treatment for recurrence.

**Results:** One hundred eighty-three patients received NACT. Median age and BMI were 64 years (range 34–85 years) and 26.8 (range 16–52.5), respectively. At time of cancer diagnosis, 7 patients (3.8%) were actively anticoagulated for a non-VTE indication and 19 (10.4%) presented with a VTE. Of the remaining 157 patients, 12 (7.6%) had a VTE diagnosed during NACT. There was no significant association between age, race, BMI, or ECOG performance status and occurrence of VTE during NACT. Three patients (1.9%) had a VTE following interval debulking surgery, 3 (2.0%) during adjuvant chemotherapy, and 12 (8.9%) during treatment for recurrence. See Table 1.
Conclusion: VTE is common among women receiving treatment for advanced OC. Most VTEs were present at diagnosis, which may have influenced the decision for NACT. Although larger studies are still needed, the high rate of VTE during NACT deserves attention, and consideration of VTE prophylaxis during NACT may be warranted.

Table 1. Association between patient demographics and VTE during NACT.

<table>
<thead>
<tr>
<th>Patient Demographic</th>
<th>All (n=183)</th>
<th>VTE during NACT (n=12)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 70</td>
<td>128</td>
<td>10</td>
<td>p = 0.52</td>
</tr>
<tr>
<td>≥70</td>
<td>55</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>66</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>25-30</td>
<td>68</td>
<td>4</td>
<td>p = 0.43</td>
</tr>
<tr>
<td>31-40</td>
<td>40</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>145</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>31</td>
<td>4</td>
<td>p = 0.79</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ECOG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>58</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>75</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>2</td>
<td>p = 0.60</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

56 - Featured Poster Session
Assessing the social determinants of health: A pilot performance improvement project

Objective: To determine the most common social needs and distress levels in patients receiving gynecologic oncology care.

Method: This was an Institutional Review Board-approved cross-sectional study in a largely immigrant and under- or uninsured population in Los Angeles. As part of a quality improvement initiative, social needs assessment and distress
screening were performed in patients receiving gynecologic oncology care in August 2018. Surveys, which were administered in person or over the phone in the patient’s primary language, were adapted from the Health Leads Screening Toolkit, the National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT), and the Emotion Thermometers Tool (ETT). Responses were retrospectively analyzed to determine needs across various domains, including food security, housing instability, financial strain, transportation, as well as social isolation and support. In addition, distress levels and emotional qualities were assessed.

Results: Survey data from 78 patients, primarily Latino (67.9%) and Spanish-speaking (60.8%), were analyzed. Mean age was 54.9 years, and 1.3% had a Patient Health Questionnaire (PHQ-2) score of 3 or greater. While 14.1% screening positive for food insecurity, 12.8% reported housing instability; 12.8% endorsed financial strain limiting ability to receive medical care; 10.2% listed transportation as a barrier to health care; 23.7% lacked social support; and 32.5% reported needing assistance with reading hospital materials. Overall, 41.6% requested assistance with social needs. Using the NCCN DT, 55.1% had scores of 5 or greater. Across the various ETT categories, 19.2% to 37.2% had scores of 5 or greater, with the highest scores noted for distress and anxiety, respectively. Compared to patients with NCCN DT scores less than 5, patients with scores greater than or equal to 5 had, on average, more social needs (2.17 vs 1.23, \( P = 0.02 \)).

Conclusion: In our patient population multiple social needs exist. Routinely assessing social stressors increases awareness and allows for referral to nutritional, social, and financial services that are pivotal to comprehensive cancer care. It is, however, important to recognize that the utility of screening tests varies between groups and that, to accurately determine needs, these tools should be tailored to individual populations.

57 - Featured Poster Session
The m.b.e.c. study: Menopause, bleeding, and endometrial cancer among black women: A community-engaged qualitative analysis
K.M. Doll\(^a\), B. Hempstead\(^b\), J. Alson\(^a\) and E. Kellogg\(^a\). \(^a\)University of Washington Medical Center, Seattle, WA, USA, \(^b\)Cierra Sisters, Seattle, WA, USA

Objective: Delays in presentation to health care settings among black women diagnosed with endometrial cancer (EC) is hypothesized to be a driver of disparity in stage at diagnosis and overall mortality by race. Yet there have been no qualitative studies to understand potential mechanisms of delay in this period prior to medical presentation.

Method: Black women with a recent (<3 year) diagnosis of EC were recruited through gynecologic oncology clinics and Cierra Sisters, a local cancer support group for black women. We created an interview guide based on the Health Belief Model, adapted with principles from the Public Health Critical Race praxis. One- to two-hour semistructured interviews included open-ended questions focused on experiences of menopause, postmenopausal bleeding (PMB), and symptom disclosure. Using directed content analysis, transcripts were coded for common themes.

Results: To date, 11 women have been recruited from Washington, California, Louisiana, and Georgia, with an age range of 47–70 years, representing stages 1–3 of diagnosis. Of these women, 91% were insured with access to routine medical care. A total of 147 pages of transcribed interviews (53,438 words) were the basis for this interim analysis. Menopause experience was marked by a lack of knowledge of normal versus abnormal symptoms, silencing about bleeding symptoms among friends and family, and specific knowledge gaps secondary to the high hysterectomy rate in participants’ social circles. Self-reliance strategies of endurance and home remedies were common both in menopause and PMB experiences. The predominant interpretation of PMB was a resumption of menstruation or prolongation of menopause. The primary cue for symptom disclosure to a medical professional was increased severity of bleeding or the onset of pain. Initial disclosure to a provider was notably marked by a casual tone despite longstanding symptoms, alongside the lack of explicit discussion of cancer as a risk by providers.

Conclusion: In this interim analysis of the prediagnostic experience of black women with EC, there are a number of concerning gaps in knowledge and maladaptive coping strategies leading to unnecessary delays in care, despite access to routine care. This is the first study to identify modifiable targets for community education directed at those at greatest risk of EC mortality.

58 - Featured Poster Session
The first nationwide Japanese multicenter study: Characterizing the cross-sectional approach to ovarian cancer
genetic testing of BRCA (CHARLOTTE)
Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, Keio University School of Medicine, Tokyo, Japan, Tohoku Medical and Pharmaceutical University, Sendai, Japan, Matsue City Hospital, Matsue, Japan, Cancer Institute Hospital, Tokyo, Japan, AstraZeneca K.K., Osaka, Japan, National Defense Medical College, Tokorozawa, Japan, Takagi Hospital, Okawa, Japan

Objective: Given the lack of health insurance coverage for germline BRCA (gBRCA) testing in Japan, prevalence data for gBRCA1/2 mutations in patients with ovarian cancer are scarce. This is the largest nationwide multicenter study to describe the prevalence of gBRCA1/2 mutations in Japanese patients with newly diagnosed ovarian cancer, including primary peritoneal and fallopian tube cancer, as well as the prevalence stratified by patient background factors, including family history of cancer. In addition, we assessed patient satisfaction with genetic counseling for gBRCA testing.

Method: In this multicenter, collaborative cross-sectional study (NCT03229122), Japanese patients aged ≥20 years with histologically confirmed FIGO stage I–IV ovarian cancer received genetic counseling about gBRCA testing. Genetic counseling was conducted mainly by a genetic specialist, genetic counselor, or gynecologist with genetic counseling training. After written informed consent was obtained, background information and blood samples were collected for gBRCA testing (Myriad Genetics Inc., UT, USA), and histopathological specimens were collected for central pathological assessment. Only deleterious or suspected deleterious mutations were defined as gBRCA mutations. Patients filled out a questionnaire to rate their satisfaction with genetic counseling.

Results: A total of 666 patients were enrolled, and 633 were included in the final analysis. The overall prevalence of gBRCA1/2 mutation was 14.7%. The prevalence of gBRCA1/2 mutations was 0%, 2.1%, 6.7%, 20.0%, and 28.5% in patients with mucinous (n = 19), clear cell (n = 187), endometrioid (n =120), low-grade serous (n = 5), and high-grade serous carcinoma (n = 274), respectively. Patients’ satisfaction with the explanation provided prior to gBRCA testing was generally high, regardless of the expertise of the counselor.

Conclusion: The overall prevalence of gBRCA1/2 mutations in ovarian cancer patients in this Japanese multicenter study was comparable with those already reported in other countries. The prevalence of gBRCA1/2 mutations in patients with high-grade serous carcinoma might be slightly higher than what has been reported by previous studies in other countries. In addition, most patients were satisfied with the gBRCA test counseling provided.

Feature Poster Session: Trials, Basic Science and Translational Science
Monday, March 18, 2019
Moderators: Joel Segundo Cardenas-Goicoechea, MD, Mount Sinai School of Medicine, New York, NY, USA
Marian Yvette Williams-Brown, MD, MMS, FACOG, University of Texas at Austin, Austin, TX, USA

60 - Featured Poster Session
Early results of a phase I evaluation of TAK-228 (TORC 1/2 inhibitor) in combination with TAK-117 (PI3K alpha inhibitor) and paclitaxel in advanced gynecologic malignancies and metastatic breast cancer

Objective: To evaluate the safety and efficacy of dual blockade of the PI3K/AKT/mTOR pathway with TAK-228 and TAK-117 combined with weekly paclitaxel.

Method: This was a standard 3+3 design phase I trial with five planned cohorts. The dosing schema for the available patients is summarized in Table 1.

Results: As of August 1, 2018, nine patients have been enrolled to this study, and the initial safety evaluation for the first three cohorts is nearing completion. No dose-limiting toxicities have occurred during the first cycle for any patient to date. Of the six evaluable patients, the response rate is 50% and the clinical benefit rate is 67%. The median progression-free survival for patients deriving clinical benefit is currently at 7 months. One heavily pretreated patient in the first cohort with platinum refractory HGSOC achieved stable disease for over 10 months, and two patients in the second cohort with endometrial cancer have ongoing partial responses for greater than 6 and 9 months, respectively. Overall, the first three cohorts have been well
tolerated. The most common toxicities requiring dose adjustments have been elevated LFTs and neutropenia. All patients had comprehensive molecular profiling prior to enrollment. Updated results will be provided at the meeting.

**Conclusion:** Preliminary results appear very promising, and the treatment has been well tolerated for patients in the early cohorts.

**Table 1.**

<table>
<thead>
<tr>
<th>Patient # and Diagnosis</th>
<th>Cohort</th>
<th>Previous Lines of Treatment</th>
<th>Dose Level TAK-228/TAK-117 (Day 2-4, 9-11, 16-18, 23-25)</th>
<th>Paclitaxel weekly dose (Day 1,8,15)</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Breast)</td>
<td>1</td>
<td>4</td>
<td>2 mg/100 mg</td>
<td>60mg/m2</td>
<td>PR</td>
</tr>
<tr>
<td>2 (HGSOC)</td>
<td>1</td>
<td>12</td>
<td>2 mg/100 mg</td>
<td>60mg/m2</td>
<td>SD</td>
</tr>
<tr>
<td>3 (Endometrial)</td>
<td>1</td>
<td>3</td>
<td>2 mg/100 mg</td>
<td>60mg/m2</td>
<td>PD</td>
</tr>
<tr>
<td>4 (Endometrial)</td>
<td>1</td>
<td>6</td>
<td>2 mg/100 mg</td>
<td>60mg/m2</td>
<td>PR</td>
</tr>
<tr>
<td>5 (Breast)</td>
<td>2</td>
<td>5</td>
<td>2 mg/200 mg</td>
<td>60mg/m2</td>
<td>Not Evaluable – Elevated LFTs in cycle 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not Evaluable – developed brain mets during cycle 1</td>
</tr>
<tr>
<td>6 (Breast)</td>
<td>2</td>
<td>5</td>
<td>2 mg/200 mg</td>
<td>60mg/m2</td>
<td></td>
</tr>
<tr>
<td>7 (Endometrial)</td>
<td>2</td>
<td>2</td>
<td>2 mg/200 mg</td>
<td>60mg/m2</td>
<td>CR</td>
</tr>
<tr>
<td>8 (HGSOC)</td>
<td>3</td>
<td>3</td>
<td>2 mg/200 mg</td>
<td>80mg/m2</td>
<td>PD</td>
</tr>
<tr>
<td>9 (HGSOC)</td>
<td>3</td>
<td>3</td>
<td>2 mg/200 mg</td>
<td>80mg/m2</td>
<td>Too early to evaluate</td>
</tr>
</tbody>
</table>

**61 - Featured Poster Session**

**Mechanisms of SWI/SNF dysfunction in the immune-reactive microenvironment of small cell carcinoma of the ovary, hypercalcemic type**

J.R. Patibandla, E. Van Oudenhove, P. Jelic and D.A. Levine. *New York University School of Medicine, New York, NY, USA, NYU Langone Health, New York, NY, USA*

**Objective:** Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a rare aggressive subtype of ovarian cancer that occurs primarily in young women and is characterized by a loss of function mutations in SMARCA4. Unexpected responses to immune checkpoint blockade have been demonstrated in SCCOHT patients, despite a low mutational burden. We sought to determine the mechanisms of response to immune checkpoint blockade in SCCOHT, a monogenic tumor with remarkably high expression of PD-L1 and other markers of an active immune microenvironment.

**Method:** SCCOHT model cell lines (BIN67 and SCCOHT-1) and HEK293T cell line with stable SMARCA4 knockdown were treated with 10 Gy of irradiation. We examined the expression of cGAS-dependent interferon-stimulated genes, *CCL5* and *CXCL10*, via real-time polymerases chain reaction (PCR) at various time points after irradiation. We also examined activation of pSTAT1 through Western blotting as a surrogate for cGAS-STING pathway activation. Finally, we performed multiparametric immunofluorescence to identify and quantify cytoplasmic micronuclei and characterized the impact of SMARCA4 loss in these model cell lines.

**Results:** BIN67 showed a 30-fold increase in *CXCL10* and a 6-fold increase in *CCL5* at 6 days post-irradiation compared to nonirradiated controls. In HEK293T with knockdown of SMARCA4, there was a 1.6-fold increase in expression of *CXCL10* ($P = 0.26$) and a 2.8-fold increase in *CCL5* ($P < 0.01$) 6 days after irradiation compared to irradiated HEK293T wildtype cells. After irradiation, there was an increased number of micronucleated cells per high-powered field in BIN67 (9.30% vs 21.24%, $P = 0.103$) and SCCOHT-1 (0.0% vs 9.38%, $P = 0.033$) compared to their nonirradiated controls. See Figure 1.

**Conclusion:** SCCOHT is an aggressive malignancy affecting young women with a poor prognosis. Understanding the immune tumor microenvironment of these tumors can further define treatment regimens. We show here that SMARCA4 loss may play an important role in activating the innate immune response, ultimately leading to response to immune checkpoint blockade.
Homologous recombination DNA repair defects in copy-number high serous-like endometrial cancers

C.W. Ashley, A.D.C. Paula, R. Kumar, D. Mandelker, X. Pei, N. Riaz, J. Reis-Filho and B. Weigelt. Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: Endometrial cancers (ECs) of copy-number high (serous-like) molecular subtype are characterized by high levels of copy-number alterations and recurrent TP53 mutations akin to high-grade serous ovarian (HGSOCs) and basal-like breast cancers, which are sensitive to platinum agents and/or PARP inhibitors. We aimed to assess whether copy-number high (serous-like) ECs show defects in homologous recombination DNA repair (HRD) akin to HGSOCs and basal-like breast cancers.

Method: Whole-exome sequencing data from ECs of copy-number high (serous-like) subtype (n = 60), HGSOCs (n = 225), and basal-like breast cancers (n = 146) from the Cancer Genome Atlas were reanalyzed. We defined genomics features that correlate with HRD, including large-scale state transitions (LSTs), mutations affecting HRD genes, small deletion length, and mutational signatures (deconstructSigs).

Results: Mutational signature analysis revealed that 55% of HGSOCs (132/225) and 46% of basal-like breast cancers (67/146) harbored a dominant mutational signature 3 associated with HRD, compared to 15% (9/60) of copy-number high (serous-like) ECs (P < 0.001 and P = 0.007, respectively). LST scores, a genomic feature of HR deficiency, were found to be significantly lower in copy-number high (serous-like) ECs (median 13, range 0–37) compared to HGSOCs (median 25, range 0–57) and basal-like breast cancers (median 23, range 0–48, P < 0.0001 for both). In addition, we observed that the average small deletion length, which in HRD defective tumors has been found to be ≥5 nucleotides, was significantly lower in copy-number high (serous-like) ECs (median 3 nucleotides, range 1–37) than in HGSOCs (median 6 nucleotides, range 1–57) and basal-like breast cancers (median 5.7 nucleotides, range 0–41.5, P < 0.05 for both). Bi-allelic genetic alterations in HRD genes were less common in copy-number high (serous-like) ECs (5%, 3/59) than in HGSOCs (29%, 71/243), or basal-like breast cancers (20%, 28/138).

Conclusion: The mutational processes involved in the tumorigenesis of copy-number high (serous-like) ECs differ from those of HGSOCs and basal-like breast cancers. Further studies are warranted to define whether ECs with HRD defects may benefit from distinct HR-directed treatment regimens.
63 - Featured Poster Session
PD-1/PD-L1 expression in BRCA1/2 mutated ovarian cancers
C.A. Penna, J. Lester, K. Bohrer, C. Moon, J. Yearley, B.Y. Karlan and C. Walsh. aCedars-Sinai Medical Center, Los Angeles, CA, USA, bMerck & Company, Inc., Whitehouse Station, NJ, USA

Objective: Accumulating evidence suggests that some cancers are dependent on the programmed cell death-1 (PD-1)/programmed cell death ligand-1 (PD-L1) pathway to evade immune destruction. Tumors with higher mutational burdens, such as those arising in BRCA germline mutational carriers, are hypothesized to be more responsive to immune checkpoint blockade. We sought to characterize tumor PD-1/PD-L1 expression in patients with primary epithelial ovarian cancer harboring BRCA1/2 germline mutations.

Method: Thirty pathologic specimens from treatment-naïve, primary ovarian cancers from women with known BRCA1 (n = 14) or BRCA2 (n = 16) germline mutations were selected for analysis of PD-1 and PD-L1 expression utilizing immunohistochemical (IHC) staining performed by Merck Research Laboratories. A semiquantitative 0–5 scoring system used by Merck Discovery pathologists across many tumor types (0 = negative, 1 = rare, 2 = low, 3 = moderate, 4 = high, 5 = very high) was used to assign scores to tumor cells and nontumor inflammatory cells. IHC scores of 2 or greater were considered "positive" for expression of PD-1 or PD-L1.

Results: PD-1 expression was observed in 30% (9/30) of the cohort and at a higher rate in BRCA1 carriers (50%) compared to BRCA2 carriers (13%) (7/14 versus 2/16, P = 0.04). PD-L1 expression was observed in 67% (20/30) of the cohort and at a higher rate in BRCA1 carriers (93%) compared to BRCA2 carriers (44%) (13/14 versus 7/16, P = 0.007). Most PD-L1 expression was seen in nontumor cells (inflammatory infiltrate) in both groups.

Conclusion: In this cohort of BRCA1/2-associated primary ovarian cancer, the rate of positive immunohistochemical staining for PD-1 and PD-L1 was high, particularly among BRCA1 carriers. These data suggest that a subset of these patients may be good candidates for PD-1/PD-L1 checkpoint inhibition therapy.

64 - Featured Poster Session
Clinical outcomes of patients with POLE-mutated endometrioid endometrial cancer

Objective: Patients with endometrioid endometrial cancer (EEC) harboring somatic POLE exonuclease domain mutations (EDMs) have been shown to be associated with favorable outcome. We sought to assess the outcome of a prospective clinical cohort of patients with POLE EDM.

Method: Patients consented to an Institutional Review Board-approved protocol of tumor-normal profiling using massively parallel sequencing (MSK-IMPACT) targeting 468 cancer-related genes. We reviewed all EECs sequenced between 2014 and 2018 and identified tumors with somatic POLE EDMs of interest (A456P, V411L, P286R, F367V, P436R). All tumors were assessed for microsatellite instability (MSI) via MSIsensor and immunohistochemical analysis for mismatch repair (MMR) proteins. Clinical data were abstracted, and descriptive statistics were employed.

Results: Of the 451 EECs sequenced, 23 had a POLE EDM (5%): 20 were primary tumors and 3 were recurrences. Not all POLE EDM EECs were stage I at diagnosis (18 cases, 78%); 3 (13%) and 2 (9%) were stages III and IV, respectively. Thirteen tumors (57%) were FIGO grades 1/2, and 10 (43%) were grade 3. All but 1 patient was treated with surgery as primary treatment (95%), and 14 patients (71%) received adjuvant radiation therapy (RT) with (n = 5, 22%) or without (n = 9, 39%) chemotherapy. EECs harbored a median of 160 somatic mutations (range 17–527) in the genes assessed. A subset of these tumors displayed loss of DNA MMR protein expression (5 samples: 1 MLH1/PMS2 and 4 MSH6), which, in all but one case, was underpinned by DNA MMR somatic mutations or MLH1 promoter methylation. MSI scores were conclusively obtained in 21 patients: 19 were microsatellite stable (MSS) and 2 MSI-high. Of the 20 patients who had germline mutation testing, none had Lynch syndrome. After a median follow-up of 20 months, 4 patients developed recurrences: 2 with initial stage I (1 MSS, 1 MSI-H) and 2 with stage III disease (1 MSS, 1 MSI-indeterminate). All were treated with a combination of surgery, chemotherapy, and RT, and all were alive at last follow-up, 3 with evidence of disease. See Table 1.
Conclusion: In this clinical cohort of EEC patients with POLE EDM, de novo metastatic disease was noted and recurrences were seen in 17% of cases. Further research is warranted to evaluate biomarkers of POLE EDM-mutant EECs that are likely to recur and are susceptible to immunotherapy.

Table 1.

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>POLE mutant tumors (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis; years (range)</td>
<td>54 (43-76)</td>
</tr>
<tr>
<td>Stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>18 (78%)</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>IV</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Adjuvant therapy</td>
<td></td>
</tr>
<tr>
<td>No adjuvant treatment</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Radiation</td>
<td>9 (39%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Radiation and chemotherapy</td>
<td>5 (22%)</td>
</tr>
<tr>
<td>Metastatic disease</td>
<td></td>
</tr>
<tr>
<td>De novo stage IV</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Recurred</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Did not recur</td>
<td>17 (74%)</td>
</tr>
<tr>
<td>Status at last follow up</td>
<td></td>
</tr>
<tr>
<td>No evidence of disease</td>
<td>20 (87%)</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Genomic Characteristic</td>
<td></td>
</tr>
<tr>
<td>Median number point mutations (range)</td>
<td>160 (17-527)</td>
</tr>
<tr>
<td>Exonuclease domain mutation</td>
<td></td>
</tr>
<tr>
<td>V411L</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>P286R</td>
<td>8 (36%)</td>
</tr>
<tr>
<td>A456P</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>F367V</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>P436R</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>MSI score</td>
<td></td>
</tr>
<tr>
<td>MSI-high</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>MSI-indeterminate</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>MSS</td>
<td>19 (83%)</td>
</tr>
<tr>
<td>MMR IHC</td>
<td></td>
</tr>
<tr>
<td>Proficient</td>
<td>18 (78%)</td>
</tr>
<tr>
<td>Deficient</td>
<td>5 (22%)</td>
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</tbody>
</table>

65 - Featured Poster Session
Safety and efficacy of a DKK1 inhibitor (DKN-01) as monotherapy or in combination with paclitaxel in patients with Wnt activated recurrent gynecologic malignancies
University of Alabama at Birmingham, Birmingham, AL, USA, Massachusetts General Hospital, Boston, MA, USA, Dana-Farber Cancer Institute, Boston, MA, USA, Sarah Cannon Research Institute Tennessee Oncology, Nashville, TN, USA, The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, University of Missouri - Kansas City, Kansas City, MO, USA, Leap Therapeutics, Inc., Cambridge, MA, USA

Objective: Wnt/β-catenin signaling is frequently dysregulated in gynecologic malignancies. Stabilizing mutations in CTNNB1, the gene encoding for β-catenin, result in constitutive pathway activation and elevated Dickkopf-1 (DKK1). DKK1 is a secreted modulator of Wnt signaling and promotes an immunosuppressive tumor microenvironment. DKN-01 (D), a mAb against DKK1, is being evaluated in recurrent gynecologic malignancies in a multicenter, phase II basket study.
**Method:** Eligible patients include recurrent endometrial cancer (EC) or platinum-resistant/refractory ovarian cancer (OC) and enriched (~50%) for tumors with stabilizing β-catenin mutations and/or Wnt signaling alterations. Patients are assigned (at physician discretion) to receive D (300 mg on days 1 and 15) monotherapy (mono) or D in combination with weekly P (80 mg/m² on days 1, 8, and 15) of a 28-day cycle. Primary endpoint is objective response rate. Exploratory endpoints include DKK1 expression (serum, plasma, and tumor); tumor genetics, infiltrating immune cells, β-catenin IHC; and peripheral MDSC and T Effector Memory cells.

**Results:** Twenty-one patients have been enrolled: D mono (n = 5, 3 EC, 2 OC); D + P combination therapy (n = 16; 9 EC, 7 OC). To date, 5/5 patients treated with D and 7/16 patients treated with D + P have mutations of interest. No treatment-related SAEs are reported to date. Most TEAEs were grade 1/2, and those reported in more than 1 patient were arthralgia, constipation, fatigue, hypokalemia, and lymphopenia (each n = 2). TEAEs equal to or greater than grade 3 included D + P related lymphocytopenia (n = 1) and unrelated vasovagal syncope (n = 1). All evaluable D mono patients had SD. Among the 8 evaluable D + P patients, 5 had stable disease, and 3 had PD. Eighteen patients remain on therapy. The trial is currently ongoing; complete cohort details and correlative work are pending. See **Table 1**.

**Conclusion:** Preliminary genetic analysis of tumors enrolled in this trial demonstrates that (~52%) of the participants have stabilizing β-catenin mutations and/or Wnt signaling alterations. To date, D mono and D in combination with P have been well tolerated with no new safety signals and evidence encouraging preliminary clinical benefit in patients with recurrent EC and platinum-resistant/refractory OC.

**Table 1.**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Total N, identified mutations</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>NE*</th>
<th>Ongoing</th>
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<tr>
<td>DKN-01 Monotherapy</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CTNNB1</td>
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<td>2</td>
<td>0</td>
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<tr>
<td>Other Wnt Alterations</td>
<td>2 (ARID1A, CREBBP, MLL2)</td>
<td>0</td>
<td>2</td>
<td>0</td>
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</tr>
<tr>
<td>No Wnt Alterations</td>
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<td>0</td>
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<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Overall</td>
<td>5</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>DKN-01 + Pac</td>
<td></td>
<td></td>
<td></td>
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<td>CTNNB1</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other Wnt Alterations</td>
<td>4 (CREBBP, ARID1A, MLL2, APC)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>No Wnt Alterations</td>
<td>9</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
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<td>16</td>
<td>0</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>13</td>
</tr>
</tbody>
</table>

*pending imaging

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**66 - Featured Poster Session**
Withdrawn at author’s request

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**67 - Featured Poster Session**

The combination of olaparib (Poly ADP-ribose polymerase inhibitor) with neratinib (pan-HER inhibitor) is synergistic in uterine serous carcinoma overexpressing HER2

G. Yadava a,b, S. Lopez a, C. Han a, G. Altwerger a,b, G. Menderes a, S. Bellone a, A. Bianchi a, E.S. Ratner a, P.E. Schwartz a and A.D. Santina a.

aYale University School of Medicine, New Haven, CT, USA, bBaylor College of Medicine, Houston, TX, USA

**Objective:** Uterine serous carcinoma (USC) represents a biologically aggressive variant of endometrial cancer and over-expresses HER2 in more than 30% of cases. Development of effective targeted treatments for recurrent, chemotherapy-resistant USC remains an unmet medical need. Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor and neratinib, a pan-HER tyrosine kinase inhibitor, are FDA-approved drugs for the treatment of platinum-sensitive ovarian cancer and early-stage HER2 + breast cancer, respectively. Recent studies in breast cancer model systems showed that high HER2 expression resulted in sensitization of breast cancer to PARP inhibitors, regardless of BRCA status. Accordingly, we evaluated the efficacy of the combination of olaparib and neratinib in primary HER2+ USC cell lines and xenografts.
Method: Cell viability experiments with olaparib, neratinib, and the combination were performed using flow-cytometry-based assays against three primary BRCA1/2-proficient USC models over-expressing HER2. Synergy of the two drugs was assessed by using CompuSyn software. Immunoblotting experiments were performed to elucidate the mechanism of action. Finally, the efficacy of the combination (olaparib + neratinib) versus single-agent olaparib and neratinib was evaluated in vivo using two HER2+ USC xenografts.

Results: The combination treatment of olaparib + neratinib displayed a more potent and superior antitumor activity when compared to the single-agent therapy in both the HER2-amplified tumor cell lines ARK 1 and ARK 2 in vitro. In contrast, ARK 4, which is not HER2-amplified, was unaffected by exposure to the combination. Immunoblotting results showed increased PARP expression in both USC cell lines treated with neratinib compared to control, and increased HER2 expression in both USC cell lines treated with olaparib compared to control. In both USC xenograft models, the combination induced a more potent tumor inhibition and a long-lasting effect when compared to single-agent olaparib or neratinib (P < 0.05).

Conclusion: Our study demonstrated the combination of olaparib and neratinib has remarkable antitumor activity against HER2+ USC. This combination may represent a novel therapeutic option for chemotherapy-resistant USC patients with HER2+, homologous recombination-proficient tumors.

68 - Featured Poster Session
Therapeutic AXL inhibition of tumor and tumor microenvironment stromal cells improves response to chemotherapy in ovarian cancer
M.M. Mullen1, E. Lomonosova1, H. Beck-Noia1, D. Wilke1, L. Guo1, A.R. Hagemann1, L.M. Kuroki1, C.K. McCourt1, P.H. Thaker1, D.G. Mutch1, M.A. Powell1 and K.C. Fuh4. 1Washington University School of Medicine in St. Louis, St. Louis, MO, USA, 4Women & Infants Hospital, Brown University, Providence, RI, USA

Objective: To determine whether inhibition of GAS6/AXL with recently granted fast-track designation AVB-S6-500 (AVB) can improve response in both tumor and tumor microenvironment (TME) stromal cells in ovarian cancer.

Method: AVB was supplied by Aravive Biologics. IHC for AXL expression, and serum GAS6 levels were performed on HGSOC tumors and blood collected pre- and post-NACT. In vitro viability assays were performed on chemoresistant tumor cells (OVCAR5 and POV71-hTERT) treated with chemotherapy ± AVB, and synergy calculations were performed. Mouse models (OVCAR8, PDX) were used to determine whether the combination of chemotherapy plus AVB reduced tumor volume. To evaluate the contribution of the TME in tumor cell invasion, AXL-expressing fibroblasts were treated with AVB prior to tumor cell invasion.

Results: Increased AXL IHC expression was seen in the post-NACT versus the pre-NACT tumors that had poor response (+5%) compared to a decrease (~15%) in AXL expression in tumors with good response to NACT (P < 0.01). Similarly, serum GAS6 levels tended to be higher in patients with poor response (20.5 vs 15.6 ng/mL). The combination of carboplatin plus AVB (2 µM, 5 µM) or paclitaxel plus AVB (1 µM) resulted in decreased cell viability compared to chemotherapy alone (P < 0.05) in both cell lines. Synergism was seen between carboplatin + AVB and paclitaxel + AVB with a weighted combination index <1. In vivo mouse models treated with chemotherapy + AVB had significantly smaller subcutaneous tumors than those treated with chemotherapy alone (3.1 mg vs 64 mg, P = 0.003 in OVCAR8 and 62 mg vs 157 mg, P = 0.0108 in the PDX model). Ovarian cancer cells treated with AVB had decreased invasion compared with those treated with vehicle alone (150 vs 225 invasive tumor cells/hpf, P < 0.01). More significantly, a decrease in tumor cell invasion was seen when only omentum-derived fibroblasts were therapeutically inhibited with AVB versus vehicle (50 vs 250 invasive tumor cells/hpf, P < 0.0001).

Conclusion: AXL and GAS6 levels are higher in post-NACT tumors of poor responders. The combination of chemotherapy with AVB has been shown to decrease tumor cell viability, tumor invasion, and tumor volume. Treatment of TME cells such as fibroblasts with AVB can inhibit tumor cell invasion, suggesting that inhibition of the TME can modulate tumor cell invasion through AXL signaling.

69 - Featured Poster Session
The combination of olaparib (Poly ADP-ribose polymerase inhibitor) with neratinib (pan-HER inhibitor) is synergistic in epithelial ovarian carcinoma overexpressing HER2.
C. Han5, G. Altwerger5, G. Menderes5, S. Bellone5, A. Bianchi5, G. Yadav5, S. Lopez5b, A. Manzano5, E.S. Ratner5, M. Azodi5, B.
Objective: Ovarian cancer (OC) remains the most lethal gynecologic tumor. Development of effective targeted treatments in ovarian cancer remains an unmet medical need. Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, and neratinib, a pan-HER inhibitor, have recently been approved in ovarian cancer and early-stage HER2 plus breast cancer, respectively. Importantly, studies in breast cancer models showed high HER2 expression resulted in sensitization of breast cancer to PARP inhibitors regardless of BRCA status. We evaluated the efficacy of the combination of olaparib and neratinib in HER2+, BRCA wildtype OC cell lines and xenografts.

Method: Cell viability experiments with olaparib, neratinib, and the combination were performed using flow-cytometry-based assays in four primary BRCA1/2-proficient OC models over-expressing HER2. Drug synergy was assessed using CompuSyn software. Immunoblotting and real-time polymerase chain reaction (RT-PCR) experiments were performed to elucidate the mechanism of drug activity. Finally, the efficacy of single-agent olaparib, neratinib, and the combination was evaluated in HER2+ OC xenograft models.

Results: In vitro, olaparib and neratinib as single agents were both effective in suppressing primary ovarian tumor cell lines growth. However, neratinib had more prominent tumor suppression activity than olaparib in HER2+ OCs. Importantly, the drug combination demonstrated synergy in all four primary OC models tested and was superior to single-agent olaparib or neratinib in vivo and in vitro. Accordingly, mice treated with the combination of olaparib and neratinib had a significantly longer overall survival when compared to control mice (P = 0.0005), mice treated with olaparib (P = 0.0005), and mice treated with neratinib (P = 0.0013). RT-PCR and immunoblotting of OC cells treated with neratinib showed decreased BRCA1/2 and increased PARP activity.

Conclusion: Our study demonstrated synergy of olaparib and neratinib in HER2+ OC models. This combination may represent a novel therapeutic option for chemotherapy-resistant OC patients with HER2+, homologous recombination-proficient tumors.

70 - Featured Poster Session
Dasatinib, paclitaxel and carboplatin in women with advanced-stage and recurrent endometrial cancer: A pilot clinical and translational study

Objective: To evaluate the impact of dasatinib therapy on EphA2 signaling and on clinical efficacy in combination with standard chemotherapy in endometrial cancer patients.

Methods: Single-agent dasatinib (150 mg orally daily × 14 days) lead-in followed by triplet dasatinib (150 mg orally daily), paclitaxel, and carboplatin chemotherapy was administered to women with measurable and tumor biopsy-amenable advanced-staged primary or recurrent endometrial cancer for up to 6 cycles (21-day cycles). Main outcomes and measures were alteration in MAPK signaling in pre- and post-dasatinib treatment tissue biopsies by Reverse Phase Protein Array (RPPA); the frequency and severity of adverse events of combination paclitaxel, carboplatin, and dasatinib; RECIST objective response rate (ORR), progression-free survival (PFS), and overall survival (OS); microRNA expression and downstream effectors of EphA2 signaling.

Results: Eighteen patients (5 with advanced-staged primary and 13 with recurrent endometrial cancer) were recruited: 17 were evaluable for toxicity and 11 for response. A previously unknown interaction in bRAF/cRaf dimerization and caveolin-1 (CAV1) was predictive of response/resistance to dasatinib. Overall, the ORR was 45% (95% CI 22–72%) with PFS of 10.5 months and OS of 30.4 months. The most common grade 3/4 adverse events were neutropenia (65%), thrombocytopenia (59%), anemia (24%), and fatigue (24%). RPPA analysis demonstrated interactions in Notch pathway signaling.

Conclusion: This unique lead-in trial design demonstrated that CAV1 expression in combination with Raf heterodimerization is responsible for resistance to EphA2 targeting by dasatinib. The triplet combination shows interesting clinical activity for this population with acceptable toxicity. The exploration for biomarker-driven and informed therapy is feasible and necessary for improving outcomes in women with advanced-stage and recurrent endometrial cancer.
71 - Featured Poster Session
Surgery induces broad changes in clinically relevant genes regulating immune and metabolic responses in murine epithelial ovarian cancer
Roswell Park Cancer Institute, Buffalo, NY, USA, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

Objective: Standard therapy for metastatic EOC involves surgical debulking and chemotherapy. Surgery in metastatic disease is noncurative, and recurrence of disease is driven by residual tumor. However, little is known about the effect of surgery on residual tumor. Our objective is to evaluate acute changes induced by surgery on the residual tumor microenvironment in syngeneic murine epithelial ovarian cancer (EOC).

Method: Female C57BL/6 (n = 30) were administered intraperitoneal ID8 murine ovarian cancer cell line (1.0 × 10^7 cells/mouse). At day 28, when visible widely metastatic intraperitoneal disease is present, the mice underwent laparotomy and partial omentectomy. On days 31 or 35, a second surgery was performed to remove the remaining omental tissue. RNA was extracted from the omental tumor. Tumor implants in the omentum were confirmed by histology. RNA-Seq libraries were prepared using Illumina TruSeq Stranded Total RNA Library Prep Kit and sequenced using 75 paired end sequencing on Illumina NextSeq500. Gene Set Enrichment Analysis was performed to compare the omental samples between groups. In addition, the omentum from each mouse that underwent surgery on day 28 was compared to the tissue extracted on day 31 or 35 from the same mouse. A twofold gene expression change was used with an adjusted P value of <0.05.

Results: We observed significant alterations (P < 0.05) in gene expression in multiple clinically relevant pathways including the IGF1/MTOR, KRAS, PD1, and HRD pathways as well as immune landscape markers including neutrophil and T cell trafficking. Comparison of day 28 with day 31 showed a total of 612 genes with a twofold increase and 398 genes with a twofold decrease in expression (P < 0.05). Comparison of day 28 with day 35 showed a total of 263 genes with a twofold increase and 455 genes with a twofold decrease in expression (P < 0.05). Our presentation will include the specific clinically relevant genes with altered expression and pathway analysis. See Figure 1.

Conclusion: Surgery induces broad changes in the expression of clinically relevant genes regulating immune and metabolic responses in murine metastatic EOC. This analysis provides insight into the surgically induced immune landscape that may influence the use of targeted chemotherapy or immunotherapy in the peri-operative period.

Fig. 1. Heatmaps showing day 28 versus 35 gene expression changes
72 - Featured Poster Session
The lack of benefit of chemotherapy for stage I uterine leiomyosarcoma patients: A retrospective analysis of 890 patients
M.T. Richardson, J.K. Chan, D.S. Kapp, A.K. Mann and C.I. Lia. Stanford University School of Medicine, Stanford, CA, USA, California Pacific Medical Center, San Francisco, CA, USA, Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

Objective: To determine the role of chemotherapy (CT) in surgically staged I uterine leiomyosarcoma (LMS).

Method: Data were obtained from the National Cancer Data Base (NCDB) from 2010 to 2014. χ² test, Cox regression, and Kaplan-Meier analyses were used.

Results: Of 890 LMS patients, the mean age was 54.5 years (range 24–90 years). Of all patients, 634 (71.2%), 193 (21.7%), 35 (3.9%), and 28 (3.1%) were white, black, Asian, and other/unknown, respectively. In the overall group, 38.8% of patients underwent lymph node dissection and 14.6% had omentectomy with their surgical staging. According to the American Joint Committee on Cancer, 7th edition, for surgical staging, 143 (16.1%) were stage IA; 634 (71.2%) were stage IB; and 113 (12.7%) were undefined stage I. A total of 528 (59.3%) underwent no CT, and 362 (40.7%) CT after surgery.

In stage I, the 5-year overall survival (OS) for no CT was 61.5% versus 60.6% for CT (P = 0.761). In stage IA, overall survival (OS) was 76.7%. The OS for no CT was 75.5% versus 80.3% for CT (P = 0.690). For stage IB, the OS was 57.2%. The OS for no CT was 55.7% compared to 59.1% for CT (P = 0.536). On multivariate analysis, older age (HR = 1.04, 95% CI 1.02–1.05, P = 0.001), black race (HR = 1.56, 95% CI 1.22–1.98, P < 0.001), higher substage (HR = 2.26, 95% CI 1.43–3.57, P < 0.001), Charlson/Deyo Score 2 (HR = 1.99, 95% CI 1.10–3.58, P = 0.022), lymph vascular invasion (HR = 1.65, 95% CI 1.17–2.32, P = 0.004), and positive peritoneal cytology (HR = 3.66, 95% CI 1.08–12.39, P = 0.037) were independent predictors of worse survival. Adjuvant CT (HR = 1.04, 95% CI 0.79–1.36, P = 0.787) were not predictors for improved survival.

Conclusion: Our data suggest that adjuvant chemotherapy was not associated with an overall survival benefit in stage I uterine leiomyosarcoma.

73 - Featured Poster Session
Profiling the metabolomic composition of the ovarian cancer secretome and ovarian cancer-induced metabolomic changes in mesothelial cells
I.M. Lazova, A. Mukherjee, H. Kenny, S. Fan, I. Blaženović, O. Fiehn and E. Lengyel. The University of Chicago Medicine, Chicago, IL, USA, University of California, Davis, Davis, CA, USA, University of Chicago, Chicago, IL, USA

Objective: We aim to understand the mechanisms driving the prometastatic interactions between epithelial ovarian cancer (OvCa) cells and human peritoneal mesothelial cells (HPMCs), the first cells encountered by OvCa during abdominal metastasis. Here, we describe the global metabolomic profile of the OvCa secretome and the OvCa-induced metabolomic changes within HPMCs.

Method: To profile the OvCa secretome, Tyk-nu cells were grown as spheroids, and their conditioned media (CM) were submitted for metabolomic analysis. HPMCs were treated with Tyk-nu CM, and morphology, stress fiber formation, gene expression, and metabolism were measured using an f-actin stain, qRT-PCR/immunoblot analysis and metabolomic analysis. Levels of amines, primary metabolites, and lipids in Tyk-nu CM and HPMCs were quantified using HILIC, gas and liquid chromatography-based mass spectrometry. Paired t tests identified the significantly altered metabolites between control and experimental groups.

Results: We identified several metabolic changes in the OvCa secretome (Tyk-nu CM) encompassing carbohydrate, fatty acid, and tryptophan metabolism. Treatment of HPMCs with Tyk-nu CM significantly changed their metabolomic profile, illustrated by increases in cholesterol esters, TCA cycle intermediates (succinate), polyamine metabolism (spermine, spermidine), and catabolic intermediates of pyrimidine and tryptophan (β-alanine and kynurenine). We show that HPMCs treated with Tyk-nu CM undergo an epithelial to mesenchymal transition (EMT) characterized by increased stress fiber formation and altered expression of established EMT markers (decreased E-cadherin and increased snail expression). These effects on EMT were reproduced by ectopic addition of individual metabolites (lactate, spermine, and kynurenine) found in the OvCa secretome. These data suggest metabolic regulation of OvCa cell-induced EMT processes in HPMCs.
Conclusion: This is the first unbiased study that comprehensively characterizes the effect of OvCa cells on HPMC metabolism. Subsequently, we show OvCa-secreted metabolites can induce EMT in HPMCs. We are actively exploring the contributions of the identified metabolic signature in augmenting the tumor-promoting nature of HPMCs. Findings will be correlated with transcriptomic and proteomic data to identify key metabolites within these metabolic pathways for targeted therapy development.

74 - Featured Poster Session
Epigenetics tells the mole story: DNA methylation identifies complete moles destined to develop into gestational trophoblastic neoplasia
LD. St. Laurenta,b, L. Lin, I. Maestá, N.S. Horowitzc,d,e, R.S. Berkowitzc,d,e, and K.M. Eliasb,e,h,j.
Massachusetts General Hospital, Boston, MA, USA, aBrigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA, bUniversity of Sao Paulo, Sao Paulo, Brazil, cUniversity of Sao Paulo State University, Botucatu, Sao Paulo, Brazil, dNew England Trophoblastic Disease Center, Boston, MA, USA, eBrigham and Women’s Hospital/Dana-Farber Cancer Institute, Boston, MA, USA, fBrigham and Women’s Hospital, Boston, MA, USA, gBrigham and Women’s Hospital, Harvard University, Boston, MA, USA, hHarvard Medical School, Boston, MA, USA, iHarvard Medical School, Boston, MA, USA

Objective: There is no method to predict which patients with complete hydatidiform mole (CHM) will develop gestational trophoblastic neoplasia (GTN). DNA methylation is a key regulatory mechanism in trophoblast development. This study sought to determine whether DNA methylation distinguishes CHM destined to develop GTN. Array-based bisulfite sequencing provides the ability to study whole genome methylation and enables discovery of epigenetic biomarkers and therapeutic targets.

Method: Genomic DNA was extracted from 22 CHM specimens collected at the time of uterine evacuation. Bisulfite modification and methylation patterns were investigated using the Illumina HumanMethylation450 array, and validated by bisulfite sequencing for selected probes. Two-way hierarchical clustering was performed, and the degree of methylation at sites throughout the genome were compared between samples. Quantitative comparison between sample clusters was used to identify significant differentially methylated regions (DMRs).

Results: Among the 22 patients, 13 had hCG normalization without treatment, and 9 developed GTN that required methotrexate. One methotrexate-resistant case required second-line therapy with pulse-ActD. Distinct methylation signatures were observed between benign CHM and CHM that progressed to GTN after two-way hierarchical clustering of DMRs (Figure 1). A total of 182 distinct genomic regions exhibited significantly different levels of methylation; 133 DMRs were hypomethylated and 47 were hypermethylated in CHM cases that progressed to GTN. DMRs were more likely to occur in coding regions followed by intergenic regions. Notable DMRs between CHM progressing to GTN compared to benign CHMs include multiple PI3K/AKT pathway members: RPTOR (2.3-fold increase, \( P = 0.022 \)), PIK3C2G (1.7-fold decrease, \( P = 0.038 \)), and PEBP4 (1.8-fold increase, \( P = 0.003 \)). TGFβ receptor SMAD3 (2.0-fold decrease, \( P = 0.05 \)) and NOTCH receptor DLL1 (2.5-fold increase, \( P = 0.008 \)) were also notably altered.

Conclusion: This is the first study to identify epigenetic markers that predict progression to GTN in CHM tissue collected at initial uterine evacuation. DMRs between these populations of CHM not only predict new biomarkers and therapeutic targets for post-molar GTN, but also suggest DNA methylation is fundamental to tumorigenesis in GTD.
Harnessing artificial intelligence and digital diffraction to advance point-of-care HPV 16 and 18 detection

C.M. Castro\textsuperscript{a}, H. Im\textsuperscript{a}, H. Lee\textsuperscript{a}, M. Avila-Wallace\textsuperscript{b}, R. Weissleder\textsuperscript{a} and T. Randall\textsuperscript{a}. \textsuperscript{a}Massachusetts General Hospital, Boston, MA, USA, \textsuperscript{b}Gillette Center for Gynecologic Oncology/Massachusetts General Hospital, Boston, MA, USA

Objective: The shift towards HPV DNA detection as standalone or co-testing for cervical cancer screening is countered by resource and cost demands in centralized settings. We sought to leverage an innovative diffraction imaging platform with readouts powered by artificial intelligence to detect HPV16 and 18 at the point of care.

Method: For HPV DNA assay, we developed a DNA detection method based on digital diffraction (Figure 1). Cells from cervical brushings were collected and their DNA extracted using disposable syringe-filters. DNA samples were mixed with polystyrene (PS) and silica beads (S) coated with DNA probes complementary to the 3’ and 5’ ends of HPV target DNA, respectively. In the presence of target DNA, the 2 bead types become linked through the target DNA and form detectable dimers. Upon LED illumination, diffraction patterns of PS, silica, and PS-silica bead dimers were captured by our new portable device and quickly analyzed by custom-built artificial intelligence algorithms we designed resulting from machine training on thousands of diffraction images. In preclinical/clinical testing, (1) to examine the specificity of our diffraction assay, we tested 3 cell lines (CaSki, HPV16+/18−; HeLa, HPV16−/18+; C33a, HPV16−/18−) for HPV16 and 18 DNA. (2) Via an approved protocol, we compared cervical brushing/biopsies from 7 patients with known HPV status (HPV 16+/18−, HPV 16−/18+, and HPV 16−/18−) to test performance and specimen requirements. (3) We collected cervical brushings from 28 high-risk patients referred to the colposcopy clinic. Our HPV diffraction readouts were analyzed blindly and then compared to results from the Cobas HPV test, the local gold standard.

Results: In all cases, readouts from brushings performed as well as biopsies for identifying HPV subtypes. Moreover, our platform detected the presence of HPV16 and/or 18 with 100% accuracy and within 2 hours.

Conclusion: Current “state-of-the-art” recommendations favoring HPV screening are poised to widen existing gaps between resource-rich and poor regions. Our rapid and accessible HPV platform performs as well as its costlier peers. By decentralizing diagnoses through point-of-care operation and artificial intelligence algorithms, our work is positioned to partner with rural and global communities where effective HPV tactics remain unmet needs.

Fig. 1. A) DNA extraction using a disposable microbead-based syringe filter. Thousands of dimer images, formed in the presence of target

DNA, were used to develop artificial intelligence readouts for an on-device analysis; b) Portable and low cost HPV device; c) Clinical performance of device against cobas HPV test using cervical brushing specimens (elevated bars equated to HPV positivity with our approach; red equals positive per cobas HPV- note correlation)

76 - Special Interest Session
Accuracy of high-risk HPV DNA detection from urine and cervical samples in abnormal pap smear women
V. Achariyapota and A. Punyashthira.  "Faculty of Medicine Siriraj Hospital, Bangkok, Thailand, Thammasat University, Pathum Thani, Thailand"

**Objective:** The aim of this study was to evaluate the clinical performance of high-risk (hrHPV) detection in paired urine and cervical samples in histology-confirmed high-grade cervical lesions (high-grade squamous intraepithelial lesion, HSIL), squamous cell carcinoma (SCC), atypical glandular carcinoma (AGC), adenocarcinoma in situ (AIS), and adenocarcinoma.

**Method:** This cross-sectional study enrolled 96 participants who had abnormal cervical cytology and attended the colposcopy clinic at Siriraj Hospital, from July 15, 2016, to January 29, 2017. The exclusion criteria were participants who had a history of cervical surgery, hysterectomy, pelvic irradiation, or chemotherapy. Either randomized void and initial stream urine samples or cervical cell samples were collected from participants before undergoing pelvic examination and colposcopy. Cervical biopsy, endocervical curettage (ECC), or cervical conization was done as a standard treatment guideline. Both specimens were sent to the microbiology department, Faculty of Medicine, Siriraj Hospital, Mahidol University, for extraction and detection of hrHPV by Anyplex II HPV high-risk testing. Moreover, the acceptability and satisfaction of individual testing were questioned.

**Results:** The results showed high sensitivity of HPV detection in urine and cervical groups, 86.2 and 94.8, respectively. Both groups were high accuracy, about 70%. The data showed very good agreement between urine and cervical group for detection of HPV. Kappa = 0.85 and 0.95 for hrHPV type 16 and 18, respectively. Higher satisfaction and acceptability were found in the urine group. See Table 1.

**Conclusion:** hrHPV detection in urine samples was an easy test and feasible; there was no need for pelvic examination; and there was high sensitivity and high accuracy. The study demonstrated an alternative choice in case of follow-up an abnormal cervical cytology or post-treatment follow-up in women who fear or reject pelvic examination. In the future, studies in large population and negative disease population may improve specificity of outcome.

### Table 1. Urine and cervical hrHPV detection in histology confirmed CIN2+ lesion

<table>
<thead>
<tr>
<th>Test result; % (95% CI)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>86.2 (74.6-93.9)</td>
<td>47.4 (31.0-64.2)</td>
<td>71.4 (59.4-81.6)</td>
<td>69.2 (48.2-85.7)</td>
<td>70.8 (61.1-79.0)</td>
</tr>
<tr>
<td>Cervix</td>
<td>94.8 (85.6-98.9)</td>
<td>39.5 (24.0-56.6)</td>
<td>70.5 (59.1-80.3)</td>
<td>83.3 (58.9-96.4)</td>
<td>72.9 (63.6-80.8)</td>
</tr>
</tbody>
</table>

*; included high grade squamous intraepithelial lesion, atypical glandular carcinoma, adenocarcinoma in situ, squamous cell carcinoma, adenocarcinoma hrHPV, high risk Human Papilloma Virus

77 - Special Interest Session
Withdrawn at author’s request

78 - Special Interest Session
Phase II randomized, double-blind, placebo-controlled evaluation of ahcc for the eradication of HPV infections in women with HPV positive pap smears
J.A. Smith, A.A. Gaikwad, B. Rech, J. Faro, J.A. Lucci III, R. Olsen and T.T. Byrd. "The University of Texas Medical School at Houston, Houston, TX, USA, University of Texas Medical School at Houston, Houston, TX, USA, Specialists in Obstetrics & Gynecology, Houston, TX, USA, Houston Methodist Hospital, Houston, TX, USA"
**Objective:** The aims of this study were (1) to evaluate the efficacy of AHCC 3 grams by mouth once daily to eradicate HPV infections in women with HPV-positive PAP smears, (2) to observe the durability of response to AHCC, and (3) to define the adverse effects of AHCC compared to placebo.

**Method:** This is an ongoing National Institutes of Health-funded phase II study (NCT02405533), reviewed and approved by the University of Texas Health Sciences Center at Houston Institutional Review Board, to evaluate AHCC 3 grams in a randomized, double-blind placebo-controlled study. Patients will be randomized to first receive either arm A, AHCC 3,000 mg (taken as 6 500-mg capsules) by mouth once daily on an empty stomach for 6 months, or arm B, placebo (6 capsules) by mouth once daily on an empty stomach for 6–12 months. HR-HPV DNA status and the immune panel were monitored at each visit. Power analysis was based on expected 10% eradication in the absence of treatment and 50% eradication with treatment. At a 0.05 confidence level, we summarize sample size and its associated statistical power. In this analysis, the planned sample was a maximum of 50 patients (n = 25 per group), which leads to 94.5% power to detect the hypothesized effect size.

**Results:** A total of 50 patients have been enrolled in this phase II study. A total of 46 patients completed the study at time of analysis with the remaining planned to conclude in February 2019. Preliminary analysis confirmed a 60% clearance of HPV infections after 6 months of AHCC including 66.7% who have had confirmed eradication for more than 12 months. Two patients (11.8%) on placebo cleared HPV infection over the 12-month study duration. Data to date also confirmed use of AHCC supplementation modulates the expression and signaling of IFNβ that is known to be elevated in chronic viral infections, such as HPV, to levels below 25 pg/mL. This was associated with a correlative increase in IFN-gamma and eradication of HPV infections.

**Conclusion:** The results of this phase II study confirmed data observed in pilot studies that AHCC supplementation for at least 6 months is associated with a 60% successful elimination of HPV infections and confirmed IFNβ correlates with eradication of persistent HPV infections. The optimal duration of AHCC supplementation required after the first negative result still needs more evaluation in future clinical studies.

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**79 - Special Interest Session**

**The world ovarian cancer coalition every woman study: Identifying global and local challenges, and the opportunities to improve survival and quality of life for women no matter where they live**

F. Reid and A. Jones. World Ovarian Cancer Coalition, London, United Kingdom, World Ovarian Cancer Coalition, LONDON, United Kingdom

**Objective:** The objectives of the World Ovarian Cancer Coalition Every Woman Study were to address the evidence gap relating to the experiences of women with ovarian cancer globally, and to identify actions to ensure that every woman with ovarian cancer has the best possible chance of survival and best quality of life.

**Method:** Guided by a Global Expert Advisory Panel with patient and clinical representation, the study included a literature review of global trends in incidence, mortality, and survival of ovarian cancer, qualitative interviews with women and clinicians in 16 countries, and an online survey available in 15 different languages (open March to May 2018). A total of 1,531 women diagnosed since 2013 from 44 countries took part. Given global 5-year prevalence, results in this survey achieve a confidence level of 95% with a confidence interval of ±2.5% where n = 1,530.

**Results:** With global incidence set to rise by 55% to 371,000 a year, 5-year survival rates of less than 50%, and 15% dying within 2 months of diagnosis, urgent action is required to improve survival. More than two-thirds of woman had not heard of ovarian cancer or knew anything about it prior to their own diagnosis. Ninety percent of respondents reported experiencing multiple symptoms prior to their diagnosis regardless of type. However, a quarter of woman waited 3 months or more before visiting a physician. One in 10 waited more than 6 months. There were wide variations between countries and in the subsequent time to diagnosis. There were wide levels of variation in genetic testing, both pre- and post-diagnosis, by country (9.6% to 80.6%, average 54.7%, P < 0.01). Of those women with 2 or more relatives with ovarian cancer, 80% had not had genetic testing prior to their diagnosis. Clinicians indicate that access to specialist treatment in high-volume centers varies widely by country and region.

**Conclusion:** Low level of awareness of ovarian cancer is a global problem resulting in delays in women seeking medical attention and being diagnosed. Women are potentially missing out on new targeted treatments for ovarian cancer, and family members are unaware of risk because of variable rates of genetic testing. Ensuring that all women have access to specialist
treatment is a vital step to improving outcomes worldwide. Reducing rates of variability between countries is an important first step.

80 - Special Interest Session

Long term consequences of cervical cancer treatment if we don’t get it right
R. Music. Jo’s Cervical Cancer Trust, London, United Kingdom

Objective: The aims of this study were to better understand the impact of living beyond a cervical cancer diagnosis and to identify gaps in provision of care and support and improvements that are needed to ensure every woman is given the best opportunity to have a good quality of life and positive health outcomes.

Method: There were 3 phases using the same question set. In phase 1 women were identified through England’s National Cancer Patient Experience Survey (CPES) (2010–2013) and agreed to be involved in future research. In phase 2 an online survey was publicized through various online and print channels throughout the period of both phase 1 and phase 3. In phase 3 the method was the same as in phase 1, using 2015 CPES participants. The total number of participants was 688.

Results: Significant numbers experienced, or continue to be affected by, several, often complex, long-term consequences of their diagnosis and treatment including the following: 86% experienced at least 1 physical long-term consequence; 63% experienced 3 or more; and 24% experienced 6 or more. Of which 67% experienced changes in their sex life; 64% suffered fatigue; 54% bowel difficulties; 54% urinary difficulties; 44% lymphedema; and 60% said employment changed due to their treatment. High numbers hadn’t sought medical advice about the difficulties experienced including 39% who had changes to bowel function and 42% urinary function; 59% with negative changes to or a complete loss of sex life; 44% affected by pain and/or fatigue; and only 32% who have experienced reduced, or even lost, fertility talked to a physician.

Conclusion: The research commissioned by Jo’s Cervical Cancer Trust, a leading cervical cancer charity, is very likely the biggest ever dataset of its type, and the results are relevant to both health professionals and patients worldwide. It highlights that high numbers of women are affected by multiple negative consequences of their treatment and demonstrates their complex, wide-ranging needs. Patients are being suboptimally managed. Women presenting with problems are not being referred or diagnosed correctly, often being told there is nothing that can be done and being left to self-manage life-changing symptoms without the right diagnosis. There needs to be increased understanding and awareness of the long-term consequences across healthcare, and women need to be empowered to feel they are able to ask questions, ask for help, and be confident their concerns will be recognized and addressed.

81 - Special Interest Session

Concurrent chemoradiotherapy for adenocarcinoma of the uterine cervix: Japanese Gynecologic Oncology Group (JGOG) multicenter retrospective study

Y. Nagai¹, M. Takekuma², R. Kitagawa³, E. Kobayashi⁴, A. Tozawa⁵, S. Nagao⁶, S. Nishio⁷, T. Toita⁸, M. Mikami⁹ and T. Sugiyama¹⁰. ¹Okinawa Prefectural Nanbu Medical Center & Children’s Medical Center, Okinawa, Japan, ²Shizuoka Cancer Center, Shizuoka, Japan, ³Tohoku Medical and Pharmaceutical University, Miyagi, Japan, ⁴Osaka University, Osaka, Japan, ⁵St. Marianna University School of Medicine, Kanagawa, Japan, ⁶Hyogo Cancer Center, Akashi, Hyogo, Japan, ⁷Kurume University School of Medicine, Fukuoka, Japan, ⁸Okinawa Prefectural Chubu Hospital, Okinawa, Japan, ⁹Tokai University School of Medicine, Isehara, Japan, ¹⁰Takagi Hospital, Fukuoka, Japan

Objective: Concurrent chemoradiotherapy (CCRT) using weekly cisplatin is the standard treatment for advanced cervical cancer. Because cervical adenocarcinoma (CxAdeno) is relatively rare and has poor prognosis after treatment with CCRT, it is unclear whether CCRT using weekly cisplatin is the standard treatment for CxAdeno. We conducted a multicenter retrospective study of CxAdeno treated with CCRT in Japan to find out the treatment outcomes and to extract the data for required information to establish a newly clinical study design for CxAdeno.

Method: We retrospectively reviewed the clinical data of patients with CxAdeno treated with CCRT between January 2000 and June 2014. Patient characteristics, methods of chemotherapy and radiotherapy, late adverse events, and oncologic outcomes were analyzed. Kaplan-Meier life table analysis and the log rank test were used to assess the survival rate. P values <0.05 were considered significant.
**Results:** We collected 413 CxAdeno cases from 47 institutions of the Japanese Gynecologic Oncology Group (JGOG). Median age was 58 years (range 24–58 years), and median tumor diameter was 50 mm (range 11–120 mm). The FIGO stages were stage I, 49; II, 139; III, 186; and IVA, 39. Median OS and DFS time in 269 patients treated with CCRT using platinum was 46.9 and 12.9 months, respectively. Median OS and DFS time in 48 patients with paraaortic node (PAN) enlargement was 29.8 and 8.0 months, respectively. For 175 patients without PAN enlargement treated with CCRT using weekly CDDP 40 mg/m² (w-P group), median DFS time and 2-year DFS was 15.6 months and 41.8%, respectively. Meanwhile, 2-year DFS in 26 patients treated with paclitaxel and weekly CDDP (TP group) was 72.5%. DFS in the TP group was superior to those in the w-P group ($P = 0.012$). Regarding late adverse events in all patients, grade 3 or more was 4.6% in small/large intestine, 1% in bladder.

**Conclusion:** This multicenter retrospective study in CxAdeno suggested that CCRT using paclitaxel and weekly CDDP may be a promising strategy for CxAdeno.

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**82 - Special Interest Session**

**Concurrent chemoradiotherapy for cervical cancer in a single institution: High-dose rate brachytherapy vs helical tomotherapy**

**S. Kim, K.J. Ryu, S. Lee and J.Y. Song. Korea University College of Medicine, Seoul, Korea, Republic of (South)**

**Objective:** We reviewed our experience, evaluated the results of intensity-modulated radiation therapy (IMRT) via helical tomotherapy (HT), and compared the disease outcome with that of high-dose-rate brachytherapy in patients with cervical cancer.

**Method:** A total of 114 patients who have been treated with concurrent chemoradiotherapy (CCRT) for newly diagnosed cervical cancer from 2008 to 2017 were retrospectively reviewed. Radiotherapy was given as a combination of whole pelvic external beam RT (EBRT) followed by high-dose-rate brachytherapy (BT) or IMRT via helical tomotherapy (HT).

**Results:** We extracted selected populations using propensity score matching with 1:1 ratio. After adjustment for age, BMI, radiation dose, prior surgery, clinical stage, and histologic type, there was no significantly different parameter between the 2 groups. OS was poorer in BT group compared to HT group (median survival 17.5 months after BT vs 30 months after HT, log rank $P = 0.034$). Four-year survival rates were 74.2% in the BT group and 100% in the HT group. However, the PFS was not different between the 2 groups ($P = 0.270$). One- and 2-year PFS rates were 85.3% and 76.3% in the BT group but 87.0% and 58.9% in the HT group, respectively. In univariate analysis, there was no significant risk factor for OS. However, in PFS, stage was the only significant risk factor for recurrence. In multivariate analysis, clinical stage was still a significant risk factor after adjusting for the other clinical parameters.

**Conclusion:** HT could be a feasible option for CCRT in patients with cervical cancer with appropriate indications. Further studies with delicate design and larger numbers from multicenter with long follow-up periods are warranted to confirm the significance of benefit of HT in CCRT in the field of cervical cancer.

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**83 - Special Interest Session**

**Safety, acceptability and efficacy of a new thermal ablation technique to prevent cervical cancer in low- and middle-income countries – preliminary results**

**L.F. Pindera,b, P. Basu,c, W. Prendiville,c, R. Mwongo,c, E. Lucas,c and G.P. Parham,b,d. aUniversity of Washington Medical Center, Seattle, WA, USA, bWomen and Newborn Hospital, University Teaching Hospital, Lusaka, Zambia, cInternational Agency for Research on Cancer, Lyon, France, dUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA**

**Objective:** We present preliminary data from a randomized controlled trial on the safety, acceptability, and efficacy of a new cordless, rechargeable, hand-held thermal ablation (TA) device for the treatment of cervical precancerous lesions in Lusaka, Zambia.

**Method:** VIA screen-positive women eligible for ablative treatment are randomized to receive TA, cryotherapy, or LLETZ. Side effects, pain, and client satisfaction are scored and recorded. Samples for HPV DNA testing are collected at baseline and follow-up. Treatment efficacy is based on VIA and HPV status at 6-month follow-up.

**Results:** Seven hundred and fourteen (95%) of 750 targeted women have been randomized (234, 240, and 240 in TA, cryotherapy, and LLETZ arms, respectively). The proportion reporting moderate to severe pain/cramps during treatment was...
lower in the TA than cryotherapy (4.7% vs 12.9%) or LLETZ (4.7% vs. 6.3%) arms. Over 97% reported no pain or least amount of pain (scores 1–3) during treatment, and 99% were highly satisfied (scores 7–9) with and willing to recommend the treatments. Treatment success rates assessed by repeat VIA at 6 months were 82%, 77%, and 81% in the TA, cryotherapy, and LLETZ arms, respectively. Overall these rates were slightly lower among all the treatment arms compared to previously reported results, likely due to high HIV positivity (53%) in the study population. Treatment success rates based on clearance of type-specific HPV (16, 18, and/or 45) and repeat VIA at 6 months were 78%, 77%, and 79% in the TA, cryotherapy, and LLETZ arms, respectively. See Figure 1.

**Conclusion:** This pilot study demonstrates the new TA device is extremely safe and highly acceptable. TA efficacy will be further confirmed in a larger trial.

**Fig. 1.**

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**84 - Special Interest Session**

**Lynch syndrome screening in thai endometrial cancer patients**

T. Manchana. *Chulalongkorn University, Bangkok, Thailand*

**Objective:** Lynch syndrome (LS) increases the lifetime risk of endometrial cancer by about 40%–60%. Universal screening with microsatellite instability (MSI) and/or immunohistochemistry (IHC) for mismatch repair (MMR) proteins have been recommended. However, IHC for MMR proteins is less expensive and more available in most centers. If expression of any MMR proteins is absent, the patients should be offered genetic counseling and genetic testing. MMR IHC screening is not yet recommended in all endometrial cancer patients in Thailand. This study aims to evaluate the prevalence of MMR-deficient and germline MMR mutation in Thai endometrial cancer patients.
**Method:** IHC for MMR proteins included MLH1, MSH2, MSH6, and PMS2 and was tested in 158 endometrial cancer patients who underwent primary surgery between 2013 and 2015. The revised Bethesda criteria using age at diagnosis and personal and family history of LS-related cancers were reviewed. Patients who were MMR deficient were referred for genetic counseling and offered germline testing using gene panel next-generation sequencing.

**Results:** Fifty-seven of 158 (36.1%) patients had loss of MMR expression; 42 had losses of MLH1 and PMS2; 10 had losses of MSH2 and MSH6, and 5 had loss of MSH6 expression. Only 34 patients (21.5%) met the revised Bethesda criteria; 30 patients were diagnosed at age younger than 50 years (19%); 10 patients (6.3%) had synchronous endometrial and ovarian or colon cancers; and only 14 patients (8.9%) had family history of LS-related cancers. Forty-two of 124 patients (33.9%) who did not meet the revised Bethesda criteria were detected as MMR deficient. Twenty-five MMR-deficient patients were contacted, and 16 patients agreed to have genetic testing. In 4 of 16 patients (25%) were germline MMR mutations detected; this included 2 MSH6, 1 PMS2, and 1 MLH1 mutation. Only 2 in 4 LS patients (50%) met the revised Bethesda criteria.

**Conclusion:** MMR deficiency could be detected in 36.1% of endometrial cancer Thai patients. In at least one-third who did not meet the revised Bethesda criteria was MMR deficiency detected. Germline MMR mutation was found in 4 patients (2.5%). If the chance to detect germline MMR mutation in MMR-deficient patients was 25%, predictive prevalence of LS in endometrial Thai patients was 9%. Therefore, screening with MMR IHC should be considered in all endometrial cancer patients aiming to diagnose and prevent LS-related cancers in both patients and their relatives.

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**85 - Special Interest Session**

Risk of recurrence and HPV type-distribution among patients with vaginal intraepithelial neoplasia

S.C. Kim\(^a\) and M.K. Kim\(^b\), \(^a\)Ewha Womans University Hospital, Seoul, Korea, Republic of (South), \(^b\)Ewha Womans University, Seoul, Korea, Republic of (South)

**Objective:** We sought to evaluate the clinical outcomes of vaginal and intraepithelial neoplasia (VAIN) and to assess the risk of recurrence and its association with high-risk HPV positivity.

**Method:** A retrospective review of the clinical-pathologic data and clinical outcomes was performed on patients who were diagnosed with VAIN at a single center between January 2000 and July 2016. Demographics, HPV positivity, treatment modalities, and clinical outcomes were abstracted from medical records.

**Results:** A total of 576 patients with VAIN1-3 were included in the study analysis. The distribution of VAIN1-3 was as follows: VAIN1 31.1%, VAIN2 45.3%, and VAIN3/in situ carcinoma (CIS) 23.6%. In VAIN2+ patients, management included observation (3.5%), topical management (6.5%), laser ablation (75.3%), excision (14.1%), and radiotherapy (0.5%) with the following rates of recurrence/progression: 46.2%, 62.5%, 26.4%, 32.7%, and 0%, respectively. HPV test was performed in 523 patients (90.8%), and 444 cases were positive for high-risk HPV types (84.9%). Among high-risk HPV+ patients with available data on HPV genotypes (n = 410), other types were more common than HPV 16 and HPV 18 (72.9% vs 19.0% and 8.0%, respectively). However, as VAIN grade increased, the proportion of HPV 16+ cases increased accordingly (P < 0.001). On multivariate analysis, high-risk HPV positivity and treatment method were found to be independent risk factors for recurrence and progression (P = 0.003 and P = 0.001).

**Conclusion:** Patients with VAIN are at high risk of recurrence. Laser or excision provides a higher regression rate than topical agent or observation, and high-risk HPV positivity is a risk factor for recurrence. Whatever treatment method is used, however, the high rate of recurrence warrants long-term follow-up surveillance.

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**86 - Special Interest Session**

Impact of metformin on survival outcome in ovarian cancer: A nationwide population-based cohort study

M.H. Baek\(^a\), Y.H. Park\(^a\) and H.B. Kim\(^b\), \(^a\)Hallym University Sacred Heart Hospital, Anyang, Korea, Republic of (South), \(^b\)Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea, Republic of (South)

**Objective:** The impact of metformin on survival outcome in ovarian cancer was studied.

**Method:** Mortality HRs according to age at diagnosis, Charlestown comorbidity index (CCI), and duration of metformin use were analyzed by using Korean National Health Insurance Service data. Cox proportional hazards regression was used to analyze HRs for OS and disease-specific survival (DSS) with 95% CI adjusting for confounding factors.
Results: Among the eligible 866 patients, 101 (11.7%) were metformin users. Median follow-up period was 6.10 and 5.74 years for nonusers and users, respectively. Overall, there was no survival difference between nonusers and users. There was no survival difference between the 2 groups in subgroup analysis according to age at diagnosis and CCI. Metformin use in long-term duration (≥720 days) was associated with better OS (adjusted HR = 0.244, 95% CI 0.090–0.664, P = 0.006). In multivariate Cox proportional hazards model, longer duration of metformin use (≥720 days) was an independent favorable prognostic factor for OS (HR = 0.193, 95% CI 0.070–0.528, P = 0.001) but not for DSS (HR = 0.599, 95% CI 0.178–2.017, P = 0.408).

Conclusion: In our nationwide population-based cohort study, metformin reduced all-cause mortality in ovarian cancer when used in long-term duration. Whether metformin reduces deaths because of ovarian cancer itself needs further investigation.

Poster Session
Sunday, March 17, 2019
Basic and Translational Science

1101 - Poster Session
Biomarker panel for early detection of endometrial cancer in the prostate, lung, colorectal, and ovarian cancer screening trial

Objective: No early detection test exists for asymptomatic women at average risk for endometrial cancer. We sought to identify early detection biomarkers for endometrial cancer using prediagnostic serum.

Method: We performed a nested case-control study of postmenopausal women in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial (n = 78,216). One hundred and twelve incident endometrial cases were matched 1:1 with controls based on age, race, study site, year of blood draw, and year of randomization. Prediagnostic serum was immunodepleted of high-abundance proteins and digested with sequencing-grade porcine trypsin via pressure cycling technology. Quantitative proteomics and phosphoproteomics were performed using high-resolution liquid chromatography-tandem mass spectrometry and highly multiplexed isobaric mass-tag combined with basic reversed-phase liquid chromatography. A set of proteins able to predict cancer status was identified with an integrated score assessed by receiver operator curve analysis.

Results: Mean time from blood draw to endometrial cancer diagnosis was 3.5 years (standard deviation 1.9 years). There were 47 differentially abundant proteins between cases and matched controls (P < 0.05). Protein alterations with high predictive potential were selected by regression analysis and compiled into an aggregate score to determine the ability to predict endometrial cancer. An integrated risk score of six proteins (complement factor B, serotransferrin, catalase, proteasome subunit beta type-6, beta-2-microglobulin, and protocadherin-18) was directly related to disease incidence in cases with blood draw ≤2 years, >2 years to ≤5 years or >5 years prior to cancer diagnosis. The integrated score was able to distinguish cases from controls with an area under the curve of 0.80 (95% CI 0.72–0.88). See Figure 1.

Conclusion: An integrated score based on six proteins using prediagnostic serum from the PLCO Cancer Screening Trial distinguishes postmenopausal endometrial cancer cases from controls. Validation is needed to evaluate whether this test can improve prediction or detection of endometrial cancer among postmenopausal women.
Inhibition of dual specificity phosphatase 6 (DUSP6) sensitizes ovarian cancer cells to chemotherapeutic agents
L.B. Beffaa, N. James, M. Oliver, R. Freiman, P.A. DiSilvestro and J. Ribeiro. aWomen & Infants Hospital, Brown University, Providence, RI, USA, bWomen & Infants Hospital, Brown University, Providence, RI, USA

Objective: Dual specificity phosphatase 6 (DUSP6) is a phosphatase that negatively regulates the extracellular-signal-regulated kinase (ERK) pathway. Established ovarian cancer clinical biomarker human epididymis protein 4 (HE4) has been shown to interact with the ERK pathway. Therefore, this study was conducted to determine the relationship between DUSP6 and HE4, with the goal of better understanding DUSP6's role in epithelial ovarian cancer (EOC).

Method: Western blot and quantitative polymerase chain reaction (PCR) following siRNA knockdowns were used to evaluate the codependence of HE4 and DUSP6. MTS assay was used to determine the effect of DUSP6 inhibition in combination with chemotherapeutic agents on cell viability. Quantitative PCR was employed for the evaluation of gene expression responses to drug treatments. Expression levels of DUSP6 in EOC tissue were evaluated by immunohistochemistry. Unpaired two-tailed Student t test was employed to determine statistical significance of results.

Results: HE4 and DUSP6 levels were noted to be codependent in SKOV3 and OVCAR8 ovarian cancer cell lines. Because HE4 has been shown to promote chemoresistance in EOC, the effect of DUSP6 on chemotherapeutic response was evaluated. Cell viability significantly decreased when cells were cotreated with a DUSP6 inhibitor (BCI) and carboplatin or paclitaxel, compared to treatment with single-agent chemotherapy alone. Furthermore, DUSP6 inhibition altered expression of phosphorylated ERK (p-ERK) response genes, including early growth response protein 1 (EGR1) and c-Jun. EGR1, a strong promotor of apoptosis, was increased when ovarian cancer cells were treated with the combination of BCI and paclitaxel or carboplatin, compared to treatment with a single chemotherapeutic agent. Alternatively, the expression of c-Jun, a proto-oncogene, decreased with cotreatment of BCI and paclitaxel or carboplatin. Finally, levels of DUSP6 were noted to be significantly upregulated in serous EOC tissue compared to adjacent normal tissue.

Conclusion: DUSP6 inhibition sensitizes ovarian cancer cells to chemotherapeutic agents and alters gene expression of p-ERK response genes. The ability to detect HE4 levels in EOC patients, coupled with the established codependence of DUSP6 with HE4, indicates that DUSP6 could plausibly function as a future novel therapeutic target.

Figure 1. A serum-based, integrated risk score to predict endometrial cancer. Protein alterations with high diagnostic potential were selected by the least absolute shrinkage and selection operator (LASSO) regression analysis and assembled into an aggregate score calculated for each case to predict the relative risk of having endometrial cancer. A: Integrated risk scores are directly related to disease incidence in patients with blood draw ≤ 2 years, > 2 years to ≤ 5 years or > 5 years prior to endometrial cancer diagnosis. B: Integrated risk scores exhibit a linear relationship from time of blood draw to receiving a diagnosis of endometrial cancer.
In vivo real time observation of tumor-host interaction during ovarian cancer cytoreductive surgery using intravital microscopy


**Objective:** Intravital microscopy (IVM) is a dynamic imaging modality that allows for real-time observation of tumor vasculature and immune cell trafficking. A recent clinical trial in melanoma patients was the first application of high-magnification, real-time IVM to patients at the time of surgery. To date there are no reports of IVM in deep-seated tumors including ovarian cancer. We tested the feasibility of using IVM during ovarian cancer cytoreductive surgery in order to characterize tumor vasculature and expand the ability of IVM from subcutaneous sites to the peritoneal cavity.

**Method:** All newly diagnosed patients with suspected ovarian cancer who were undergoing primary cytoreductive surgery at our center from December 2017 to July 2018 were offered to participate in the study. On entry via laparotomy the omentum was visually evaluated for tumor. Patients underwent a 15-minute observational period using fluorescent IVM of cancer-infiltrated omentum under 100x magnification. During the observation period 2–10 mL of AK-FLUOR 25% fluorescein was administered IV to delineate the tumor vasculature and to demonstrate patency through support of blood flow.

**Results:** Baseline imaging of tumor blood vessels was successful in all six patients with fluorescein present within the vasculature. Average vessel diameter was 18.00 ± 1.39 µm. Images from the first patient were suboptimal due to tissue motion related to the patient's pulses and respirations. This obstacle was overcome in the remaining four out of five patients with use of the Thompson retractor rail clamps and two angled arms while placing the mobilized omentum over the arms for tissue stabilization. This technique was not applicable in one patient as the omentum was immobile. Following adoption of the Thompson retractor technique, four patients were successfully observed with at least 15-minute observation time and minimal movement. There were no reported patient adverse events or toxicity other than temporary fluorescein-related urine color changes. See Figure 1.

**Conclusion:** Visualization of an intraperitoneal tumor and associated vasculature using IVM is safe and feasible in patients undergoing surgery for suspected gynecologic malignancy. This new in vivo technique will allow for future studies to examine real-time characterization of tumor vessels, immune cell trafficking, anti-angiogenic therapy, and chemotherapy delivery.

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**Single cell RNA-sequencing identifies unique immune cell profiles across metastatic sites in a case of primary ovarian cancer**


University of Minnesota, Minneapolis, MN, USA, University of Minnesota Cancer Center, Minneapolis, MN, USA, University of Minnesota Medical Center, Minneapolis, MN, USA

**Objective:** Knowledge of the specific immune cell composition of a solid tumor can help predict a patient's response to immunotherapy. Little is understood about the immune cell profile of ovarian cancer (OC) or the impact of this profile on response to immunotherapy and chemoresistance. The purpose of this study was to utilize single-cell sequencing techniques to analyze the immune cell profile of tissue obtained from different metastatic sites in a single patient with high-grade OC.
Method: Seven different tumor samples from 4 metastatic sites (2 omentum, 1 liver, 2 peritoneum, 2 diaphragm) in a single patient with high-grade serous ovarian cancer were submitted for single-cell sequencing using the 10X Genomics platform and Illumina HiSeq. Clustering techniques, including graph-based clustering, principal component analysis (PCA), t-Distributed Stochastic Neighbor Embedding (tSNE), and clustering through imputation and dimensionality reduction (CIDR), were used to define groups of cells with similar gene expression patterns. An "immune signature," previously validated from bulk sequencing, was used to further define immune subsets of cells.

Results: Transcript expression was characterized for an average of 1,522 (range 1,054–2,368) cells per sample, with a mean of 176,433 (range 98,436–244,591) reads per cell in the seven sites. Based on differentially expressed gene expression, we defined cell clusters as epithelial, stromal, immune, or endothelial. We identified cellular heterogeneity across all seven tumor samples by unsupervised clustering of the scRNA-Seq matrix and by using known signature genes for various cell types. The average expression of immune cells was 41.3% (21%–57%) across sites. Among various immune cells, macrophages predominated across all samples.

Conclusion: Single-cell sequencing offers a new method of describing immune profiles within OC. In the future, immunotherapy-based trials for OC could be enhanced by using this technique to identify patients most likely to benefit from such treatment strategies.

1105 - Poster Session
Single cell exome analysis of hereditary breast and gynecologic cancer loci
S.M. Bedella, Z. Chang, Y. Zhang, L. Uppendahl, A. Grad, S. Talukdar, A. Wilhite, R. Zhang, J. Wang, S.A. Mullaney, T. Starr and B. Winterhoff. University of Minnesota, Minneapolis, MN, USA, University of Minnesota Cancer Center, Minneapolis, MN, USA, University of Minnesota Medical Center, Minneapolis, MN, USA

Objective: To assess the technical quality and potential diagnostic utility of single-cell DNA sequencing in ovarian cancer (OVCA) for detecting subclonal heterogeneity of clinically relevant mutations.

Method: Four patients were recruited as part of a prospective precision medicine program in OVCA. Twenty-four tumor cells were isolated from each tumor at the time of primary debulking using Fluidigm C1 and subsequent whole exome-sequencing. Initial analysis was restricted to 31 genes related to the pathogenesis and predisposition of OVCA (Dicer1, Mre11a, MutYH, Rad50, Smarca4, Pold1, Brca1, Brca2, Stk11, Brrip1, Msh2, Msh6, Mlh1, Pms2, EpCAM, Rad51c, Rad51d, ATM, Cdh1, Chek2, Nbn, Nf1, Palb2, Pten, Tp53, Bard1, Rb1, Csmd3, Cdk12, Fat3, and Gabra6). Variant calling was performed with FreeBayes, and variants were annotated with Annovar for review by a molecular pathologist. Results were compared to parallel germline medical Exome sequencing to discriminate somatic versus germline origin in the single-cell data.

Results: Four patients (two high-grade serous, one mucinous borderline, and one mucinous carcinoma) had 24 cells each captured. Next-generation sequencing (NGS) analysis of these 31 gene loci revealed a range from 116 to 186 potentially pathogenic somatic mutations detected per patient across all 24 cells. Coverage demonstrated heterogeneity among patients and within individual samples. There was evidence of subclonal mutations within clinically relevant genes such as Brca2, Atm, and Pold1. All variants were confirmed somatic with comparison to paired germline data. Whole exome-sequencing of bulk tumor tissue from each patient is ongoing. Comparison of single-cell and high-depth bulk sequencing will characterize the analytic performance of each.

Conclusion: Subclonal mutational heterogeneity may drive resistance to standard therapy and promote disease recurrence. The best approach to interrogate this disease characteristic is not defined. We demonstrate that potentially pathogenic mutations in these four patients show evidence for subclonal heterogeneity in single cell Exome-sequencing data. Comparisons to paired bulk sequencing data will illustrate whether there is need for further development of higher resolution techniques like single-cell DNA sequencing to accurately assess the drivers and identify possible therapeutic targets for each individual patient.

1106 - Poster Session
Ultrasonographic visualization of ovaries according to age in women of different body types
**Objective:** The ultimate limits of modern ultrasonographic instrumentation to resolve human ovaries have not been fully characterized. The objective of this study was to determine how age, menopausal status, weight, and BMI influence visualization of the ovaries when using transvaginal ultrasonography (TVUS) to detect ovarian and adnexal masses.

**Method:** A total of 29,877 women were selected who had both ovaries visualized on their first examination and were followed over 202,639 prospective TVUS examinations as part of the University of Kentucky Ovarian Cancer Screening Program. Landmarks for proving structure consisted of identifying the iliac vessels in the pelvic sidewall and the tubal vessels located posterior and parallel to the fallopian tubes. Pressure was applied to three or more regions of the abdominal surface to achieve bowel repositioning in order to assist visualizations. All images were reviewed by a physician. Multiple comparisons in one-factor ANOVA were performed, as were $\chi^2$ analyses.

**Results:** Visualization of both ovaries decreased with age with only 50% of patients aged 75–76 years having both ovaries identified (dashed line in Figure 1). A crossover point is noted for women in their mid-80s where nonvisualization of both ovaries surpassed visualization. Visualization of both ovaries was very well fitted ($R = 0.9992$) to an equation that can be used to calculate the probability of visualization over the range 25–90 years of age ($y = 102.097937 - 5.571464X + 2.739043X^2 - 0.626314X^3 + 0.048908X^4 - 0.001299X^5$). Both ovaries were visualized in ~93% of premenopausal women and ~69% of postmenopausal women. Adjustable probe frequency allowed both ovaries to be visualized in ~72% of women who weighed more than 300 lb and in ~70% of women who had a BMI over 40 with no more than 4% differences over 100–300+ lb or BMIs of 16–40+.

**Conclusion:** The ovaries can be visualized well past the menopause. Body habitus was not limiting to ovarian imaging, and TVUS should be considered capable of imaging both ovaries in one of every three women older than 80 years.

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**1107 - Poster Session**

**Dinaciclib persistently inhibits patient-derived high-grade ovarian carcinoma growth**

California Pacific Medical Center, San Francisco, CA, USA, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA

**Objective:** High-grade ovarian cancer (HG-OVCA) is currently being treated with aggressive surgery followed by platinum-taxane chemotherapy. Platinum resistance develops within six months in ~30% of patients. Our objective is to identify more effective therapies for HG-OVCA.
Method: We employed a high-throughput drug screen, precision medicine approach to identify antitumor agents efficacious in inhibiting HG-OVCA growth in culture and in vivo. Ten patient-derived cultures (PDC) and patient-derived xenograft cultures (PDX-C) were grown as three-dimensional tumorspheres and screened for drug sensitivity using a 60-drug combination panel. In vivo validation studies were performed next.

Results: Dinaciclib, a small molecule inhibitor of CDK 2/7/9/12, induced between 70% and 90% apoptosis across seven HG-OVCA samples, performing significantly better than standard chemotherapies. In vivo validation studies using both epithelial and serous-derived HG-OVCA PDX models were conducted and confirmed the therapeutic efficacy of dinaciclib at doses not associated with toxicity. Furthermore, the effect of dinaciclib resulted in persistent tumor inhibition in vivo, while carboplatin and paclitaxel combined induced only transient suppression of tumor growth. Dinaciclib induced 68% tumor reduction from vehicle control compared with 12% tumor reduction induced by chemotherapy (paclitaxel plus carboplatin). Tumor growth inhibition by dinaciclib was 56% superior compared to the standard of care. Statistical analyses showed that dinaciclib versus vehicle effect was significant ($P = 0.0130$), as well as the dinaciclib versus paclitaxel plus carboplatin effect ($P = 0.0367$, both two-tailed t test). Mechanistically, dinaciclib appears to coordinately modulate levels of the APC (anaphase promoting complex) and tumor suppressor (TP73, TP57) proteins resulting in cell cycle arrest and apoptosis. Immunohistochemical analyses of PDX tissues posttreatment displayed significant decrease in proliferation index by Ki-67 staining in dinaciclib-treated samples versus control.

Conclusion: Dinaciclib is an effective targeted therapy against patient-derived HG-OVCA tumors. Ongoing studies in our laboratory are exploring the utility of dinaciclib in combination with chemotherapy and PARP inhibitors as possible maintenance therapies for HG-OVCA, and identification of patient populations that will respond best to dinaciclib for use in future clinical trials.

1108 - Poster Session
A novel STAT3 inhibitor YHO-1701 inhibits ovarian and endometrial cancer cell growth, with augmented cytotoxicity in combination with an mTOR inhibitor
K. Hasegawa,a A. Yoshinaga,b D. Shintani,c M. Tsuganeb, S. Satoa, H. Abutanid, H. Takahashid, S. Ishiic, F. Nishisakab and K. Fujiwarad
Saitama Medical University International Medical Center, Hidaka, Japan, Yakult Central Institute, Yakult Honsha Co., Ltd., Tokyo, Japan, Yakult Honsha Co., Ltd., Tokyo, Japan, Saitama Medical University International Medical Center, Saitama, Japan

Objective: The signal transducer and activator of transcription (STAT) 3 plays a critical role in the regulation of cell growth, metastasis, and survival. STAT3 signaling is constitutively activated in various cancers including gynecological cancer. To investigate the potential cytotoxic effect of a new oral STAT3 inhibitor, YHO-1701, in ovarian and endometrial cancer, we evaluated its antitumor activity using an SKOV3 abdominal dissemination xenograft model. Efficacy of combination therapy with YHO-1701 and everolimus was analyzed in vitro based on the combination index (CI) using the median effect method. The downstream signaling pathways were investigated by Western blot.

Method: PDCs were isolated from 37 cases of surgical specimens or ascites cells from ovarian or endometrial cancer patients, and the growth inhibitory effect of YHO-1701 on cell lines or PDCs was evaluated by standard colorimetric assays. Antitumor activity of YHO-1701 was assessed using an SKOV3 abdominal dissemination xenograft model. Efficacy of combination therapy with YHO-1701 and everolimus was analyzed in vitro based on the combination index (CI) using the median effect method. The downstream signaling pathways were investigated by Western blot.

Results: We observed growth inhibitory effects of YHO-1701 in both ovarian and endometrial cancer cell lines, A2780, CaOV3, OVCAR3, SKOV3, and Ishikawa, with IC50 ranging from 0.44 to 2.21 μM. We tested the potential antitumor activity of orally administered YHO-1701 in a mouse intraperitoneal dissemination model of ovarian cancer using SKOV3. We observed decreased numbers of peritoneal metastasis in mice treated with YHO-1701 compared with those treated with vehicle control ($P < 0.05$). A total of 37 PDCs were treated with YHO-1701 and showed a remarkable growth inhibition compared with the control group ($P < 0.0007$ and $P < 0.0001$ for ovarian and endometrial cancer cells, respectively). We further investigated the potential pathways influenced by YHO-1701 and found decreased levels of p70S6K and p4EBP-1 as well as pSTAT3 and survivin. We also found an additive or synergistic effect in combination with everolimus in three of four cell lines tested.

Conclusions: Our results demonstrated efficacy of YHO-1701 for ovarian and endometrial cancer both in vitro and in vivo through STAT3 and mTOR pathways. Combination therapy of YHO-1701 and everolimus might show enhanced efficacy.
1109 - Poster Session
Blocking metastatic behavior of MUC16/CA-125-expressing cancer by targeting galectin-3
E. Smith, M. Stasenko, T.D. Rao, N.Z. Feit, E. de Stanchina, T. White, B. Weigel, I.C. Lorenz and D. Spriggs. aMemorial Sloan Kettering Cancer Center, New York, NY, USA, bWeill Cornell Medical College, New York, NY, USA, cMassachusetts General Hospital, Boston, MA, USA

Objective: Galectin-3 (gal-3) and MUC16 (CA125) interact on the cell surface to promote ovarian cancer metastatic invasion and growth. As a novel therapeutic approach for the prevention of ovarian cancer metastasis, we aimed to modulate the expression and activity of gal-3 and alter the metastatic efficiency and organotropic behavior of cells in vitro and in vivo.

Method: Gal-3/LGALS3 was silenced using short-hairpin (sh) RNAs (shLGALS3) in a MUC16-positive cancer cell line, MDA-MB-231. Invasion assays were performed with MDA-MB-231 wildtype (WT) and shLGALS3 cells in the presence or absence of a highly specific anti-gal-3 murine monoclonal antibody (MAb), 14D11.2D2. Two murine experiments were conducted: mice were inoculated with (1) either WT (n = 10) or shLGALS3 cells (n = 10) and observed for 12 weeks, and (2) WT cells and either mock-treated with phosphate-buffered saline (n = 10) or treated with anti-gal-3 MAb (n = 10) for 20 weeks and observed for a total of 36 weeks. Metastatic behavior was observed and survival data were collected for both experiments. Data were analyzed using unpaired t tests and Kaplan-Meier survival analyses with log rank tests.

Results: MDA-MB-231 shLGALS3 cells showed a significant decrease in invasion compared to WT cells (P = 0.005). In addition, significantly decreased invasion activity of WT cells was observed upon MAb exposure (P = 0.002). In the murine models, mice inoculated with shGAL3 cells had a significantly longer overall survival compared to mice inoculated with WT cells (P = 0.018). Survival difference did not reach statistical significance in mice treated with MAb compared to untreated mice (P = 0.081), although this could be due to small cohort numbers.

Conclusion: Our findings demonstrate that galectin-3 expression modification and MAb inhibition of gal-3 interferes with the metastatic activity and establishment of tumor metastases in MUC16-positive cancers. These results are the basis for further studies to assess gal-3 inhibition for the blockade of metastatic invasion and colonization in ovarian cancer.

1110 - Poster Session
The association of hematologic toxicities and outcomes in the treatment of cervical cancer with definitive chemoradiation
A.K. Yoder, C. Mach, S. Dalwadi, T.R. Hall, M.L. Anderson and M. Ludwig. aBaylor College of Medicine, Houston, TX, USA, bUniversity of Houston, Houston, TX, USA

Objective: To examine the prognostic significance of hematologic toxicities during cervical cancer treatment, and to analyze the risk factors for these toxicities.

Method: Patients treated between August 2012 and July 2015 for cervical carcinoma with definitive chemoradiation were identified. Toxicities were assessed during weeks 1–6 of concurrent external beam radiation and chemotherapy. Outcomes were analyzed using Cox survival regression analysis. The variables associated with toxicities were assessed using logistic regression.

Results: There were 121 patients eligible for analysis with FIGO stage I–III disease. Median age at diagnosis was 45 years (IQR 40–52 years) with median follow-up time of 34 months (95% CI 30.8–37.2). The majority of the patients were Hispanic (n = 83, 69%), followed by African-American (n = 30, 25%), and Caucasian (n = 8, 6%). Squamous cell carcinoma (SCC) was the most common histology (n = 101, 84%). All patients experienced some grade of hematologic toxicity. The most common toxicities greater than grade 3 were low absolute lymphocyte count (n = 115, 95%), low WBC count (n = 21, 17%), and anemia (n = 11, 9%). The most common grade 4 toxicity was lymphopenia, experienced by 36% of patients (n = 44). Grade 4 lymphopenia was associated with reduced overall survival (OS) (HR = 4.5, P= 0.005, see Figure 1), progression-free survival (PFS) (HR = 3.4, P= 0.001), and local control (LC) (HR = 4.1, P= 0.047). Anemia grade 3–4 was also associated with reduced OS (HR = 4.1, P= 0.014). Neutropenia was not associated with any change in outcomes (all P > 0.05). After controlling for race, stage, treatment factors including number of chemotherapy cycles, and comorbid conditions, grade 4 lymphopenia remained significantly associated with reduced OS and PFS (HR = 11.1, P = 0.006; HR = 2.7, P = 0.020), though not LC (HR = 1.5, P = 0.711). On univariate regression analysis, higher stage, SCC histology, and lower BMI were associated with increased chance of grade 4 lymphopenia. On multivariate analysis only stage III disease remained associated with grade 4 lymphopenia (OR = 5.8, P = 0.003).
Conclusion: Severe lymphopenia was associated with reduced OS and PFS in patients undergoing definitive chemoradiation for cervical cancer even after controlling for number of chemotherapy cycles. Continued work is needed to explore treatments that do not deplete lymphocyte count during cancer treatment.

Fig. 1. Overall Survival and Grade 4 Lymphopenia

1111 - Poster Session
Postirradiation PD-L1 expression is a predictor of an improved prognosis after carbon ion radiotherapy for uterine cervical adenocarcinoma
M. Iijima\textsuperscript{a,b}, N. Okonogi\textsuperscript{b}, K. Banno\textsuperscript{a}, K. Tsuji\textsuperscript{a}, Y. Kobayashi\textsuperscript{a}, E. Tominaga\textsuperscript{a}, S. Hasegawa\textsuperscript{b} and D. Aoki\textsuperscript{a}. \textsuperscript{a}Keio University School of Medicine, Tokyo, Japan, \textsuperscript{b}National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan

Objective: Carbon ion radiotherapy (CIRT) is expected to be an effective therapeutic option for uterine cervical adenocarcinoma. Programmed cell death-ligand 1 (PD-L1) has been shown to predict clinical outcomes for several types of cancers. The aim of this study was to examine the effect of CIRT on PD-L1 expression in uterine cervical adenocarcinoma and to identify prognostic factors for outcomes after CIRT.

Method: The subjects were 48 patients with uterine cervical adenocarcinoma who were treated with CIRT. Among them, biopsy specimens were taken from 33 patients before CIRT started (pre-CIRT) and after 12 Gy of CIRT (post-12Gy-CIRT). The remaining 15 biopsy specimens were taken only pre-CIRT. Expression of PD-L1 in tumor cells was detected by immunohistochemistry. Changes in PD-L1 expression after CIRT and correlations with clinical outcomes and clinicopathologic parameters were analyzed.

Results: Among the patients whose biopsy specimens were taken both pre-CIRT and post-12Gy-CIRT, PD-L1 expression was significantly elevated post-12Gy-CIRT, compared to pre-CIRT ($P = 0.046$). There was no significant difference of PD-L1 expression in terms of age, clinical stage, histological subclassification, maximum tumor size, or lymph node metastasis. Kaplan-Meier analysis showed that there was no significant relationship between pre-CIRT PD-L1 status and clinical outcomes such as local control (LC), progression-free survival (PFS), and overall survival (OS). On the other hand, post-12Gy-CIRT PD-L1 expression correlated with better PFS ($P = 0.008$) but not with LC and OS. See Figure 1.

Conclusion: Postirradiation PD-L1 expression is a predictor of a better prognosis after CIRT in patients with uterine cervical adenocarcinoma. Moreover, CIRT can induce PD-L1 expression in uterine cervical adenocarcinoma. This finding supports
utilization of immune checkpoint inhibitors in combination with CIRT.

Fig. 1.

1112 - Poster Session
Mutational signature analysis of primary and metastatic endometrial cancer reveals associations with molecular subtypes and shifts during tumor progression
C.W. Ashley, A.D.C. Paula, R. Kumar, D. Mandelker, X. Pei, N. Riaz, J. Reis-Filho and B. Weigelt. Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: Mutational signatures provide insights into the biological processes shaping tumor genomes and may inform patient therapy. We aimed to define the mutational signatures of primary endometrioid and serous endometrial carcinomas (ECs), stratified into molecular subtypes, and of matched primary and metastatic ECs.

Method: Whole-exome sequencing data from primary endometrioid and serous carcinomas (n = 232) from the Cancer Genome Atlas and matched primary and metastatic ECs (n = 61, 26 patients; Gibson et al. 2016) were reanalyzed. Mutational signatures were defined using deconstructSigs, and results were correlated with clinicopathologic and genomic data.

Results: ECs of POLE (ultramutated) and MSI (hypermutated) molecular subtypes displayed dominant mutational signatures associated with POLE mutations (e.g., signatures 10 and 14, 15/17 cases) and microsatellite instability (i.e., signatures 6, 15, and 26; 55/65 cases), respectively. The impact of specific POLE mutations on the mutational processes varied, with M444K or P286R mutations being strongly associated with signature 10, whereas mutations in V411L-mutated ECs were additionally associated with aging (signature 1) or MSI (signatures 6/15). Most copy-number low (endometrioid, 79/90 cases, 88%) and copy-number high (serous-like, 42/60 cases, 70%) ECs displayed a dominant aging-associated signature 1. At variance with high-grade serous carcinomas of the ovary, only a small subset of copy-number high (serous-like) ECs (15%, 9/60) had a dominant signature 3, associated with homologous recombination DNA repair deficiency (HRD). Survival analysis based on the mutational signatures mimicked those based on the molecular subtypes reported by TCGA. Finally, we observed shifts from aging- or POLE-related mutational processes to MSI mutational processes in the progression from primary to metastatic ECs in a subset of cases.

Conclusion: Mutational signatures of POLE and MSI subtype ECs correlate with their molecular subtype and alterations of DNA repair-related genes, whereas copy-number low and copy-number high ECs demonstrate primarily aging-associated mutational signatures. A small subset of copy-number high (serous-like) ECs displays genomics features of HRD. Shifts in the mutational signatures may take place in the progression of ECs.
1113 - Poster Session
Impact of SPR064, a prodrug of paclitaxel, on ovarian cancer cell proliferation and tumor growth
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, Sphaera Pharma, Singapore, Singapore, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

Objective: SPR064 (Sphaera) is a prodrug of paclitaxel that is not cremaphor-based, thereby decreasing the risk of hypersensitivity reactions. We sought to compare the antitumorigenic effects of SPR064 versus paclitaxel in ovarian cancer (OC) cell lines and a high-grade serous OC mouse model (K18-GR121; p53fl/fl; Brca1fl/fl; KpB).

Method: Human OC cell lines (OVCAR5, OVCAR433, OVCAR3, IGROV, SKOV3, ES2) were treated with paclitaxel and SPR064. Cell proliferation and apoptosis were assessed by MTT and Annexin V assays, respectively. Cell cycle progression was determined by flow cytometry. Reactive oxygen species (ROS) were measured by DCFH-DA assay. Adhesion and invasion were assessed by laminin and wound healing assays, respectively. Western immunoblotting evaluated effects of paclitaxel and SPR064 on cell cycle control, cellular stress, apoptosis, and invasion. AdCre was injected at 6 weeks of age to induce invasive OC in KpB mice. After tumor onset, mice were treated with placebo, SPR064 (6 mg/kg, IP Q3 days), or paclitaxel (6 mg/kg, IP weekly) for 4 weeks (n=8–10 mice per group).

Results: SPR064 and paclitaxel inhibited cell proliferation in a dose-dependent manner in all OC cell lines after 72 hours of treatment, with similar IC50s between both drugs (range 1–10 nM). At the same doses of treatment, both drugs caused an increase in G2 cell cycle arrest (P < 0.05) as well as decreased expression of CDK4 and CDK6. SPR064 and paclitaxel induced apoptosis and ROS production (P < 0.05) at equivalent dosing. Western immunoblotting found increased expression of the cellular stress proteins, PERK, Calnexin, and PDI, and decreased expression of the anti-apoptotic proteins, BCL-XL and MCL-1. SPR064 and paclitaxel similarly reduced cell adhesion and migration (P < 0.05) that was accompanied by decreases in Slug, Snail, and VEGF. Both SPR064 and paclitaxel reduced tumor weight in KpB mice compared to their respective controls (67% decrease for SPR064, 59% decrease for paclitaxel, P < 0.05) after 4 weeks of treatment.

Conclusion: SPR064 has antitumorigenic effects in OC that are equivalent to paclitaxel, suggesting that SPR064 may be a promising therapy for OC without the risk of the significant hypersensitivity reactions seen for paclitaxel.

1114 - Poster Session
PD-1 inhibitor treatment impacts both immune and metabolic pathways in obesity-driven endometrial cancer
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, Sphaera Pharma, Singapore, Singapore, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

Objectives We investigated the antitumorigenic potential of PD-1 inhibitor therapy in a genetically engineered mouse model of obese endometrioid endometrial cancer (EC) (LKB1fl/fl/p53fl/fl) and its impact on immune and metabolic pathways.

Method: LKB1fl/fl/p53fl/fl mice were fed a low-fat diet (LFD, 10% calories from fat, lean) versus a high-fat diet (HFD, 60% calories from fat, obese) to mimic diet-induced obesity, starting at 3 weeks of age. AdCre was injected at 6 weeks of age to induce invasive EC. Mice were treated with placebo or a mouse PD-1 inhibitor (BioXCell) (10 mg/kg, 2X/week, IP) for 4 weeks (n=8–10 mice per group). RNAseq was performed to determine differences in immune pathways between obese and lean ECs. Global, unbiased metabolomics/lipidomics were used to identify obesity-dependent effects of PD-1 inhibitor treatment in the ECs. CD4+ and CD8+ T cells in the ECs were evaluated using flow cytometry.

Results: Obesity resulted in a doubling of tumor size (P < 0.05). Expression of genes related to T-cell/B-cell receptor, NF-kappa B, and TNF pathways were upregulated in obese versus lean ECs. Lipid and energy metabolism were dramatically upregulated in ECs from obese versus lean mice. PD-1 inhibitor treatment decreased tumor weight by 73% in obese and 77% in lean mice (P < 0.05). PD-1 inhibitor therapy increased PD-1 expression on CD4+ and CD8+ T cells in both obese and lean ECs; however, the % number of CD4+ T cells increased in obese and lean ECs, but CD8+ T cells increased in only the lean ECs. Metabolomic profiling revealed differences between obese and lean mice treated with the PD-1 inhibitor (P < 0.05). PD-1 inhibitor therapy reversed the upregulation of lipid biosynthesis in the obese ECs, resulting in altered lipid degradation and beta-oxidation rates as evidenced by decreased cholesterol esters/phospholipids and increased 3-hydroxybutyrate. In contrast, glycolysis was stimulated by PD-1 inhibition in only the lean ECs. Bile acids, which modulate gut microflora and...
glycolysis/lipid metabolism, were decreased in only obese ECs with PD-1 inhibitor therapy. Eicosanoids were increased in obese ECs with PD-1 inhibition, suggesting enhanced immune response.

Conclusion: PD-1 inhibitor treatment had efficacy in an EC mouse model through modulation of both immunity and metabolism, with distinct effects depending on obesity status.

1115 - Poster Session

SPR064, a highly soluble taxane, exhibits anti-tumorigenic effects in endometrial cancer

A. Staley a, K. Tucker b, Y. Fan c, X. Zhao c, Y. Yin c, Z. Fang c, W. Sun c, S. Sen b, S. Dugar d, Y. Zhang c, C. Zhou d and V.L. Bae-Jump e, d

aUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, bSphaera Pharma, Durham, NC, USA, cSphaera Pharma, Singapore, Singapore, dUniversity of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

Objective: Paclitaxel is one of the most effective and widely used therapeutics against many cancers, including endometrial cancer (EC). Because of paclitaxel’s poor solubility, the drug is formulated in a mixture of ethanol and castor oil, Cremaphor®. Hypersensitivity reactions to Cremaphor® are encountered in 30%–45% of treated patients. SPR064 is a modified, highly soluble form of paclitaxel, which may allow for improved formulation and minimize hypersensitivity reactions. Thus, we assessed SPR064’s antitumorigenic potential in EC using cell lines and a genetically engineered mouse model (LKβ1f/flp53f/fl) of endometrioid EC.

Method: The human EC cell lines, ECC, HEC-1, Ishikawa, and RL-952, were used. Cell proliferation and apoptosis were assessed by MTT and Annexin V assays, respectively. Cell cycle progression was assessed by flow cytometry. Reactive oxygen species (ROS) were measured using a DCFH-DA assay. AdCre was injected at 6 weeks of age to induce invasive EC in LKB1f/flp53f/fl mice. Following tumor onset, mice were treated with placebo, SPR064 (6 mg/kg, every three days, intraperitoneal) or paclitaxel (6 mg/kg, weekly, intraperitoneal) for 4 weeks (n = 8–10 mice per group).

Results: SPR064 and paclitaxel potently inhibited cell proliferation in a dose-dependent manner in all four EC lines. The IC50 for SPR064 in each cell line was similar to that of paclitaxel (range 5–10 nM). At the same doses of treatment, SPR064 and paclitaxel induced annexin V expression, caused cell cycle G1 arrest, and increased ROS production in the EC cell lines (P < 0.05). Both SPR064 and paclitaxel reduced tumor weight (77% decrease for SPR064, 74% decrease for paclitaxel) in LKB1f/flp53f/fl mice compared to their respective control groups (P < 0.01).

Conclusion: SPR064 exhibited similar antitumorigenic effects to paclitaxel in EC cell lines and mouse models, suggesting that SPR064 may be a promising therapy for EC without the significant risk of hypersensitivity reactions seen for paclitaxel.

1116 - Poster Session

SPR589: A novel metabolome targeted therapy for obesity-driven endometrial cancer

K. Tucker a, A. Staley a, Y. Yin a, W. Sun a, Z. Fang b, Y. Zhang b, D. Lee b, S. Sen b, S. Dugar c, C. Zhou e and V.L. Bae-Jump e, d

aUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, bOmic Insight, LCC, Durham, NC, USA, cSphaera Pharma, Durham, NC, USA, dSphaera Pharma, Singapore, Singapore, eUniversity of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

Objective: Mitochondrial dysfunction has been implicated in the pathogenesis of endometrial cancer (EC), obesity, and diabetes. SPR589 [(−)-Epicatechin] is an oral, well-tolerated natural product and a novel inducer of mitochondrial biogenesis. SPR589 improves the levels of metabolic syndrome biomarkers (insulin, glucose, and lipids) in obesogenic animal models and patients. Thus, we sought to investigate the antitumorigenic potential of SPR589 in a genetically engineered mouse model of endometrioid EC (LKB1f/flp53f/fl).

Method: LKB1f/flp53f/fl mice were fed a control low-fat diet (LFD, 10% calories from fat, lean) versus a high-fat diet (HFD, 60% calories derived from fat, obese) to mimic diet-induced obesity, starting at 3 weeks of age. AdCre was injected at 6 weeks of age to induce invasive EC. Following tumor onset, mice were treated with placebo or SPR589 (3 mg/kg, oral) for 4 weeks (n = 10–15 mice per group). Global, unbiased metabolomics and lipidomics were used to identify the obesity-dependent effects of SPR589 in the endometrial tumors.

Results: HFD-fed mice (obese) had tumors double in size of those of LFD-fed mice (lean) (35.58 vs 24.49, P < 0.01). SPR589 decreased tumor weight/size by 72% in the obese mice and 47% in the lean mice (P < 0.05). Metabolomic profiling revealed
significant differences between obese and lean mice treated with SPR589 or placebo \((P < 0.05)\). Lipid and protein biosynthesis was dramatically upregulated in ECs from obese control compared to lean control mice. Tricarboxylic acid cycle intermediates were increased in both lean and obese tumors with SPR589, indicating induction of mitochondrial biogenesis. SPR589 reversed the obesity-driven upregulation of lipid biosynthesis in the endometrial tumors, resulting in beta-oxidation and lipid degradation as evidenced by decreased cholesterol esters and diacylglycerols/acyl-carnitines and increased 3-hydroxybutyrate in obese versus lean mice. Bile acids, which modulate gut microflora activity and glycolysis/lipid metabolism, were decreased only in obese ECs with SPR589.

**Conclusion:** SPR58 inhibited tumor growth in an endometrioid EC mouse model via induction of mitochondrial biogenesis, and its anticancer effects aligned with obesity status. Thus, SPR589 may have promise as a metabolically targeted agent in obesity-driven EC.

### 1117 - Poster Session

**ONC201 has anti-tumorigenic effects in obesity-driven endometrial cancer**

K. Tucker\(^a\), A. Staley\(^a\), S.R. Pierce\(^a\), Y. Fan\(^a\), Y. Yin\(^a\), W. Sun\(^a\), X. Zhao\(^a\), Y. Zhang\(^a\), D. Lee\(^b\), V. Prabhu\(^c\), C. Zhou\(^d\) and V.L. Bae-Jump\(^d\).

\(^a\)University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, \(^b\)Omic Insight, LLC, Durham, NC, USA, \(^c\)Oncceutics, Inc., Philadelphia, PA, USA, \(^d\)University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

**Objective:** ONC201 (Oncoceutics), a dopamine receptor D2 (DRD2) antagonist, is actively being explored in clinical trials for endometrial cancer (EC). DRD2 is a G protein-coupled receptor that activates the trimeric G-protein complex Ras, modulating downstream metabolic pathways such as Ras- and Akt-signaling, which are highly dysregulated in obesity-driven EC. Thus, we sought to investigate the antitumorigenic potential of ONC201 in a genetically engineered mouse model of endometrioid EC (LKB1\(^{f/f}\)/p53\(^{f/f}\)).

**Method:** LKB1\(^{f/f}\)/p53\(^{f/f}\) mice were fed a control low-fat diet (LFD, 10% calories from fat, lean) versus a high-fat diet (HFD, 60% calories derived from fat, obese) to mimic diet-induced obesity, starting at 3 weeks of age. AdCre was injected at 6 weeks of age to induce invasive EC. Following tumor onset, mice were treated with placebo or ONC201 (130 mg/kg, Qweek, oral) for 4 weeks \((n = 8-10\) mice per group). Global, unbiased metabolomics and lipidomics were used to identify the obesity-dependent effects of ONC201 in the endometrial tumors.

**Results:** HFD-fed mice (obese) had tumors double in size as those of LFD-fed mice (lean) \((P < 0.05)\). ONC201 decreased tumor weight/size by 79% in the obese mice and 59% in the lean mice \((P < 0.05)\). Metabolic profiling revealed significant differences between obese and lean mice treated with ONC201 or placebo \((P < 0.05)\). Lipid and protein biosynthesis were dramatically upregulated in ECs from obese control compared to lean control mice. Treatment with ONC201 in the obese ECs resulted in a switch from obesity-driven upregulation of lipid biosynthesis to lipid degradation and oxidation, as evidenced by decreased cholesterol esters and diacylglycerols/triacylglycerols and increased lysolipids. In contrast, ONC201 reduced glycolysis in the lean but not in the obese ECs. ONC201 decreased availability of amino acids for protein biosynthesis in both obese and lean ECs. Eicosanoids were increased in obese but not lean ECs with ONC201, suggesting enhanced immune response in the setting of obesity.

**Conclusion:** ONC201 inhibited tumor growth in an endometrioid EC mouse model and had increased efficacy in obese versus lean endometrial tumors. Given this, ONC201 may have promise as an antitumorigenic agent in obesity-driven EC via downstream metabolic pathways.

### 1118 - Poster Session

**Mutation profiles of paired ovarian cancers across time**

J. Fehninger\(^a\), A.A. Berger\(^b\), L. Gay\(^c\), J.A. Elvin\(^a\), D.A. Levine\(^a\) and D. Zajchowski\(^d\).

\(^a\)NYU Langone Health, New York, NY, USA, \(^b\)New York University School of Medicine, New York, NY, USA, \(^c\)Foundation Medicine, Inc., Cambridge, MA, USA, \(^d\)Clearity Foundation, San Diego, CA, USA

**Objective:** We analyzed comprehensive tumor sequencing results from paired ovarian cancer tumor samples to identify changes in mutational events over time.

**Method:** DNA from two or more FFPE tumor samples collected serially as part of clinical care from 50 ovarian cancer patients in the Clearity Foundation Data Repository was analyzed for genomic mutations (GM), copy number alterations (CNA),
microsatellite instability (MSI), tumor mutation burden (TMB), and loss of heterozygosity (LOH) by hybrid-capture, next-generation sequencing of up to 315 genes (Foundation Medicine, Cambridge, MA). Genomic profiles were compared between samples from the same patient excluding subclonal GM and equivocal CNA. Six pairs were excluded because of poor quality metrics; an additional nine had poor quality CNA data.

**Results:** For the 44 paired samples analyzed, median age at diagnosis was 59 (range 35–77) years. The majority of patients had advanced-stage disease (34, 77%) with serous histology (31, 30%). Twenty-two pairs consisted of a primary and recurrent sample (PR), and 22 pairs were from two recurrent tumors (RR). Patients received a median of 3 treatment regimens (range 1–13) between paired samples. There was a median of 2 GM (range 0–5) and 1 CNA (range 0–6) in each sample. No samples demonstrated MSI. TMB was consistent between samples in all but one case; the majority (33, 75%) of patients had low TMB in both samples. Among 32 patients with paired LOH data, only 2 (6%) demonstrated LOH changes between samples. The majority of GM and CNA were consistent across paired samples; 12 (27%) patients had discordant GM and 16 (36%) had discordant CNA. There were no changes in therapeutically relevant GM between paired samples. Twelve (27%) patients had changes in GM or CNA that could have affected clinical trial eligibility. There was no relationship between clinical or treatment variables and discordant GM or CNA.

**Conclusion:** Paired ovarian cancer samples demonstrate stability in GM and CNA across time. Repeat tumor testing may be useful in the determination of eligibility for molecularly targeted clinical trials.

**1119 - Poster Session**
**Mechanisms of response to anti-angiogenesis therapy in CTNNB1-mutated endometrial cancers**
A.A. Berger, P. Jelinic and D.A. Levine. New York University School of Medicine, New York, NY, USA, NYU Langone Health, New York, NY, USA

**Objective:** To test whether CTNNB1 exon 3 mutations drive VEGFA expression and are associated with therapeutic response to antiangiogenesis therapy in endometrial cancer (EC). The prognosis of advanced EC is poor, and limited therapies are available. β-catenin is thought to increase VEGFA expression and tumor vascularity. To date, antiangiogenesis trials in EC have had limited success. Results from GOG-86P suggested an improved outcome for patients with CTNNB1 mutations treated with bevacizumab (Bev).

**Method:** We measured VEGFA RNA and protein levels in CTNNB1-mutated and wildtype EC and colorectal (CRC) cell lines, using RT-PCR, Western blots, and ELISA. We also transiently and stably over-expressed wildtype and mutant CTNNB1 in EC and CRC cell lines, respectively. shRNA transduction was used to create stable CTNNB1 knockdown in these cell lines. Publicly available data from the endometrial Cancer Genome Atlas (TCGA) project were used for external validation.

**Results:** CTNNB1-mutated cell lines showed higher expression of β-catenin target genes, including CCND1 and MMP7, and were also associated with higher VEGFA expression compared to CTNNB1 wildtype cell lines. Transient CTNNB1 overexpression in 3 EC and 1 CRC cell lines led to expected increases in β-catenin protein levels and increased VEGFA gene expression. Stable over-expression of mutated CTNNB1 in three EC cell lines resulted in higher levels of intracellular VEGFA protein measured by Western blotting and higher levels of secreted VEGFA protein measured by ELISA. Knockdown of mutated CTNNB1 in one CRC cell line showed decreased cellular and secreted VEGFA protein expression. An analysis of published TCGA microsatellite-stable, TP53-wildtype, endometrioid EC showed a 1.4-fold increase in VEGFA gene expression in tumors with CTNNB1 mutations compared to those without (P = 0.01).

**Conclusion:** We have shown in vitro and in silico that CTNNB1 exon 3 mutations are consistently associated with increased VEGFA expression. Ongoing experiments will study the mechanism of VEGFA activation and response to treatment in vitro and in vivo. These findings are being translated into biomarker-stratified clinical trials and individualized treatment for women with advanced EC.

**1120 - Poster Session**
**Differential cell surface protein expression in response to PARP inhibition in BRCA1 mutant isogenic ovarian and breast cancer cells using a novel proteomic technique**
A. Freeman, S. Bakker, A. Weeks, M.E. Diolaiti, D. Quigley, J.S. Chapman, L.M. Chen and A. Ashworth. UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA, University of California, San Francisco, San Francisco, CA, USA
**Objective:** Poly(ADP-ribose) polymerase inhibitors (PARPi) have shown tremendous promise as chemotherapeutic agents targeting tumors with defective homologous recombination repair. Recent data suggest that PARPi may modulate immune response independent of BRCA status. However, little is understood about cellular changes induced by PARPi. We sought to evaluate changes in gene expression by BRCA1 mutant and wildtype (WT) ovarian and breast cancer cells following PARPi therapy.

**Method:** We used stable isotope labeling by amino acids in cell culture (SILAC) with quantitative mass spectrometry to quantify protein levels in isogenic BRCA1 cell pairs for ovarian (UWB1.289) and breast (SUM149) cancer. Cells were grown in both high (1 μM) and low (50 nM) doses of olaparib. Cell surface protein enrichment was performed; median log2 ratios for each protein were calculated; and volcano plots were generated using a significance of log2 ratio >1 or <-1 and P < 0.01 (Mann-Whitney test). RNA sequencing was performed under identical experimental conditions to determine whether altered surface protein levels correlated with differential transcription.

**Results:** We find a total of 54 surface proteins with significantly different expression in BRCA1 mutant versus WT ovarian cancer cells. After exposure to PARPi, a total of 46 and 32 proteins showed significantly altered expression in UWB1.289 and SUM149 isogenic pairs, respectively. Of note, multiple components of the integrin signaling pathway are upregulated among BRCA1 mutant cells treated with olaparib, and urokinase-type plasminogen activator receptor (uPAR or PLAUR), a regulator of cell adhesion, migration, and signaling is upregulated in the BRCA1 mutant UWB1.289 cells relative to the BRCA-WT line.

**Conclusion:** Using a novel quantitative proteomic technique, we demonstrate that PARPi treatment alters cell surface protein expression. Our proteomic data suggest that cells may undergo a morphological change in response to PARP inhibition, potentially altering the integrin signaling pathway, interactions with the extracellular matrix, cell adhesion, signaling, and/or tumor invasion.

**1121 - Poster Session**  
**Subsequent therapies and survival after immunotherapy in recurrent ovarian cancer**  
Y.L. Liu, V.N. Emengoa, C.F. Friedman, J. Konner, R.E. O'Cearbhailla, C.A. Aghajaniana and D. Zamarinb, aMemorial Sloan Kettering Cancer Center, New York, NY, USA, bWeill Cornell Medical College, New York, NY, USA

**Objective:** Immune checkpoint inhibitors (ICIs) have shown modest activity in ovarian cancer (OC), yet little is known about their effect on subsequent treatment. Preclinical studies suggest activation of T cells with ICIs may enhance response to chemotherapy. We sought to evaluate the impact of ICIs on subsequent therapies and survival in women with recurrent OC.

**Method:** Retrospective review identified 79 women with recurrent OC who received ICI and ≥1 subsequent treatment at a single institution between January 2013 and July 2018. Patient characteristics were abstracted and verified by two independent reviewers. Duration of treatment after ICI was defined as time from initiation of current treatment to time of event (initiation of new treatment, radiographic disease progression in those without subsequent treatment, or death in those without subsequent treatment or progression), or last follow-up for those without events. Kaplan-Meier survival analysis was used to estimate treatment durations and overall survival (OS) defined from end of ICI treatment course to death or last follow-up.

**Results:** Mean age was 60 years (SD 9.1), and 67 (85%) women had platinum-resistant disease at the time of ICI. Median time from diagnosis to ICI was 43 months (range 10–411 months), with a median of 4 prior treatment lines (range 1–12). All but two women received ICI on protocol, and most received a PD1/PD-L1 inhibitor (42%) or combination PD1/PD-L1 and CTLA-4 inhibitor (34%). Median time on ICI was 2.8 months (range 0.6–14.0 months). Median number of treatment lines after ICI was 2 (range 1–8). Median duration of treatment for the first line after ICI was 4.9 months (95% CI 3.3–6.4) and declined with each subsequent line (line 2, n = 58, 4.0 months, 95% CI 3.0–5.4; line 3, n = 35, 3.0 months, 95% CI 2.0–4.7; line 4, n = 20, 2.7 months, 95% CI 1.9–5.4). The most common therapies after ICI were taxanes (21%), platinum-based regimens (20%), and pegylated liposomal doxorubicin (11%). Bevacizumab was used in 30% of regimens. Median follow-up was 15.6 months, and there were 45 observed deaths. Median OS after ICI was 18.7 months (95% CI 13.2–23.5). See Figure 1.

**Conclusion:** In this heavily pretreated population of recurrent OC patients, therapies after ICI resulted in promising clinical benefit, with mOS of 18.7 months, suggesting ICI may have a positive impact on response to subsequent chemotherapy. These findings support the rationale for trials evaluating ICI in combination with specific cytotoxic agents.
Fig. 1. Overall Survival after ICI

1122 - Poster Session
Cytomegalovirus and systemic inflammation is associated with worse outcomes in serous ovarian cancer patients
L.D. Uppendahl\textsuperscript{a}, C.M. Dahl\textsuperscript{b}, A. Messelt\textsuperscript{c}, M. Felices\textsuperscript{d}, H.H. Nelson\textsuperscript{e}, K.L.M. Boylan\textsuperscript{f}, A.P.N. Skubitz\textsuperscript{g}, K. Geschwind\textsuperscript{h}, R.I. Vogel\textsuperscript{a} and M.A. Geller\textsuperscript{i}. \textsuperscript{a}University of Minnesota, Minneapolis, MN, USA, \textsuperscript{b}Northwestern University Feinberg School of Medicine, Chicago, IL, USA, \textsuperscript{c}University of Minnesota Cancer Center, Minneapolis, MN, USA

Objective: Cytomegalovirus (CMV) is a common infection that establishes latency in healthy people. The role of CMV is not well established in human cancer, but it does strongly influence the immune repertoire and can emerge from latency during times of immunosuppression. CMV reactivation is associated with increased inflammation, which may have an adverse impact on patient outcomes. We aimed to investigate the association of CMV status and systemic inflammation with outcomes in women with high-grade serous ovarian cancer.

Method: A registry of biobanked specimens at our institution was queried for diagnosis of serous ovarian cancers from 2006 to 2009. A total of 149 patients were identified, with 106 included in the final analysis. Medical records were reviewed and demographic, surgical, and pathological variables collected. We assessed CMV status and systemic inflammation by measuring CMV immunoglobulin G and C-reactive protein (CRP), respectively, in banked serum specimens from time of debulking surgery. After stratification into four groups by CMV and CRP status, recurrence-free survival (RFS) and overall survival (OS) were calculated. Comparisons were conducted using χ\textsuperscript{2} and Fisher exact tests for categorical variables and Student t tests and Wilcoxon rank sum tests for continuous values. OS and RFS were summarized using Kaplan-Meier methods. Comparisons of groups used log rank tests and Cox proportional hazards adjusted for age.

Results: Of the 106 women eligible for inclusion, 40 (37.7%) were CMV+/CRP+, 24 (22.6%) were CMV+/CRP−, 19 (17.9%) were CMV−/CRP+, and 23 (21.7%) were CMV−/CRP−. There were no significant differences in demographic, surgical, or pathologic factors between groups. The median RFS was 20.6 months (95% CI 17.8–27.1), and median OS was 54.5 months (95% CI 46.1–61.3) for the entire cohort. Median RFS and OS for women who were CMV+/CRP+ at time of debulking surgery was 16.9 months (95% CI 9.0–21.1) and 31.7 months (95% CI 25.0–48.7), respectively, and had significantly worse RFS (aHR = 1.85, 95% CI 1.05–3.24, \(P = 0.03\)) and OS (aHR = 2.12, 95% CI 1.17–3.82, \(P = 0.01\)) compared to women who were CMV−/CRP−. The CMV+/CRP− group displayed the longest OS (89.3 months). See Figure 1.

Conclusion: Patients who tested positive for CMV and CRP at debulking surgery had worse RFS and OS compared to women who tested negative. Interestingly, the CMV+/CRP− group had the longest OS, indicating that CMV status alone, in the absence
of inflammation, might have protective properties.

Fig. 1.

1123 - Poster Session
Complex immune checkpoint signatures in a subset of endometrial cancers
A. Ramosa, S.A.M. Fortina, D. Jenkinsb, W.B. Growdenc and D.R. Borgera. aMassachusetts General Hospital, Boston, MA, USA, bTESARO Inc, Waltham, MA, USA, cGillette Center for Gynecologic Oncology/Massachusetts General Hospital, Boston, MA, USA

Objective: Immune checkpoint inhibition has revolutionized cancer therapy. Endometrial cancers can harbor microsatellite instability (MSI) that is associated with response to PD-1 monotherapy, which may be improved with combination checkpoint blockade. This study is an exploratory analysis investigating the presence of immune checkpoints in endometrial cancer that could allow for development of combination immune therapies.

Method: Diagnostic endometrial tumor samples representing 6 histologic groups were chosen from the Massachusetts General Hospital Tumor Registry, including MSI high-grade endometrioid (MSIH, n = 21), microsatellite stable high-grade endometrioid (MSSH, n = 21), MSI low-grade endometrioid (MSIL, n = 20), MSS low-grade endometrioid (MSSL, n = 19), carcinosarcoma (MMMT, n = 11), and uterine serous carcinoma (USC, n = 11). RNA expression signatures from 214 gene targets including immune checkpoints CTLA4, PDCD1 (PD-1), CD274 (PDL1), LAG3, and HAVCR2 (TIM-3) and immune cell markers were evaluated from tissue lysates using a flow cytometry-based platform. RNA analysis results were verified with immunohistochemistry staining.

Results: The cohort consisted of 101 patient samples. Overall, 51 patients had stage 1A disease; 18, stage 1B; 11, stage II; 12, stage III; and 10, stage IV disease. Recurrences were seen in 12 patients. Recurrent disease was not associated with significant differences in immune checkpoint expression. The MSIH group had significantly elevated levels of CD8+ cell infiltration compared to the MSSH and MSSL groups (P = 0.01 and P = 0.002). Compared to the MSSH group, MSIH tumors had significantly higher levels of the CTLA-4 and PD-1 immune checkpoints (P = 0.04 and P = 0.008). Compared to MSSL patients, MSIH patients had elevated levels of CTLA-4 (P = 0.004), PD-1 (P = 0.02), LAG-3 (P = 0.002), PD-L1 (P = 0.04), and PD-L2 (P =
Regression analysis revealed dependent co-expression of multiple immune checkpoints in a subset of MSIH patients, suggesting the possibility of simultaneous immune checkpoint upregulation of CTLA-4, PD-1, LAG-3, TIM-3, PD-L1, and PD-L2 in this group ($P < 0.001$).

**Conclusion:** MSI, high-grade endometrioid tumors co-express multiple immune checkpoints, specifically CTLA-4 and PD-1, suggesting that multitarget immunotherapy may be a consideration in endometrial carcinomas.

**1124 - Poster Session**

**Circulating mirnas in a low-volume disease murine model of BRCA mutated high-grade serous ovarian cancer**

A.A. Gockley, S. Fiascone, K. Hasselblatt, W. Fendler, R.S. Berkowitz, and K.M. Elias. *Harvard Medical School, Boston, MA, USA, Brigham and Women’s Hospital, Boston, MA, USA, Dana-Farber Cancer Institute, Boston, MA, USA, Medical University of Lodz, Poland, Lodz, Poland*

**Objective:** The primary objective of this study was to validate a serum microRNA (miRNA) signature and the kinetics of miRNA expression in a murine xenograft model of human BRCA-mutated high-grade serous ovarian cancer (HGSOC). The secondary objective was to relate miRNA expression to volume of disease.

**Method:** Thirty NSG mice were injected with 500,000 cells of one of three luciferized BRCA-mutated HGSOC cell lines (COV362, Kuramochi, or OVSAHO). Ten control mice were injected with PBS. All mice underwent a submandibular blood collection prior to injection. After a week, mice underwent a second bleed and bioluminescent imaging to verify tumor engraftment. Mice underwent a final bleed and imaging at 1 month. Tumors were harvested for live imaging and histologic assessment. Within the sera, 23 miRNAs were measured in each sample in duplicate, selected from a published serum signature for human ovarian cancer using the FirePlex miRNA Assay (Abcam, Cambridge, MA). Samples were randomized 2:1 to training and testing sets, and then a neural network was created and employed to differentiate samples from tumor-bearing or naive mice.

**Results:** Tumors were identified through microdissection and verified by histologic assessment including both conventional stains and immunohistochemical staining for PAX8. Chemiluminescent live tissue imaging identified tumors <1 mm. The neural network analysis was a more sensitive predictor of tumor presence than bioluminescent imaging alone. The algorithm identified the presence of cancer with an area under the curve of 0.94 with 80% sensitivity and 90% specificity (**Figure 1**).

**Conclusion:** Human serum signatures of ovarian cancer are recapitulated in murine xenografts, suggesting that these are feasible models for study of miRNA kinetics of BRCA-mutated HGSOC. miRNA serum signatures are sensitive for low-volume disease, which may be a useful adjunct to CA-125 in patients with disease below the size threshold for imaging.

**Fig. 1.** Neural network based on 14 miRNAs
**Objective:** To determine the clinical significance of PD-L1 expression in tumor and PD-1 expression in tumor-infiltrating immune cells (TIC) in squamous cell carcinoma of the cervix (SCC).

**Method:** A total of 198 patients with SCC were identified, and 60 had evaluable tumor specimens and clinical data. Immunohistochemistry on PD-L1 and PD-1 expression using tissue microarrays was performed. PD-L1 expression was classified as negative (<1%), low (1%–50%), and high (>50%). PD-1 expression of TIC was analyzed as low or high based on the median number of TIC per mm². Correlation between PD-L1 and PD-1 expression and clinical parameters was analyzed using χ² or Fisher exact test. Cumulative 5-year survival was calculated by the Kaplan-Meier method and analyzed by the log rank test.

**Results:** Of the 60 patients, 90% were black, 55% between ages 30–55 years, and 40% older than 55 years. Thirty-three patients had poorly, 20 moderately, and 7 well-differentiated tumors. At 5-year follow-up, 14 patients died of disease, 40 were alive, and 6 lost to follow-up; 12 of the 60 patients recurred. The percentage of tumors with positive staining for PD-L1 was 93.3%, with 56.7% showing high expression. Patients aged 30–55 years showed a higher rate of PD-L1 staining and high expression ($P = 0.047$). These patients also had higher PD-1 expression on TIC ($P = 0.013$). Mean disease free survival (DFS) was 43.7, 36.5, and 6.3 months for high, low, and negative PD-L1 expression, respectively ($P = 0.002$). In patients with stage I–II disease, mean DFS was 52.2, 42.6, and 7.6 months for high, low, and negative PD-L1 expression, respectively ($P = 0.001$). In patients with stage III–IV disease, mean DFS was 26.1, 10.7, and 3.6 months for high, low, and negative PD-L1 expression, respectively ($P = 0.37$). OS analysis also showed similar correlations. Early-stage tumors had significantly higher PD-1 expression on TIC ($P = 0.009$), but there was no correlation between survival and PD-1 expression on TIC. See Figure 1.

**Conclusion:** Contrary to previous studies, our results showed a remarkably high rate of PD-L1 expression in SCC. High PD-L1 expression was associated with longer DFS and OS, especially in early-stage tumors. PD-1 expression on TIC was higher in patients with early-stage tumors, but there was no correlation between PD-1 expression and cervical cancer survivals.

![Figure 1](image.png)

**Fig. 1.** Five-year disease-free survival of patients with cervical squamous cell carcinoma based on the PD-L1 expression on tumor cells.
1126 - Poster Session
Evaluation of cancer stem cell drug response assay in the treatment of recurrent ovarian cancer patients
N. Bou Zgheiba, C.M. Howard, A. Huck, M. Parsons, J. Vallur and P.P. Claudio.
*Marshall University School of Medicine, Huntington, WV, USA, University of Mississippi Medical Center, Jackson, MS, USA, Marshall University, Huntington, WV, USA

Objective: Recurrent epithelial ovarian cancer (EOC) is associated with significant mortality and a median survival rate of only 12–18 months. Disease recurrence is common in these patients, and most of them eventually develop platinum-resistant or refractory disease. Unfortunately, over the past 20 years the prognosis of EOC has not improved. This is due in large part to the presence of chemoresistant cancer stem cells (CSCs) that contribute to tumor propagation, maintenance, and treatment resistance. We are using ChemoID, a CLIA-certified and CAP-accredited drug response assay to identify the most effective chemotherapy treatment against CSCs and bulk of tumor cells from a panel of chemotherapies, offering great promise for individualized cancer management.

Method: Fresh tissue samples (surgical biopsies, ascites, and pleural fluid) were collected for drug sensitivity testing from 45 patients affected by poor prognosis (third to fifth relapse) recurrent ovarian cancer. Test results from ChemoID assay to measure the sensitivity and resistance of CSCs and bulk of tumor cells challenged with 15 chemotherapy single agents or their combinations were correlated to the clinical response of the treated patients, independently of other biomarkers. Patients were all treated with FDA-approved chemotherapies with or without debulking surgery, depending on the status of the disease. CT and PET scans were used to prospectively monitor patients for tumor response, time to recurrence, PFS, and OS.

Results: We found that recurrent ovarian cancer patients (third to fifth relapse) treated with ChemoID-guided chemotherapy (>50% cell kill for CSCs and >60% cell kill for bulk of tumor) had a median PFS of 9.5 months for third relapse, 7 months for fourth relapse, and 6.5 months for fifth relapse, compared to historical data showing PFS of 5.6 months for third relapse, 4.4 months for fourth relapse, and 4.1 months for fifth relapse, respectively.

Conclusion: The data suggest that the ChemoID CSCs drug response assay has the potential to help guide individualized chemotherapy choices to improve ovarian cancer patient outcomes.

1127 - Poster Session
Molecular profiling of endometrioid ovarian carcinomas
*Memorial Sloan Kettering Cancer Center, New York, NY, USA, +British Columbia Cancer Agency, Vancouver, BC, Canada, University of British Columbia, Vancouver, BC, Canada

Objective: Endometrioid ovarian carcinomas (EOCs) account for 5%–10% of all ovarian cancers and commonly co-occur with synchronous endometrial cancer. We sought to examine the molecular characteristics of pure EOCs in patients without a concomitant endometrioid endometrial cancer (EEC).

Method: Following gynecologic pathology and chart review, DNA samples obtained from EOCs and matched blood were subjected to massively parallel sequencing targeting 341–468 cancer-related genes \((n = 8)\) or to whole-genome sequencing \((n = 28)\). Mutational frequencies of EOCs were compared to those of high-grade serous ovarian cancers \((\text{HGSOCs}, n = 224)\) and endometrioid endometrial cancers \((\text{EECs}, n = 186)\) from The Cancer Genome Atlas (TCGA), as well as synchronous EOCs \((n = 23)\).

Results: EOCs were heterogeneous at the genetic level, frequently harboring mutations affecting \(\text{KRAS}(39\%), \text{PIK3CA}(32\%), \text{CTNNB1}(29\%), \text{PTEN}(25\%), \) and \(\text{TP53}(21\%)\) but few copy number alterations. At the mutational level, EOCs were distinct from HGSOCs, less frequently harboring TP53 mutations but more frequently displaying KRAS, PIK3CA, PIK3R1, PTEN, and CTNNB1 mutations. Compared to EECs, EOCs showed lower PTEN, ARID1A, CTCF, and PIK3R1 but higher KMTD2 mutation frequencies. Similar results were obtained when comparing pure EOCs to synchronous EOCs, which are clonally related to their respective EECs, and pure EOCs less frequently harbored ARID1A, CTCF, PTEN, and PIK3R1 mutations than EOCs with synchronous EECs. Akin to EECs, EOCs could be stratified into the four molecular subtypes: POLE (ultramutated) \((1/36, 3\%)\), MSI (hypermutated) \((7/36, 19\%)\), copy-number-high (serous-like) \((6/36, 17\%)\) and copy-number-low (endometrioid) \((22/36, 61\%)\) cancer, however, at frequencies distinct from those found in EECs.
**Conclusion:** EOCs are genetically distinct from HGSOCs. Despite the similarities in the repertoire of somatic mutations between pure EOCs, synchronous EOCs, synchronous EECs, and pure EECs, the frequencies of mutations affecting known driver genes and of the molecular subtypes differ. Further studies are required to define the clinical impact of the EEC molecular subtypes on the outcomes and therapeutic responses of EOC patients.

**Objective:** Calcium Calmodulin Kinase Kinase 2 (CaMKK2) is selectively expressed in cancer cells of solid malignancies and is known to be involved in both cell cycle arrest and a regulatory feedback loop involving the retinoblastoma (Rb) tumor suppressor. Here, we examined CaMKK2 expression, Rb protein expression, and clinical response in high-grade serous ovarian cancer (HGSOC) patients. We investigated the role of pharmacologic inhibitors of CaMKK2 in vitro.

**Method:** Immunohistochemical (IHC) staining for CaMKK2 and Rb protein expression was performed on a tissue array of 55 HGSOC patients, and a 4-point scale was used to evaluate staining intensity for tumor samples (0 = negative, 1 = weak, 2 = moderate, and 3 = strong). Data were analyzed using log rank, Kaplan-Meier survival analysis, or Fisher exact tests. In vitro, proliferation, and migration assays were used to evaluate high- and low-grade serous ovarian cancer cell lines after treatment with CaMKK2 inhibitors (STO-609 and GSK190132) and siRNA.

**Results:** High CaMKK2 expression was significantly associated with worse PFS (Figure 1A) in patients with HGSOC (14.7 versus 17.5 months, \( P < 0.045 \)). STO-609 decreased proliferation by up to 70% in low-grade serous ovarian cancer (LGSOC) cell lines. CaMKK2 knockdown and pharmacologic inhibition significantly increased migration in HGSOC cell lines, while decreasing migration in LGSOC cell lines. Cell lines with elevated Rb exhibited a less migratory phenotype. High Rb expression was significantly associated with worse PFS (11.5 versus 33.2 months, \( P < 0.01 \)) and overall survival (35.3 vs 90.4 months, \( P < 0.008 \)) in HGSOC patients. Loss of Rb expression was significantly associated with platinum-sensitive disease (\( P < 0.005 \)), whereas CaMKK2 expression was not. Patients with high co-expression of CaMKK2 and Rb had significantly worse PFS (\( P < 0.025 \)) (Figure 1B) and worse OS (\( P < 0.036 \)).

**Conclusion:** High CaMKK2 and Rb expression were associated with worse outcomes in HGSOC patients and represent potential biomarkers in future clinical trials. CaMKK2 could represent a therapeutic target in high- and low-grade serous ovarian cancers. Further studies are warranted to determine the mechanism of CaMKK2’s role in ovarian cancer biology.
**Objective:** Tumor-associated macrophages (TAMs) are associated with poor outcomes in ovarian cancer because of their immunosuppressive, protumor, and proangiogenic factors. This subset of macrophages is thought to express folate receptor beta (FRβ); therefore, we analyzed patient ascites samples for expression of FRβ and the ability of an anti-FRβ antibody (m909) to mediate antibody-dependent cellular cytotoxicity (ADCC).

**Method:** Ascites samples from ovarian cancer patients were provided by the University of Pennsylvania Tumor Tissue and Biospecimen Bank. For FRβ expression studies, samples were stained with anti-CD14, anti-CD11b, and anti-FRβ (m909) antibodies and analyzed using flow cytometry. For ADCC assays, samples were first sorted using CD11b magnetic beads. The CD11b positive population was then cultured overnight with healthy donor NK cells from the University of Pennsylvania Human Immunology Core at an E:T ratio of 10:1 with different concentrations of m909. Cytotoxicity was determined by counting the remaining live cells using CountBright absolute counting beads by flow cytometry. Statistical analysis (t test, ANOVA) was performed using Prism.

**Results:** Fifteen individual ovarian ascites samples were analyzed for FRβ expression. The average percentage of total ascites cells that expressed FRβ was 20.8% (range 3.7–45.1). When the samples were gated on TAMs (CD14+ and CD11b+), the percentage of FRβ+ cells was 61.6% (range 19.1–84.9) showing that most TAMs express FRβ. ADCC assays were performed using two patient samples (1572 and 1585). After CD11b bead sorting to isolate TAMs, sample 1572 and 1585 were 85.8% and 84.8% positive for FRβ, respectively. For sample 1572, a single dose of 10 μg/mL of m909 resulted in a 66.1% (95% CI 33.7%–98.4%, P > 0.005) decrease in the number of live cells compared to control. Treatment of sample 1585 with escalating doses of m909 resulted in a statistically significant decrease in the number of live cells in a dose-dependent manner. At the highest concentration, 10 μg/mL, cell viability was reduced by 74.1% (95% CI 65.5%–82.7%, P > 0.005) (Figure 1).

**Conclusion:** FRβ is expressed on most TAMs in primary ascites samples, and these cells can be targeted and killed in vitro through ADCC with the anti-FRβ antibody m909. Given that increased TAMs is a poor prognostic factor, reduction of TAMs could lead to improved clinical outcomes.

**Fig. 1.** ADCC assay using CD11b+ cells from patient sample 1572(A) and 1585(B) incubated overnight donor NK cells with escalating doses of m909 compared to control. Number of live cells expressed as a percentage of control.
1130 - Poster Session
DKK1, a Wnt signaling modulator, promotes ovarian cancer progression and immune evasion in mice
I. Betella, T. Szul, W.J. Turbitt, B. Wu, A. Alba Martinez, R.C. Arend, A.A. Katre, L.A. Norian and M.J. Birrer. aUniversity of Alabama at Birmingham, Birmingham, AL, USA, bMassachusetts General Hospital, Boston, MA, USA

Objective: New molecular targets are needed to better control epithelial ovarian cancer (EOC), a heterogeneous group of diseases that are the most lethal gynecological cancers in the United States. Endometrioid (EC) and clear cell (CCC) carcinoma, two histotypes of EOC, are characterized by functional mutations of the Wnt pathway, which is involved in oncogenesis. Dickkopf-related protein 1 (DKK1), a secreted modulator of Wnt signaling, has recently been identified as a potential therapeutic target in several cancer types. However, its role in EOC is still controversial. Here, we aimed to clarify the role of DKK1 in EOC.

Method: We examined a panel of human and murine EOC cell lines for expression and secretion of DKK1. Using a monoclonal antibody against DKK1, we tested the in vitro effects of DKK1 inhibition on proliferation, migration, and invasion of ES2 cells, a CCC cell line expressing high endogenous levels of DKK1. We then studied the role of DKK1 in the tumor microenvironment, using a syngeneic mouse model in which mice were challenged with either parental ID8 cells, which express low levels of DKK1, or a DKK1-over-expressing ID8 variant (5 mice/group).

Results: Human EOC cells showed high expression of DKK1. ES2 and TOV21G (CCC cell lines) and TOV112D (a EC cell line) showed the highest levels of secreted DKK1. A luciferase reporter assay measuring activation of the Wnt pathway showed that DKK1 inhibition promotes Wnt signaling in vitro. Inhibition of DKK1 in ES2 cells did not affect in vitro proliferation, migration, or invasion. In contrast, injection of murine ID8 cells over-expressing DKK1 into syngeneic mice resulted in higher numbers of tumor lesions > 1 mm in diameter compared to control ID8 cells (mean 5 vs 1.2, P = 0.085). Furthermore, in vivo, over-expression of DKK1 decreased CD45+ leukocyte infiltration into the peritoneum, reducing both CD8+ T cells and NK cells.

Conclusion: Inhibition of DKK1 in vitro had no effects on the phenotypical behavior of human ES2 EOC cells. In contrast, in vivo over-expression of DKK1 was correlated with higher tumor volume and decreased immune infiltrate. Our results suggest that DKK1 inhibition does not directly affect ovarian cancer cells. Instead, DKK1 acts in vivo primarily by suppressing antitumor immunity to foster a cancer-promoting tumor microenvironment. Thus, our findings confirm DKK1 as a valuable new therapeutic target in EOC.

1201 - Poster Session
Dkn-01: A promising strategy for targeting the Wnt pathway in ovarian cancer
I. Betella, W.J. Turbitt, T. Szul, B. Wu, A. Alba Martinez, R.C. Arend, A.A. Katre, L.A. Norian and M.J. Birrer. aUniversity of Alabama at Birmingham, Birmingham, AL, USA, bMassachusetts General Hospital, Boston, MA, USA

Objective: Functional mutations in the Wnt pathway are a hallmark of clear cell and endometrioid ovarian carcinoma (OC). However, no drugs targeting the Wnt pathway are approved for clinical use. Dickkopf-related protein 1 (DKK1), an endogenous modulator of the Wnt pathway, has emerged as a promising therapeutic target. An ongoing phase II clinical trial is investigating DKK1 blockade through administration of the monoclonal antibody DKN-01, but to date, no preclinical data are available using this drug in ovarian cancer. Therefore, our goal was to examine the effects of DKN-01 on tumor burden and immune markers in mouse models.

Method: In a syngeneic mouse model, we explored the effect of DKN-01 on cancer cell growth and tumor immune infiltrates. C57BL/6 mice were challenged with an intraperitoneal (IP) injection of the murine OC cell line (ID8). In addition, we tested the antitumor efficacy of DKN-01 against human OC cells (ES2) in a xenograft model. Here, T cell-deficient nu/nu mice were challenged with IP injections of ES2 cells (expressing DKK1 endogenously) and ES2 cells with knockout (KO) DKK1. For each group, mice were randomized to receive 10 mg/kg (syngeneic model) or 5 mg/kg (xenograft model) of mDKN-01 (a surrogate murine form of DKN-01) versus control IgG2a IP biweekly. After sacrifice (at day 56 for the syngeneic mouse model and day 20 for the xenograft), tumor burdens were scored and peritoneal immune infiltrates were evaluated by flow cytometry.

Results: Treatment with mDKN01 did not significantly alter survival outcomes or tumor burdens in any model of ovarian cancer examined. However, mDKN01 increased natural killer (NK) cell infiltration (P = 0.045) and NK PD-L1 expression (P = 0.001) in the syngeneic model. Moreover, in the xenograft model, mDKN01 increased dendritic cell, macrophage, and NK cell infiltration independently of DKK1 expression by cancer cells.
Conclusion: DKN-01 is an effective modulator of antitumor immunity in preclinical ovarian cancer models. In particular, DKN-01 exerts its role through NK cells and myeloid cells. Further experiments are ongoing to identify underlying mechanisms.

1202 - Poster Session
Resuming chemotherapy after interval cytoreductive surgery in ovarian cancer: The impact of time and temperature
M. Clarka, A. Kollarb, T. Mayc and T.J. Brownb.
aUniversity of Toronto, Toronto, ON, Canada, bLunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada, cPrincess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

Objective: To investigate the impact of interval cytoreductive surgery (ICS) on tumor progression in an orthotopic mouse model of ovarian cancer and the impact of intraperitoneal (IP) cisplatin delivered perioperatively or on days 7 or 28 following surgery.

Method: Luciferase-expressing ID8 murine ovarian cancer cells were implanted intrabursally and IP to C57BL/7 mice. Once disease was established by bioluminescence imaging, 2 cycles of neoadjuvant cisplatin were administered, and animals were stratified to receive ICS (removal of the injected bursa/primary tumor) or anesthesia alone with postsurgical chemotherapy administered on the day of ICS/anesthesia or 7 or 28 days later. To determine the impact of warmed cisplatin administered on the day of ICS, a parallel group of mice was treated similarly except that a heated or ambient temperature cisplatin was administered following surgery or anesthesia. Disease progression was quantified serially with in vivo bioluminescence imaging.

Results: Animals in all groups were evenly matched for tumor burden at stratification. There was no accelerated growth of residual tumor cells after interval cytoreduction compared to controls. Animals who received chemotherapy on postoperative day (POD) 0 and on POD 7 had significantly better disease control compared to standard-of-care POD 28. There was no significant difference in tumor volume in animals receiving heated IP chemotherapy compared to ambient.

Conclusion: Although limited by being an animal model, surgical wounding after neoadjuvant chemotherapy does not cause accelerated tumor growth of residual disease compared to findings in previously published studies in primary surgical models. This also adds to a growing body of basic science and clinical research suggesting benefits to earlier postoperative resumption of chemotherapy.

1203 - Poster Session
The role of transforming growth factor-β (TGF-β) in epithelial ovarian cancer progression via immunosuppression
B.M. Roane, S. Meza-Perez, I. Betella, W. Goldsberry and R.C. Arend. University of Alabama at Birmingham, Birmingham, AL, USA

Objective: Increased TGF-β signaling is associated with poorer prognosis in advanced-stage epithelial ovarian carcinoma (EOC). We sought to demonstrate the role of the TGF-β-mediated immune suppression in the progression of EOC.

Method: Ovarian cancer cell lines, MOC-1 and SKOV3, were treated with LY2157299, a small molecule inhibitor of TGF-βR1. Western blot was used to measure p-Smad2 and p-p38 as markers of the canonical and noncanonical pathway for TGF-β signaling. Migration and invasion were analyzed in vitro using Bowden chamber-based assays. In vivo murine models were created using EG7 tumor cells. Mice injected with EG7 cells were treated with anti-TGF-β monoclonal antibody versus the corresponding isotype, and tumor burden was measured. Mice with macrophage-specific deletions of TGF-β were used to assess the lack of monocyte expression of TGF-β on tumor burden. Flow cytometry was used to quantify specific markers of immune activity and suppression. Student t test was used to demonstrate significant differences.

Results: Western blots of MOC-1 and SKOV3 cells showed baseline p-Smad2 and p-p38, which was expectedly increased with exposure to TGF-β. However, LY2157299 silenced TGF-β signaling at baseline and with exogenous TGF-β. Tumor cells exposed to TGF-β showed increased migration and invasion. This effect was eliminated with TGF-β inhibition. Murine models injected with EG7 cells showed significant reduction in tumor burden when treated with the anti-TGF-β monoclonal antibody. To determine the source of TGF-β, mice with macrophage-specific deletion of TGF-β were injected with EG7 tumor cells. In the absence of macrophage-specific TGF-β, tumor growth was reduced. Flow cytometry showed that loss of TGF-β in macrophages did not reduce the frequency of tumor-specific CD8+ T cells, but did decrease expression of PD-1 and the number of Treg cells, equating to a decrease in immunosuppression without TGF-β.
Conclusion: Increased amounts of TGF-β contribute to increased tumor invasion and migration, while loss of TGF-β results in both a decrease in tumor burden and a decrease in suppressors of T cell activity. Inhibition of TGF-β, demonstrated here with a small molecule inhibitor, can effectively reduce TGF-β signaling in tumor cells, and impairment of TGF-β function is an important contributor for tumor development and Treg activation.

1204 - Poster Session
Autotaxin in malignant ascites promotes invadopodia formation via reactive oxygen species in ovarian cancer
J.A. Choi, H. Cho, D.B. Chay, H. Kwon, G.H. Han and J.H. Kim. Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Objective: Malignant ascites correlate with the peritoneal spread of ovarian cancer and contain cytokine, angiogenic, and growth factors contributing to cell growth and tumor invasion. Autotaxin (ATX) is the primary enzyme producing lysophosphatidic acid (LPA), which correlates strongly with their aggressiveness and invasiveness. However, little is known about the role of ATX of ascites in ovarian cancer (OC) progression.

Method: OC samples from 172 patients were analyzed for ATX by IHC on TMAs using an H-score (0–300). The secreted ATX was measured by ELISA assay in ascites and serum from 153 OC patients. The ROC curves were generated to determine the optimal cutoff values of ATX and CA-125 levels for the prediction of OC. Invasion activity was examined by invadopodia assay and Matrigel assay. Intracellular reactive oxygen species (ROS) was monitored by FACS-based analysis.

Results: We observed that ATX, an LPA-producing enzyme, is highly expressed in ovarian cancer tissue compared to normal tissue. Interestingly, we found that the released ATX was more strongly detected in the ascites of ovarian cancer patients than in benign tumors, suggesting the possibility that ATX plays a critical role in ovarian cancer progression. Furthermore, we observed that ATX silencing contributes to distribution of F-actin remodeling and impairs invadopodia, actin-rich protrusions, which have been observed in a variety of invasive cancer cell formation. FACS analysis revealed that the levels of intracellular reactive oxygen species (ROS) are markedly attenuated by loss of ATX. Pretreatment of an antioxidant N-acetyl-L-cysteine (NAC) significantly inhibited the formation of invadopodia formation.

Conclusion: Taken together, these data indicate that ATX has a critical role for invadopodia formation along the ROS signaling cascade, subsequently contributing to invasion activity in ovarian cancer. This is the first study to show the possibility that ATX in malignant ascitic fluid correlates with multifocal dissemination of ovarian tumors cells on peritoneal surface.

1205 - Poster Session
Bispecific engager immunotherapy targeting the retained portion of MUC16 (MUC16<sub>ecto</sub>) is efficacious against ovarian cancer
O. Yeku<sup>a</sup>, T.D. Rao<sup>b</sup>, T. Purdon<sup>b</sup>, R.J. Brentjens<sup>b</sup> and D. Spriggs<sup>a</sup>. <sup>a</sup>Massachusetts General Hospital, Boston, MA, USA, <sup>b</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: The presence of tumor-infiltrating lymphocytes in ovarian cancer has been correlated with improved overall survival. Immunotherapeutic options utilizing immune checkpoint blockade, vaccine therapy, and adoptive cellular therapy have yielded mixed to disappointing results for ovarian cancer. Bispecific T cell engagers (BiAbs) represent another form of immunotherapy that harnesses the patients' T-cells against their cancer. BiAbs are small molecules consisting of two tandem linked single-chain variable fragments (scFv). One scFv binds to a predetermined tumor associated antigen (TAA), and the other scFv engages CD3 expressed on T cells. This results in redirection of polyclonal T cells to the tumor expressing the TAA, formation of immune synapses, and cytolysis. BiAbs for ovarian cancer have been limited by the availability of suitable TAAs. MUC16 is a TAA over-expressed on most epithelial ovarian cancer cells. MUC16 is cleaved into a soluble form (CA-125), leaving a retained extracellular fragment (MUC16<sub>ecto</sub>) on ovarian cancer cells. We have engineered and evaluated BiAbs targeting MUC16<sub>ecto</sub>. The objective of this preclinical study was to design and evaluate the efficacy of MUC16<sub>ecto</sub>-specific BiAbs.

Method: In collaboration with Eureka therapeutics, we screened an E-ALPHA® human phage display library to identify suitable clones with MUC16<sub>ecto</sub> specificity. scFv derived from positive clones were conjugated to an antihuman CD3 scFv antibody to generate functional BiAbs.

Results: MUC16<sub>ecto</sub>-BiAbs displayed MUC16-specific cytotoxicity in vitro when cocultured with MUC16<sup>+</sup> tumor cells and activated human T cells. In vivo, tumor-bearing mice treated with MUC16<sub>ecto</sub>-BiAbs had significantly delayed tumor
progression, increased systemic IL-2 and IFN-g, and exhibited prolonged survival compared to untreated mice and cohorts treated with T cells alone.

**Conclusion:** We have successfully designed and characterized fully human MUC16-directed bispecific engager antibodies. These BiAbs are effective in a preclinical model of metastatic ovarian cancer and have the potential to mitigate toxicity because of the targeting of only the tumor-retained portion of MUC16.

### 1206 - Poster Session
**Discovery of transcriptional signature of glucocorticoid receptor (GR) activation in ovarian cancer using selective GR modulators**

J.L.T. Venerisa,b, A. Panchamukhi,c, A.T. Pearsonb, G.F. Flemings and S.D. Conzenb. aDana-Farber Cancer Institute, Boston, MA, USA, bThe University of Chicago Medicine, Chicago, IL, USA, cUniversity of Chicago, Chicago, IL, USA

**Objective:** To identify transcriptional targets of glucocorticoid receptor (GR) involved in modulating ovarian cancer chemotherapy response and risk of recurrence.

**Method:** Three ovarian cancer cell lines with high GR protein expression (CAOV3, OVSAHO, and HEYA8) were serum-starved and treated in duplicate for 8 hours with vehicle, glucocorticoid (dexamethasone, 100 nM), or dexamethasone with a GR modulator (mifepristone, 100 nM, or Corcept 125134, 1 μM). RNA was sequenced on the Illumina Hi-Seq 2500 and aligned with the hg38 human reference genome. One sample did not generate a library and was excluded from subsequent analysis. Differential expression was determined by cuffdiff, DEseq2, edgeR, and limma. RT-PCR was used to validate genes of interest. Pathway analysis was performed with Ingenuity Pathway Analysis. Least absolute shrinkage and selection operator (LASSO) was used to develop a model for ovarian cancer recurrence in a discovery patient cohort, and will be tested in a validation patient cohort.

**Results:** Principal component analysis segregated the 29 samples by cell type (Figure 1). A total of 5,378 genes were differentially expressed by RNA sequencing with a fold-change of 1.2 and false discovery rate of 0.1. Across all conditions and cell lines, one gene was significantly differentially expressed: the canonical GR target gene FKBP5. Other canonical GR target genes (e.g., SGK1 and DUSP1) were differentially expressed in two of the three cell lines by RNA sequencing and confirmed by quantitative RT-PCR. Gene expression pathway analysis demonstrated enrichment in cell cycle, cytoskeletal, phosphotidyl inositol, IL-2, and IGF signaling pathways. Genes (n = 195) differentially expressed in at least 2 cell lines following GR-modulator treatment were used to generate a statistical model of recurrence in a discovery data set (Tothill et al. CCR 2008; 14(16):5198–5208). The signature is being tested in a validation cohort from The Cancer Genome Atlas.

**Conclusion:** Expression of a 195-gene GR transcriptional signature stratifies ovarian cancer patients with poor outcomes. Validation of the signature in additional patient cohorts with gene expression and clinical follow-up data is ongoing and will be presented. Prospective assessment of the score in preclinical ovarian cancer PDX experiments is planned, with consideration of exploring GR modulation in conjunction with chemotherapy as an approach to improve outcome.
Fig. 1. A) GR expression in panel of ovarian cancer cell lines by Western blot. B) PCA segregates ovarian cancer cell lines by cell type. C) Canonical GR target genes are among genes differentially expressed by RNA-seq following treatment with dexamethasone and selective GR modulators. D) GR targets SGK1 and DUSP1 validated by RT-PCR. E) 195-gene GR signatures stratifies the Discovery patient cohort by probability of recurrence.

**1207 - Poster Session**

**Tumor associated macrophages (TAMs) mediate the oncogenic effect of fibroblast growth factor -18 (FGF18) in ovarian cancer**

B.M. Roane\(^a\), S.C. Mok\(^b\), W. Wei\(^l\), I. Betella\(^d\), W. Goldsberry\(^d\), R.C. Arend\(^a\) and M.J. Birrer\(^a\), \(^a\)University of Alabama at Birmingham, Birmingham, AL, USA, \(^b\)The University of Texas MD Anderson Cancer Center, Houston, TX, USA, \(^c\)Mass General North Shore Cancer Center, Danvers, MA, USA

**Objective:** We sought to investigate the role of tumor-associated macrophages (TAMs) in the progression of ovarian cancer via mediation of nuclear factor kappa-B (NF-κB) induced expression of fibroblast growth factor 18 (FGF18).

**Method:** Immunohistochemistry (IHC) was used to measure the presence of TAMs in ovarian cancer specimens over-expressing FGF18. Murine orthotopic models were created using SKOV3 and A224 cells that over-expressed FGF18. Clodrolip was used for depletion of murine monocytes, while TPCA-1 was used to decrease NF-κB signaling via inhibition of the IKKβ-mediated canonical pathway, and tumor growth was measured. In vitro studies using a transwell insert-based co-culture system were used to further investigate the TAM/NF-κB/FGF18 axis. Co-culturing with THP-1 significantly activated NF-κB signaling, while TPCA-1 was used to inhibit this pathway. Student t test was used where indicated, and correlation coefficient was determined by Spearman ρ test.

**Results:** Using 188 samples of ovarian cancer specimens, IHC staining for FGF18 and CD163, as a marker of M2-specific TAMs, showed a strong correlation in expression levels (Spearman ρ = 0.674, \(P < 1 \times 10^{-15}\)). In orthotopic murine models with cancer
cells over-expressing FGF18, monocyte depletion with Clodrolip showed significant reduction in tumor burden and mitotic index ($P < 0.005$). THP-1 was used to induce NF-κB signaling in co-culture with A224 and SKOV3 cells over-expressing FGF-18. This stimulated increased production of cytokines creating a pro-inflammatory environment, which was proportional to the amount of THP-1 exposure and therefore the amount of NF-κB signaling. However, this effect was abrogated by TPCA-1 inhibition of NF-κB signaling. The use of TPCA-1 following tumor challenge in mouse models created using SKOV3 cells over-expressing FGF18, showed a significant reduction in tumor burden ($P = 0.0007$) as well as in macrophage infiltration ($P = 0.0004$).

**Conclusion:** FGF18 triggers NF-κB activation with resultant cytokine production. A correlation has also been demonstrated between FGF18 and TAM infiltration in patient specimens and murine xenografts. These findings are associated with progression of ovarian cancer. The feedback loop involving FGF18, NF-κB, and TAM presents an opportunity for targeted therapy aimed at reducing FGF signaling or M2 macrophage infiltration via inhibition of NF-κB.

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**1208 - Poster Session**  
The amount of circulating cell-free DNA present in plasma of endometrial cancer patients is associated with surgical stage, histology and MRI-defined tumor volume  
*Memorial Sloan Kettering Cancer Center, New York, NY, USA*  

**Objective:** The role of circulating cell-free DNA (cfDNA) analysis as a biomarker for endometrial cancer (EC) has yet to be defined. Here we sought to evaluate the associations between cfDNA concentration in plasma from EC patients and tumor histology, surgical stage, and MRI-derived tumor volume.

**Method:** Following consent to an Institutional Review Board-approved protocol, whole blood was prospectively collected (Streck tubes) from 44 patients with biopsy-proven EC prior to surgery and cfDNA was extracted. cfDNA, tumor DNA, and normal DNA samples are currently being subjected to targeted massively parallel sequencing. Preoperative pelvic MRIs were performed on 34/44 (77%) patients, and tumor volume and a radiologic tumor stage were assigned. Of the 44 patients, 43 underwent complete surgical staging, and a final surgical stage was assigned using the 2009 FIGO staging system.

**Results:** The majority of the 44 patients included in our study presented with early-stage disease; 66% (29/44) were surgical stage IA; 9% (4/44) stage IB; 21% (9/44) stage III; and 5% (2/44) stage IV. The most common histologic subtype was endometrioid (61%), followed by serous (18%), carcinosarcoma (14%), clear cell (5%), and undifferentiated (2%). The cfDNA concentrations obtained per milliliter of plasma varied between patients (median 2.92 ng/mL, range 0.6–20.62 ng/mL), and univariate analysis revealed that surgical stage was significantly associated with cfDNA concentration ($P = 0.002$): stage IA, 3.11 ng/mL; stage IB, 5.12 ng/mL; stage III, 4.04 ng/mL; and stage IV 11.86 ng/mL. cfDNA concentrations were also associated with histology, as endometrioid (2.72 ng/mL), carcinosarcoma (2.36 ng/mL), and clear cell (3.01 ng/mL) ECs had the lowest concentrations, while serous (5.44 ng/mL) and undifferentiated (8.89 ng/mL) the highest concentrations. Bivariate linear correlation modeling between preoperative cfDNA concentrations and MRI-defined total tumor volume found a high level of correlation between the two ($P < 0.001$) with an $R^2$ value of 0.66.

**Conclusion:** The levels of cfDNA in plasma of EC patients are associated with tumor stage, tumor volume, and more aggressive pathology. The results of the sequencing of cfDNA and tumor tissue will be available for presentation at the meeting.

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**1209 - Poster Session**  
RNA expression analysis of immune checkpoints in a subset of cervical cancers: A pilot study  
*Massachusetts General Hospital, Boston, MA, USA*  
*TESARO Inc, Waltham, MA, USA*  
*Gillette Center for Gynecologic Oncology/Massachusetts General Hospital, Boston, MA, USA*  

**Objective:** Immune checkpoint inhibitor therapy has been approved for use in patients with recurrent cervical cancer. However, the immune checkpoint landscape of cervical cancers has never been explored, and response rates may be improved with the identification of multiple, concurrently expressed immune targets for combined immunotherapies. This was a pilot study describing the immune checkpoint presence in a cohort of patients with cervical cancer.
Method: Diagnostic cervical tumor samples representing 3 histologic groups were chosen from the Massachusetts General Hospital Tumor Registry, including squamous cell, adenocarcinoma, and adenosquamous carcinoma of the cervix. RNA expression signatures from 214 gene targets including immune checkpoints CTLA4, PDCD1 (PD1), CD274 (PDL1), LAG3, and HAVCR2 (TIM3) and immune cell markers were evaluated from tissue lysates using a flow-cytometry-based platform. RNA analysis results were verified with immunohistochemistry staining. Immune checkpoint expression of cervical cancer was compared to a cohort of endometrial tumor tissue samples.

Results: Ultimately 19 patients were chosen for analysis. Of these, 10 patients had stage IBI disease, 4 had stage IB2, 2 had stage IIA, 2 had stage IIB, and 1 had stage IIIB disease. Of the 19 patients, 7 had squamous cell carcinoma of the cervix (SCC), and 12 had adenocarcinoma (AC). When the AC histologic group was compared to the SCC group, there were no significant differences in the quantity of CD8+ cell RNA expression and there were no significant differences in the relative RNA expression levels of the immune checkpoints CTLA-4, PD-1, LAG-3, TIM-3, and PD-L1. When compared to a cohort of 79 endometrioid endometrial tumor tissue samples, adenocarcinoma and squamous cell carcinomas of the cervix were found to express significantly higher levels of CTLA4 (P = 0.0001), HAVCR2 (P = 0.0004), CD274 (P = 0.02), and PDCD1LG2 (PD-L2) (P = 0.01) with similar levels of LAG3 and PDCD1 immune checkpoint expression. Expression of CD8+ was similar between endometrioid and cervical cancers suggesting similar immune cell infiltration patterns.

Conclusion: This pilot study suggests that cervical cancer tissues express multiple immune checkpoints that may allow for rational development of combination immunotherapies. When compared to endometrioid-type cancers, expression of these immune checkpoints is significantly elevated.

1210 - Poster Session
Cut to the chase: Should we use tumor microarrays to evaluate the tumor microenvironment?
O.D. Lara, Y.A. Lyons, R.L. Dood, Z. Wang, S. Pradeep and A.K. Sood. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bUniversity of Iowa Hospitals and Clinics, Iowa City, IA, USA, cHouston Methodist Hospital, Houston, TX, USA

Objective: Small tumor biopsy samples are frequently used for clinical trials and monitoring response to treatment; however, it is not known to what extent such biopsies are reflective of the immune cell population. The objective of our study was to assess the correlation between core biopsies and larger tumor specimens in high-grade serous carcinoma (HGSC).

Method: Immunohistochemical (IHC) staining for CD68 and CD8 on archived samples of high-grade serous carcinoma was performed. Vectra 3.0 automated imaging system and inForm cell analysis were used to quantify slides. Data were analyzed by Spearman rank correlation.

Results: We evaluated 10 cores per sample from 26 high-grade serous carcinoma (total n = 260 cores). A tumor microarray was created consisting of cores taken randomly, centrally, or peripherally from the larger tumor specimen. inForm cell analysis was utilized to develop an algorithm to distinguish stroma from tumor and intensity of positive staining cells. The mean stromal percentage and percentage of positive staining cells for larger tumor was then compared to cores based on location. There was a strong correlation between mean stromal percentage of core biopsy and larger tumor, independent of site of the biopsy (random cores, r = 0.538; central cores, r = 0.502; peripheral cores, r = 0.548). There was a weak correlation in CD68 count between core biopsies and larger representative tumor specimen made stronger if the core was taken centrally (random cores, r = 0.236; central cores, r = 0.323; peripheral cores, r = 0.259). Finally CD8 counts were not correlated between cores and larger tumor (random cores, r = −0.01; central cores, r = 0.062; peripheral cores, r = −0.0176).

Conclusions: Our results suggest that intratumoral heterogeneity of immune markers is dependent upon the marker assessed. Stromal percentage and macrophage counts were reliably discerned by smaller tumor samples with only minimal influence by location of biopsy. Based on the data, a tissue microarray-based approach to evaluating the tumor microenvironment with select markers may be valuable.

1211 - Poster Session
Tumors from ovarian cancer patients receiving neoadjuvant chemotherapy have unique protein profiles that associate with volume of residual disease after interval debulking surgery
**Objective:** Epithelial ovarian cancer is the most lethal gynecologic malignancy with nearly 75% of women diagnosed with advanced disease. This study sought to assess proteomic alterations in matched chemotherapy naïve and neoadjuvant chemotherapy (NACT)-treated high-grade serous ovarian cancer (HGSOC) patients and determine differences in profiles based on optimal (R0) and suboptimal (R1) surgical debulking.

**Method:** Tumor cell populations were enriched (>95%) by laser microdissection from matched HGSOC \(n = 25\) patient pre- and post-NACT formalin-fixed, paraffin-embedded tissues. Collections were digested by pressure cycle technology with trypsin and analyzed via a multiplexed, quantitative proteomics strategy. Protein alterations in pre- and post-treated NACT tissues were assessed relative to residual disease status (R0 = no residual/microscopic vs R1 < 1.0 cm disease) and further by functional pathway analyses, as well as in comparison with DFS in a public proteomic data set of HGSOC patients \(n = 154\).

**Results:** One hundred twenty-three and 140 proteins were identified as significantly (LIMMA \(P \leq 0.05\), Figure 1) altered in HGSOC tumors that achieved R1 versus R0 surgical debulking prior to and after exposure to NACT, respectively; approximately 10% of ±1.5-fold altered proteins overlapped. Functional inference revealed proteins involved in promoting cell invasion signaling in pre-NACT tissues, but inhibiting the pathway in post-NACT-treated tissues. The pro-invasion protein periostin (POSTN) was significantly decreased (R1 vs R0 LogFC = −1.34, LIMMA \(P = 0.024\)) in patients who achieved R1 status post-NACT. Notably, POSTN has been identified to be significantly elevated in patients with residual disease (R1, \(n = 70\)) (Zhang H et al. 2016, Proteogenomic of Ovarian Cancer) (LIMMA \(P = 0.024\)). Proteins significantly altered between R1 versus R0 disease in pre- and post-NACT tissues in the analysis were assessed for association with DFS in a publicly available proteomics data set \(n = 154\). Proteins significantly associated with altered DFS outcome were largely co-altered in R1 versus R0 patient tissues from pre- versus post-NACT-treated samples.

**Conclusion:** Proteomic alterations in ovarian tumors following NACT reveal distinct profiles between R1 versus R0 tissues associated with altered cell invasion potential and association with DFS survival in HGSOC patients.

**Fig. 1.** Supervised analysis of quantitative proteomic data collected from matched FFPE tissues collected from high-grade serous ovarian cancer patients exhibiting residual (r1, \(n=6\)) or no residual r0, \(n=14\) in pre- vs post- neoadjuvant chemotherapy (NACT) treatment.
Exploration of markers of synergistic lethality of PARP and PI3K-akt-mTOR inhibitors in women's cancers

aOregon Health and Science University, Portland, OR, USA, bThe University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: The objective was to identify molecular mechanisms and protein networks involved in synthetic lethality as well as mechanisms of adaptive changes to the combination of olaparib combined with inhibitors of the PI3K-AKT axis.

Method: One hundred ten patients with recurrent ovarian, endometrial, and triple negative breast cancer were treated with a combination of olaparib and vistusertib or capivasertib (mTORC1/2 and AKT inhibitors, respectively). We have previously reported durable clinical efficacy of these combinations, regardless of BRCA status. Tumor samples were collected pretreatment and 30 days post-treatment, and reverse-phase protein array (RPPA) was performed. Baseline expression was assessed, and change in expression was calculated. Bioinformatics and statistical methods were developed to assess activity of signaling pathways. Pathway scores were determined based on the expression of sets of proteins known to be involved in a specific pathway, including PI3K, RAS/RAF, and DNA damage repair. Association between protein expression and treatment efficacy was determined.

Results: We analyzed a total of 55 paired samples from patients treated with olaparib/vistusertib (n = 25) and olaparib/capivasertib (n = 30). These included 20 endometrial (37% PR, 31.5% SD, 31.5% PD), 21 ovarian (10% PR, 55% SD, 35% PD,) and 14 triple negative breast (15% PR, 23% SD, 62% PD) tumors. Response to olaparib/vistusertib was associated with low pretreatment mTOR pathway activity (Figure 1) and led to altered immune activity based on decreased CD4 and PD1 expression. Resistance to olaparib/vistusertib was associated with high pretreatment cell proliferation (high CCNB1, CDK1, and PLK1 protein expression). In contrast, response to olaparib/capivasertib was associated with adaptive responses indicated by decreased mTOR activity and induction of the DNA damage checkpoint (high phospho-CHK1, -WEE1 and -CDC2). Resistance was associated with high pretreatment RTK activity levels (high phospho-HER3, -EGFR, -IGFR, -MET) and AKT-independent activation of mTOR in the on-treatment samples.

Conclusion: Analysis of pre- and on-treatment samples from responders and nonresponders to PARP and PI3K pathway combination therapy identified biomarkers of patients likely to benefit from therapy and helps to understand molecular mechanisms involved in response and resistance to these drug combinations.

Fig. 1. mTOR pathway activity in pre- and on- treatment samples.

Comprehensive molecular profiles of low-grade serous ovarian carcinoma


University of Tennessee West Cancer Center, Memphis, TN, USA, Caris Life Sciences, Irving, TX, USA, Fox Chase Cancer Center, Philadelphia, PA, USA, Wayne State University, Detroit, MI, USA, Florida Hospital Cancer Institute, Orlando, FL, USA, Western Pennsylvania Hospital, Pittsburgh, PA, USA, Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, WVU Healthcare, Morgantown, WV, USA, UC Health Barrett Cancer Center, Cincinnati, OH, USA, Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA

Objective: Low-grade serous ovarian cancer (LGSOC) is unique among epithelial ovarian cancer, differing from high-grade serous ovarian carcinoma (HGSOC) in terms of its pathogenesis, molecular, genetic, and clinical features. To date, molecular studies on these malignancies have been hampered by small sample sizes. As such, mutation rates of the different cohort
studies have shown a wide range of KRAS and BRAF mutation frequencies. The purpose of this study is to better understand aberrations inherent to LGSOC in a homogenously tested, and histologically confirmed, cohort.

**Method:** In all, 185 LGSOC specimen results were retrospectively evaluated from a CLIA-certified lab (Caris Life Sciences, Phoenix, AZ) using hot-spot (46 genes) and whole exon (592 genes) next-generation sequencing (NGS) technologies interrogating DNA, fusion gene analysis interrogating RNA (52 genes), fragment analysis (FA), in situ hybridization (ISH), and/or immunohistochemistry (IHC). PD-L1 (SP142 antibody) positivity was 2+ staining intensity in at least 5% of tumor cells. Specimens are currently being validated to confirm LGSOC histology.

**Results:** Most specimens (99.5%, 184/185) underwent hot-spot (n = 106) or whole exon (n = 78) NGS. The most frequently mutated genes included KRAS (27.2%, 50/184), NRAS (10.3%, 19/184), BRAF (7.1%, 13/184), and PIK3CA (2.2%, 4/184). Copy number alterations (CNA) were detected in few genes: ADGRA2, FGFR1, HOOK3, NSD3, PCM1, RPL5, SMAD2, and ZNF703 (all 1.3%, 1/77). For hormonal biomarkers, expression rates were as follows: AR, 41.5% (35/82); ER (using a cutoff of 2+ staining in 75% of tumor cells), 81.5% (150/184); and PR, 31.5% (58/184). PD-L1 expression was 3.7% (6/163), and no MMRd (0.0%, 0/6) by IHC was noted. No gene rearrangements (0.0%, 0/9), microsatellite instability (0.0%, 0/78), or high tumor mutational burden (0.0%, 0/74 using a cutoff of ≥17 mutations/Mb) was found.

**Conclusion:** This study represents the largest cohort of molecular profiling in LGSOC, enriched by independent confirmation of histology. Based on our analysis, LGSOC has multiple targets supporting the use of hormone therapy and therapies against the MAPK pathway. Given the tumor genomic stability and low PD-L1 expression, immunotherapies are not expected to have significant efficacy. Further studies to evaluate the prognostic value of different molecular profiles are ongoing.

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### 1214 - Poster Session

**Genomic analysis of immunosuppressive and pro-angiogenic genes in recombinant HE4 treated immune cells and implications for T cell cytotoxicity in ovarian cancer cell co-culture**


aWomen & Infants Hospital, Brown University, Providence, RI, USA, bWomen & Infants Hospital, Brown University, Providence, RI, USA, cHofstra - North Shore Long Island Jewish School of Medicine, Manhasset, NY, USA, dUniversity of Rochester Medical Center, Rochester, NY, USA

**Objective:** To determine the effect of HE4 on expression of immune-related genes in CD8+ T cells and explore the role of HE4 in immunosuppression and angiogenesis in epithelial ovarian cancer (EOC).

**Method:** Tissue HE4 levels and T cell counts were determined by immunohistochemistry (IHC). Recombinant HE4 (rHE4)-mediated gene expression in CD8+ T cells was measured by qPCR array. Cytokine levels were determined using a human cytokine array. Cell viability of ovarian cancer cells co-cultured with pooled peripheral blood mononuclear cells (PBMC) in the presence or absence of rHE4 was determined using MTS cell viability reagent. P values were determined by unpaired 2-tailed Student t test. Activation of STAT3 was evaluated by Western blot, and the interaction of STAT3 and HE4 was queried by immunoprecipitation of STAT3. Finally, HE4 and IL8 levels were measured by IHC in a microarray of human EOC and normal adjacent tissue (NAT), and levels were correlated using Spearman rank test.

**Results:** Tissue HE4 levels correlated with CD8+ T cell counts in EOC. rHE4 treatment of CD8+ T cells upregulated expression of a panel of immunosuppressive and pro-angiogenic genes, including VEGF, HIF1A, STAT3, IDO1, FOXP3, and IL8. IL8 was most robustly upregulated (99-fold vs control). HE4 also resulted in alterations in cytokine levels in ovarian cancer cells co-cultured with PBMCs. OVCAR8 and SKOV3 ovarian cancer cell lines were treated with rHE4, and levels of phospho-STAT3—a known regulator of IL8—were measured. HE4 was found to activate STAT3 in a time-dependent manner, which occurred in the absence of a physical interaction between HE4 and STAT3. rHE4 treatment of OVCAR8 and SKOV3 cells co-cultured with PBMCs suppressed PBMC-mediated cytotoxicity. Finally, IL8 and HE4 mean levels were elevated in EOC tissue compared to NAT and significantly correlated (R = 0.49332, P = 0.00142).

**Conclusion:** HE4 upregulates expression of genes involved in promoting a pro-angiogenic and immunosuppressive microenvironment in EOC, which may play a role in reduced cytotoxic ability of immune cells. Upregulation of IL8 may occur via HE4 regulation of STAT3 signaling. Future directions include testing the effect of HE4 on endothelial cell angiogenesis and determining whether STAT3 and VEGF inhibitors modulate HE4 suppression of immune cell cytotoxicity.
Whole exome sequencing (WES) reveals novel therapeutic targets in cervical cancer

S. Lopez\textsuperscript{a,b}, C. Han\textsuperscript{b}, G. Altwerger\textsuperscript{b}, G. Menderes\textsuperscript{b}, L. Zammataro\textsuperscript{b}, S. Bellone\textsuperscript{b}, A. Bianchi\textsuperscript{b}, B. Zeybek\textsuperscript{b}, E.S. Ratner\textsuperscript{b}, P.E. Schwartz\textsuperscript{b} and A.D. Santin\textsuperscript{b}.

\textsuperscript{a}Magna Graecia University, Catanzaro, Italy, \textsuperscript{b}Yale University School of Medicine, New Haven, CT, USA

Objective: Management of persistent or recurrent cervical cancer has not improved significantly with modern chemotherapy. Novel more effective treatment modalities remain an unmet medical need.

Method: We analyzed 54 fresh-frozen and 15 primary cervical cancer cell lines by whole-exome sequencing (WES). We also evaluated preclinical activity of afatinib/neratinib (irreversible erbB-inhibitors), copanlisib (PIK3CA inhibitor), and their combination against HER2/neu and PIK3CA-mutated versus wildtype tumors in in vitro and in vivo experiments.

Results: We found recurrent somatic missense mutations in 32 genes (including PIK3CA, STK11, ERBB2, and GNAS) and a widespread APOBEC cytidine-deaminase-mutagenesis-pattern (TCW-motif). Somatic copy number variation (CNV) identified 13 copy-number gains and 38 copy-number losses. Since 5.8% and 27.5% of cervical tumors (including several primary cell lines, Figure 1) harbored ERBB2 and PIK3CA mutations, we evaluated the effect of afatinib, neratinib, and copanlisib on cell growth, cell-cycle distribution, and signaling of fully sequenced primary cell lines. We found the IC\textsubscript{50} values in response to afatinib and neratinib to be significantly lower in the group of mutated cell lines than in the nonmutated control group of tumors (mean ± SEM = 0.418 ± 0.065 vs 1.589 ± 0.071 and 0.175 ± 0.008 vs 0.420 ± 0.018 μM, P < 0.0001, for afatinib and neratinib, respectively). In the mutated cell lines, afatinib and neratinib growth inhibition was associated with a dose-dependent dephosphorylation of HER2 and S6. Afatinib and neratinib were both highly active in vivo against HER2/neu-mutated cervical cancer xenografts (P = 0.001 and P = 0.0002, respectively). Copanlisib was effective in inducing a significant tumor growth inhibition in primary cell lines regardless of PIK3CA status. Importantly, when the combination of copanlisib and neratinib was evaluated, a synergistic effect was consistently detected in all cell lines tested. Importantly, in vivo, the combination of copanlisib and neratinib was highly synergistic and induced a long-lasting tumor regression when compared to vehicle (P > 0.0001), neratinib (P = 0.003), and copanlisib (P < 0.003) single agents.

Conclusion: HER2-mutated cell lines were highly sensitive to afatinib and neratinib. The combination neratinib/copanlisib may represent a novel therapeutic strategy in cervical tumors harboring genetic alterations in the HER2/PIK3CA/AKT/mTOR pathway.

Fig. 1.
Talc induces a pro-oxidant state in normal and ovarian cancer cells through gene point mutations in key redox enzymes

A.K. Harper\textsuperscript{a}, N.M. Fletcher\textsuperscript{b}, I. Memaj\textsuperscript{b}, R. Fan\textsuperscript{b}, I.K. Singh\textsuperscript{b}, R.T. Morris\textsuperscript{a} and G.M. Saed\textsuperscript{b}, \textsuperscript{a}Karmanos Cancer Center/Wayne State University, Detroit, MI, USA, \textsuperscript{b}Wayne State University School of Medicine, Detroit, MI, USA

**Objective:** Genital use of talcum powder is associated with increased ovarian cancer risk. Recent data from our laboratory suggest talc induces inflammation and pro-oxidant state in normal and ovarian cancer cells. We have previously reported that alterations in key pro-oxidant and antioxidant enzymes lead to a persistent pro-oxidant state in epithelial ovarian cancer (EOC) cells that is associated with specific single nucleotide polymorphisms (SNPs) in these enzymes. Here, we sought to determine whether talc enhances the pro-oxidant state in normal and ovarian cancer cells through the induction of point mutations corresponding to known SNPs in the key redox enzymes.

**Method:** Normal ovarian, human epithelial ovarian cells (HOSEpic), normal fallopian tube (FT33), and EOC (A2780, SKOV-3, TOV112D) cell lines were treated with talc (100 µg/mL) for 48 hours. TaqMan\textsuperscript{®} Genotype analysis utilizing the QuantStudio 12K Flex was used to assess SNPs in genes corresponding to target enzymes: catalase (CAT), inducible nitric oxide synthase (NOS), superoxide dismutase (SOD3), glutathione peroxidase (GPX1), and glutathione reductase (GSR). Enzyme-linked immunosorbent assay (ELISA) was used to measure activities/levels of these key redox enzymes with point mutations in response to talc treatment. Data were analyzed with one-way ANOVA followed by Tukey’s post hoc tests with Bonferroni correction.

**Results:** Of the enzymes tested, we identified an induction of specific mutations in only CAT, NOS, and GPX1 that correlated with alterations of their activities in talc-treated cells compared to their controls (see Table 1).

**Conclusion:** Here we report a mechanism by which talc enhances the pro-oxidant state in normal and ovarian cancer cells through induction of gene point mutations in key oxidant enzymes, altering their activities.

**Table 1.**

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<th>A</th>
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<th>CAT (rs769217)</th>
<th>NOS2 (rs2297518)</th>
<th>GSR (rs8190955)</th>
<th>GPX1 (rs3448)</th>
<th>SOD3 (rs2536513)</th>
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<th>B</th>
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<td>Cell Lines</td>
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<td>C/T</td>
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<td>SKOV-3-Control</td>
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<td>SKOV-3-Talc</td>
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<td>Normal Ovarian-Talc</td>
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Whole exome sequencing (WES) of primary, metastatic and recurrent ovarian cancer reveals c-MYC gains as potential target for BET inhibitors

B. Zeybek, E. Bonazzoli, S. Lopez, C. Han, G. Altweger, G. Menderes, S. Bellone, A. Bianchi, E.S. Ratner, P.E. Schwartz and A.D. Santin. *Yale University School of Medicine, New Haven, CT, USA, Magna Graecia University, Catanzaro, Italy*

**Objective:** To investigate the pathogenetic mechanisms and evolutionary history of ovarian cancer for evaluation of new therapeutic targets.

**Method:** We analyzed the mutational landscape of 90 primary, 41 metastatic, and 17 recurrent fresh-frozen tumors along with matched-normal DNA, by whole-exome sequencing (WES). We also sequenced 13 pairs of synchronous bilateral ovarian cancer (SBOC) to evaluate the evolutionary history and to understand whether right and left tumors arise independently or represent primary and metastatic tumors. Finally, to search for new therapeutic targets we evaluated the in vitro and in vivo activity of BET inhibitor (i.e., JQ-1 and GS-626510) on primary tumors and xenografts harboring gain-of-function mutations in c-MYC.

**Results:** The large majority of germline and somatic mutations were found in *BRCA1/2* (20.8%) and *TP53* (70.1%) genes, respectively. Among mutations in known cancer driver genes, 77% were transmitted from primary tumors to metastatic tumors, and 80% from primary to recurrent tumors, indicating that driver mutations are commonly retained during ovarian cancer evolution. Importantly, the number, mutation spectra, and signatures in matched primary metastatic tumors were extremely similar suggesting transcoelomic metastases represent an early dissemination process using pre-existing metastatic ability rather than an evolution model. Similarly, comparison of SBOC showed extensive sharing of somatic mutations, unequivocally indicating a common ancestry in all cases. We also found that 7/77 primary tumors and 4/41 metastatic tumors contained at least one somatic mutation in a mismatch repair gene associated with Lynch syndrome. Most of these tumors had mixed or endometrioid histology. Copy number gains at 3q26 and 8q23-24 encompassing PIK3CA and c-MYC genes demonstrated a greater prevalence of amplification in recurrent tumors, compared to metastatic and primary tumors (*P* = 0.01). In in vitro and in vivo experiments with primary cell lines and xenografts BET inhibitors were highly effective in inducing tumor regression of chemotherapy-resistant disease.

**Conclusion:** Our findings suggest early transcoelomic spreading capability may represent an intrinsic feature of ovarian cancer posing a formidable challenge for early ovarian cancer detection. BET inhibitors may represent a novel class of active drugs in patients with recurrent/chemotherapy-resistant ovarian tumors.

Comprehensive genomic profiling of mucinous ovarian carcinoma with comparisons to mucinous colorectal carcinoma

N.L. Jones, D. Arguello, R.W. Holloway, T.J. Herzog, A.C. ElNaggar, I. Winer, T.C. Krivak, G.M. Mantia-Smaldone, V. Galvan-Turner and J. Brown. *Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, Caris Life Sciences, Irving, TX, USA, Florida Hospital Cancer Institute, Orlando, FL, USA, UC Health Barrett Cancer Center, Cincinnati, CO, USA, University of Tennessee West Cancer Center, Memphis, TN, USA, Wayne State University, Detroit, MI, USA, Western Pennsylvania Hospital, Pittsburgh, PA, USA, Fox Chase Cancer Center, Philadelphia, PA, USA, WVU Healthcare, Morgantown, WV, USA, Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA*

**Objective:** Advanced mucinous ovarian cancer (MOC) is a chemo-resistant disease with poor outcomes compared to serous ovarian cancer (SOC). It is often confused with mucinous colorectal carcinoma (MCRC) metastatic to the ovary. Studies have explored CRC chemo regimens for the treatment of MOCs because of their histologic similarities. Herein we use comprehensive technologies to further our understanding of MOC.

**Method:** A total of 140 MOC specimens were evaluated by Caris Life Sciences from 2015 to 2018 using next-generation sequencing (NGS), fragment analysis (FA), in situ hybridization (ISH), and immunohistochemistry (IHC); 188 MCRC were used for comparison. *χ*² analysis was conducted using SPSS.

**Results:** The most frequent mutations in MOC were *KRAS* (64.7%), *TP53* (56.0%), *ARID1A* (50.0%), *CDKN2A* (18.7%), *PIK3CA* (11.7%), and *ATM* (8.2%). *ERBB2* (HER2) amplification was 12.2%. *BRCA1* and *BRCA2* mutation rates were 0.0 and 2.4%, respectively. Markers of immunogenicity were rare: MSI-H in 4.2%, tumor mutational burden (TMB) in 4.8%, and PD-L1 in 5.3%. Significant differences between MOC and CRC were found in the following pathways: Wnt (*APC*, 4.7% vs 61.7%),
P13K/AKT/mTOR (ARID1A, 50.0% vs 0.0%, and FBXW7, 3.7% vs 12.5%), MAPK (BRAF, 2.4% vs 11.9%), and cell cycle control (CDKN2A, 18.7% vs 0.0%). Significant differences were also seen in ERBB2 (HER2) amplification (12.2% vs 0.0%) and hormone receptor expression (ER, 12.8% vs 0.0%; PR, 15.9% vs 0.0%). High rates of KRAS (64.7%, 73.5%) and TP53 (56.0%, 46.7%) mutations were common to both tumor types. Compared to MOC, right-sided CRC were more likely to have mutations in CDH1 (0.0% vs 6.7%) and PTCH1 (0.0% vs 6.7%), while left-sided CRC were more likely to have mutations in FOXO3 (0.0% vs 5.9%) and IDH2 (0.0% vs 5.9%). See Table 1.

Conclusion: Our findings suggest that MOC is a unique disease with multiple potential targets. At the molecular level, this disease shows similarities and differences compared to MCRC that may help to differentiate diseases in cases of unclear primary tumor. A phenotype analysis with ARID1A, CDKN2A, HER2, ER, or PR distinguishes MOC from MCRC, as does the absence of CDH1, FOXO3, or IDH2. Dysregulation of the Wnt, P13K/AKT/mTOR, and MAPK pathways may represent novel targets. Understanding the molecular profile of this rare histology will help direct future therapeutic studies.

Table 1.

<table>
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<th>mCRC %</th>
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1219 - Poster Session
Predicting novel therapies and targets in ovarian and uterine cancers
A. Villar-Prados, S. Ma, C. LaFargue, J. Roszik and A.K. Sood
aUniversity of Puerto Rico, San Juan, PR, USA, bThe University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Systematic approaches for novel drugs with specific cancers are needed. We developed and aimed to biologically validate our Therapy Prediction Tool (TPT) for the repurposing of targeted therapies for specific tumor types by testing the role of Bromodomain and Extra-Terminal motif inhibitors (BETis) in inhibiting BRD4 function and downregulating Notch3 signaling in ovarian cancer.
Method: The TPT integrates multiple platforms to identify drug-tumor type pairs. Utilizing well-established ovarian cancer preclinical models that endogenously over-express BRD4, we carry out in vitro and in vivo studies using clinically relevant BETis to determine their therapeutic effect as well as their impact on Notch3 signaling.

Results: The TPT identified BETi as a leading candidate, especially for ovarian cancers with Notch3 upregulation. Treatment with either the BETis CPI203 and CN210 or BRD4 knockdown with short interfering RNA (siRNA) resulted in decreased cell viability and growth by reducing cell proliferation and increasing cell apoptosis of ovarian cancer cells in vitro. In vivo studies demonstrated that treatment with CPI203 decreased tumor growth and that chronic knockdown of BRD4 with doxycycline inducible short hairpin RNA increased survival up to 50% ($P < 0.001$). Treatment with either BETis or BRD4 siRNA decreased Notch3 expression both in vitro and in vivo in ovarian cancer cell lines. Furthermore, chromatin immunoprecipitation revealed that BRD4 was present at the Notch3 promoter. In addition, BRD4 inhibition decreased the expression of Notch3 downstream targets, such as $HES1$, in ovarian cancer cells.

Conclusion: Our findings provide biological validation for the TPT by demonstrating the BETis can be an effective therapeutic avenue for ovarian cancer treatment and identifying Notch3 as a novel downstream target for BRD4. The TPT could rapidly identify candidate drugs for ovarian cancer along with companion biomarkers.

1220 - Poster Session
A new epha 2 inhibitor for targeted therapy in uterine cancer

W. Hu, C. Ivan, Y. Sun, S. Ma, L.S. Mangala, R.L. Coleman and A.K. Sood. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Treatment of advanced-stage/recurrent endometrial cancer is difficult with few effective therapeutic options, necessitating a search for new agents and targets. We have previously identified EphA2 as an important target in this disease. Recently, a new EphA2 inhibitor (ALW11) was reported to have high affinity for EphA2 and an improved selectivity profile relative to dasatinib (a clinical available EphA2 inhibitor). Here, we examined the antitumor activity of ALW11 alone and in combination with a rationally selected drug (trametinib) in uterine cancer and the underlying mechanisms.

Method: We evaluated the effects of EphA2 inhibition alone or in combination with a MEK inhibitor using in vitro functional and mechanistic studies and identified a set of biomarkers of response by RPPA and TCGA data analyses.

Results: Our previous data showed that dasatinib induced BRAF/CRAF dimerization and MAPK activation in dasatinib-resistant cells (HEC1A and Ishikawa cells). To determine the impact of ALW11 on MAPK activation, we treated SKUT2, HEC1A, and Ishikawa cells with ALW11 at 24 and 48 hours and found that pMAPK was inhibited in SKUT2 cells (sensitive to EphA2-targeted therapy), but slightly increased in HEC1A and Ishikawa cells (resistant to EphA2-targeted therapy). On the basis of these results, we next examined the biological effects of combined ALW11 and trametinib in uterine cancer. The combination significantly increased the apoptosis in HEC1A, Ishikawa cells, and RL-95 cells, compared with those treated with a single drug alone ($P < 0.01$). Western blot analysis revealed that the combination increases cleaved PARP, BIM, and EphrinA1 in uterine cancer cells, but pMAPK and cMyc were significantly decreased in the combined-treated HEC1A and Ishikawa cells, highlighting the importance of the cross talk between EphA2 and other pathways (Notch/cMyc) in uterine cancer. We further explored the correlation between EphA2/MAPK alterations and Notch pathway in uterine cancer by using TCGA data and found that upregulation of EphA2/MAP3K13/15 was significantly correlated with JAG1/MYC, Notch1/3 expression, respectively ($P < 0.01$).

Conclusion: Our findings demonstrate that concurrent MAPK and Notch pathway activation occurs in uterine cancer and a new EphA2 inhibitor alone or in combination with a MEK inhibitor results in significant apoptosis in uterine cancer models. Dual targeting of both EphA2 and MEK should be considered for future clinical development.

1221 - Poster Session
Sacituzumab govitecan (IMMU-132) in uterine serous carcinoma

C. Han, A. Bianchi, S. Bellone, G. Altweger, G. Mendere, B. Zeybek, K. Haines, S. Lopez, M. Azodi, B. Litkouhi, D.A. Silasi, G.S. Huang, E.S. Ratner, P.E. Schwartz and A.D. Santin. aYale University School of Medicine, New Haven, CT, USA, bMagna Graecia University, Catanzaro, Italy
Objective: Uterine serous carcinoma (USC) is an aggressive variant of endometrial cancer with poor prognosis. Sacituzumab govotecan (IMMU-132) is a novel antibody-drug conjugate (ADC) targeting trophoblast antigen 2 (Trop-2), a cell surface glycoprotein highly expressed in many epithelial tumors including USC, to deliver SN-38, the active metabolite of irinotecan. The objective of this study was to preclinically evaluate the efficacy of IMMU-132 against primary USC cell lines and xenografts.

Method: Trop-2 expression in primary tumor cell lines and USC cell viability after exposure to IMMU-132 ADS (hRS7-CL2A-SN-38), nontargeting control ADC (h679-CL2A-SN-38), and naked antibody hRS7 IgG were evaluated using RT-PCR and flow-cytometry-based-assays. Antibody-dependent cell cytotoxicity (ADCC) against Trop-2+ and Trop-2- USC cell lines was evaluated in vitro using 4 hour Chromium release assays. Finally, in vivo activity of Sacituzumab govotecan was tested against Trop-2+ USC xenografts by 3 twice-a-week retro-orbital injection of 500 μg of IMMU-132, control-ADC, and hRS7 naked-IgG.

Results: Over-expression of Trop-2 was detected in 67% (8 out of 12) of primary USC cell lines. Primary tumors over-expressing Trop-2 were significantly more sensitive (i.e., lower IC50) to IMMU-132 (hRS7-CL2A-SN-38) when compared to control ADC (h679-CL2A-SN-38). Both sacituzumab govotecan (IMMU-132) and the naked antibody hRS7 induced high level of ADCC against Trop2+ USC cell lines, while no cytotoxicity was detected against Trop-2 negative tumors. In vivo experiments comparing IMMU-132 activity to control ADC and hRS7 showed a dramatically improved tumor suppression and increased survival in IMMU-132 treated mice when compared to controls ($P = 0.0001$ and $P = 0.0002$, respectively).

Conclusion: IMMU-132 demonstrated remarkable antitumor activity against biologically aggressive USC over-expressing Trop-2. Our preclinical results combined with the dramatic clinical response recently reported in an USC patient treated with IMMU-132 (https://doi.org/10.1016/j.gore.2018.05.009) strongly supports further clinical development of sacituzumab govotecan in USC patients with advanced/recurrent disease (i.e., clinical trial IND 140394).

1222 - Poster Session
Lymphocyte-specific protein tyrosine kinase expression predicts survival in ovarian high-grade serous carcinoma
E.M. Hinchcliff1, C. Paquette1, J. Roszik2, S. Keltig3, M.H. Stoler4, S.C. Mok5, T. Yeung6, Q. Zhang7, M. Yates8, W. Peng9, P. Hwu9 and A.A. Jazaeri10, 1The University of Texas MD Anderson Cancer Center, Houston, TX, USA, 2Women and Infant’s Hospital, Brown University, Providence, RI, USA, 3University of New Mexico Health Sciences Center, Albuquerque, NM, USA, 4University of Virginia Health System, Charlottesville, VA, USA

Objective: Cellular immune response, specifically tumor-infiltrating lymphocytes (TILs), correlates with survival in ovarian carcinoma; however, specific gene expression patterns for this response remain poorly understood. Our objective was to evaluate the impact of a subset of immune-related gene expression on prognosis ovarian high-grade serous carcinoma (OHGSC), with a focus on lymphocyte specific kinase (LCK). Prognostic value of LCK status was compared to the previously validated metric of cytolytic activity score (CYT).

Method: Survival analyses were performed using cohorts stratified by immune-related gene expression in OHGSC data from The Cancer Genome Atlas (TCGA). An independent set of 72 OHGSC data was analyzed by immunohistochemistry (IHC) for validation. Correlated gene expression and gene ontology enrichment were additionally explored using BRB Array tools. A pan-tumor analysis of high and low LCK cohorts in TCGA was compared to the prognostic capability of CYT, as defined by perforin and pro-apoptotic granzymes.

Results: In 535 ovarian cancer samples, mRNA upregulation of LCK correlates with the largest improvement in survival compared with the other immune-related genes investigated. Patients with high LCK expression had a longer median PFS versus lower LCK (29.4 vs 16.9 months, $P = 0.003$) and longer OS of 95.1 versus 44.5 months ($P = 0.001$). This was confirmed by IHC in the independent cohort ($P = 0.04$). LCK was found to be a more significant predictor of prognosis than CYT across tumor types (e.g., ovarian cancer OS, LCK, $P = 0.009$; CYT, $P = 0.66$). B cell related changes, including chemokine, immunoglobulin complex, and major histocompatibility complex (MHC) class II receptor genes, were enriched in high LCK samples. CD20, a B cell marker, confirmed this correlation with LCK in the independent cohort using IHC. See Figure 1.

Conclusion: LCK upregulation is strongly predictive of survival in both TCGA and validation cohorts. The results presented demonstrate that LCK is a better prognostic indicator than the previously validated CYT, and that LCK expression correlates with not only T cell but also B cell related transcripts. Thus, the improved prognostic ability of LCK may be because the activity of both cell types is reflected in LCK expression.
Fig. 1. (A) Kaplan Meier analysis of progression free survival high LCK tumors (red) compared to tumors without high LCK (blue). (B) Kaplan Meier analysis of overall survival in high LCK tumors (red) compared to tumors without high LCK (blue).

1223 - Poster Session
Endometrial cancers in BRCA1 or BRCA2 germline mutations carriers
E. Smith\textsuperscript{a}, A.D.C. Paula\textsuperscript{a}, K.A. Cadoo\textsuperscript{a}, N.R. Abu-Rustum\textsuperscript{a}, X. Pei\textsuperscript{b}, N. Riaz\textsuperscript{a}, M.E. Robson\textsuperscript{b}, J. Reis-Filho\textsuperscript{b}, D. Mandelker\textsuperscript{a} and B. Weigelt\textsuperscript{a}, \textsuperscript{a}Memorial Sloan Kettering Cancer Center, New York, NY, USA, \textsuperscript{b}Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Objective: Bi-allelic alterations in BRCA1 or BRCA2 (BRCA1/2) are associated with genomic features of homologous recombination DNA (HRD) repair deficiency. We aimed to determine whether endometrial cancers (ECs) arising in BRCA1/2 germline mutation carriers harbor bi-allelic alterations and/or features of HR deficiency.

Method: EC patients with BRCA1/2 germline mutations whose tumors were subjected to (a) massively parallel sequencing targeting 410 cancer-related genes under an Institutional Review Board-approved protocol at Memorial Sloan Kettering Cancer Center (n = 7) and (b) whole-exome sequencing (WES) by The Cancer Genome Atlas (n = 3) were identified. Sequencing data were analyzed to define somatic mutations, copy number alterations, loss of heterozygosity (LOH), and microsatellite instability (MSI); in cases subjected to WES, genomic features of HRD were assessed.

Results: Of the 10 ECs included, 6 and 4 were from patients with pathogenic BRCA1 and BRCA2 germline mutations, respectively. The median age at EC diagnosis was 60 (range 44–78) years. The ECs were of various histologic types, including endometrioid (grade II, n = 1; grade III, n = 5), serous/clear cell (n = 2), and carcinosarcoma (n = 2). Staging information was available for 8 cases, and ECs presented at all stages (stage I, n = 3; stage II, n = 1; stage III, n = 3; stage IV, n = 1). Allele-specific copy number analysis revealed that 5 (83%) and 1 (25%) ECs harbored bi-allelic BRCA1 and BRCA2 alterations, respectively, uniformly through LOH of the wild-type allele. All ECs analyzed, regardless of the presence of mono- or bi-allelic BRCA1/2 alterations, harbored somatic TP53 mutations. Of note, 1 BRCA1 and 1 BRCA2 EC with mono-allelic alterations had a high mutational burden and were MSI-high by MSIsensor. The three ECs subjected to WES harbored BRCA1 bi-allelic alterations were of grades II and III endometrioid subtype, and displayed genomic features of HRD, including high large-scale transition scores and a dominant mutational signature 3

Conclusion: Our findings demonstrate that a small subset of patients with ECs arising in patients with pathogenic germline BRCA1/2 mutations harbor bi-allelic alterations, and may benefit from HR-directed treatment regimens. Another subset of BRCA1/2-associated ECs, however, may be sporadic and MSI high.
Immune response changes in HPV-related vulvar malignancy

E.M. Hinchcliff, J. Roszik, A. Yemelyanova, M. Yates, P. Hwu and A.A. Jazaeri. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bUniversity of Alabama at Birmingham, Birmingham, AL, USA

Objective: Evasion from immunosurveillance favors viral persistence and subsequent transformation to malignancy in HPV-related tumors. Therefore, our objective was to determine differences in immune-related gene expression profiles in HPV positive and negative vulvar cancer, in order to identify possible immunoescape mechanisms and opportunities for immune therapy.

Method: Data were abstracted for a selected group of women with primary vulvar cancer, including demographics, survival, and HPV and smoking status. RNA was extracted from formalin-fixed paraffin embedded tissue, and multiplexed gene expression analysis was conducted using NanoString PanCancer Immune Profiling (a 770-gene panel of immune cell markers and response genes). An initial set of 12 tumors was profiled followed by a validation set, and tumor/peritumor comparisons were additionally performed on a subset of these samples.

Results: Tumors from 19 women were included, 9 of which were HPV positive (47.4%). The patients had a median age of 57 (44–92) years and were most commonly stage 1B at diagnosis (52.6%), and 8 (42.1%) were smokers. In the comparison between HPV positive/negative tumors across primary and validation sets, a total of 6 genes were found to be differentially expressed after controlling for the false discovery rate. In pathway analysis, all 6 genes were involved in cellular immune response and downregulated in HPV positive tumors; 4 were involved specifically in antigen presentation, which was the top-rated pathway. CD1D, a nonclassical major histocompatibility complex (MHC) class II molecule involved in the presentation of lipid antigens to natural killer (NK) cells, demonstrated the highest fold change across sets (9.5-fold higher in HPV negative tumors, \( P = 0.002 \)). Tumor/peritumor comparison revealed TNFRSF14 (Hepesvirus entry mediator) was significantly lower in tumor samples. In addition, immune-related genes trended to be higher in smokers than in nonsmokers but did not reach statistical significance.

Conclusion: Altered immune response genes, such as CD1D, may serve as potential targets to prevent immune evasion in HPV-related vulvar malignancy. Further investigation into the role of NK cells and NK-targeting immune therapies will be important in identifying new treatment strategies for these malignancies.

Downregulation of RNA binding protein CIRBP (cold-inducible RNA-binding protein) promotes ovarian cancer progression by regulating MAP2K4 mRNA stability and translation

D. Zou, D. Wang, Q. Zhou and J. Yu. aChongqing University Cancer Hospital, Chongqing Cancer Institute and Chongqing Cancer Hospital, Chongqing, China, bInstitute of Basic Medical Sciences, Chinese Academy of Medical Sciences (CAMS), Chongqing, China

Objective: Understanding the mechanisms underlying ovarian cancer is important for development of novel therapeutic strategies. Recently, accumulating evidence showed that RNA-binding proteins (RBPs) play important roles in tumor initiation and progression. The objective of this study is to identify ovarian cancer-related RBP candidates and reveal the underlying mechanisms.

Method: Ovarian cancer-related RBP candidates were identified by comparing their expression levels and amplification/depletion statuses in normal and ovarian cancer tissues by bioinformatics analysis. The results were further verified by qRT-PCR and Western blot with tissues from patients. Next, the effect of cold-inducible RNA binding protein, CIRBP (the best matched candidate), on ovarian cancer cells was examined in siRNA-mediated CIRBP-knockdown cells and control cells in vitro as well as in a cells-derived xenograft (CDX) model in vivo. The target mRNAs of CIRBP were identified by RNA immunoprecipitation (RIP) followed by RNA-sequencing, and the stability of the target mRNAs was examined in cells treated with 4-thiouridine (4SU). The effect of CIRBP on the translation of target mRNAs was examined by polysome profiling followed by qRT-PCR. The effect of MAP2K2 (identified target of CIRBP) on ovarian cancer was also examined using the experiments as mentioned above. Rescue experiments were employed to demonstrate the role of MAP2K2 in CIRBP-associated ovarian cancer.

Results: CIRBP was identified to be downregulated or depleted in ovarian cancer tissues. Knockdown of CIRBP significantly promoted the proliferation, migration, and invasion of ovarian cancer cells in vitro and in vivo; however, the apoptosis was suppressed. Mechanistic analysis showed that CIRBP binds MAP2K and increases its stability; downregulation of CIRBP thus
activates MAPK pathways and therefore promotes ovarian cancer. The tumor suppressor role of MAP2K in ovarian cancer was further identified in vitro and in vivo. The critical role of MAP2K in CIRBP-associated ovarian cancer was demonstrated by rescue experiments.

**Conclusion:** Our study illustrated that CIRBP is a novel tumor suppressor in ovarian cancer, and stabilization of MAP2K mRNA is the underlying mechanism. This work indicates a novel therapeutic strategy for human ovarian cancer caused by aberrant CIRBP downregulation.

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**1226 - Poster Session**

**Analysis of the utilization of next generation sequencing in gynecologic malignancies**

*B.M. Roane, N. Goel, A. Londono, M.D. Toboni and R.C. Arend. University of Alabama at Birmingham, Birmingham, AL, USA*

**Objective:** We investigated the utilization of next-generation sequencing (NGS) for gynecologic malignancies at our institution.

**Method:** From September 2015 to July 2018, 262 patients underwent NGS testing with Foundation One (FO) testing. Archival tumor samples were evaluated for mutations using a validated panel of 315 genes. Utilization of NGS was up to the patient’s provider throughout the course of treatment. There was no out-of-pocket cost for any patient who had NGS testing. We collected data on patient demographics, tumor site and histology, mutations detected, specifically targetable mutations, and which drugs were utilized based on NGS results. Targetable mutations were defined as mutations that have been linked to an FDA-approved therapy.

**Results:** The FO gene panel identified mutations in all but 4 patients with an average of 5 mutations per patient. The average time to generate a report was 2 weeks. The majority of testing was for ovarian cancer (65%) followed by uterine cancer (28%). The most common mutation identified was p53 (14%), consistent with the prevalence of ovarian cancer in our dataset. However, the remaining top 9 mutated genes each account for 5% or less of all mutations found, demonstrating the diversity of the results within the tumors. The average number of targetable mutations detected was 1.4 with 71% of patients having an FDA-approved therapeutic option based on their NGS results. Out of the patients with a targetable mutation, an average of 4 drugs was available for use. Based on our experience, 26% of patients were placed on targeted therapy based on their NGS results. Patients on targeted therapy for other indications (e.g., germline positive mutations) were not included. The most frequently used class of drugs was mTOR inhibitors (24), followed by PARP inhibitors (19). The average duration of therapy was 201 days with 5 patients on targeted therapy in excess of 500 days. When comparing BRCA germline to BRCA somatic results, we found that 111 patients had congruent results (19 BRCA and NGS positive, 92 BRCA and NGS negative), while 8 patients had positive NGS BRCA testing without a germline mutation and 3 patients with negative NGS BRCA testing and positive germline BRCA mutation.

**Conclusion:** NGS testing provides clinically useful options for additional lines of therapy in patients with gynecologic malignancies. Continued research will likely move the field toward utilization of NGS as a standard diagnostic tool in the workup of these patients.

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**1227 - Poster Session**

**Effect of nodal metastasis size on survival in advanced-stage endometrial cancer**

*E. Cantillo, J.B. DiSilvestro, E. Kalife, C. Raker and C.A. Mathews. Women & Infants Hospital, Brown University, Providence, RI, USA*

**Objective:** To determine the influence of nodal metastasis size on recurrence free survival (RFS) and overall survival (OS) in endometrial cancer.

**Method:** This was a single-institution retrospective review of surgically staged endometrial cancers with positive lymph nodes \((n = 131)\). Cases were identified from the tumor registry from 2004 to 2014 and reclassified to 2009 FIGO staging. Cases with missing data, synchronous malignancies, or stage IV disease were excluded \((n = 26)\). The size of the largest metastatic focus within each positive node was measured by a single pathologist, blinded to clinical outcomes, and demarcated at increments of 0.1 mm. Isolated tumor cells (ITC) were defined as measuring ≤0.2 mm, micrometastasis (MI) as >0.2 mm but ≤2.0 mm, and macrometastasis (MA) as >2.0 mm. Clinical data were compared between groups utilizing Fisher exact test and the log rank test.
1228 - Poster Session
A comprehensive proteogenomic analysis of uterine cancer
M.L. Anderson, L. Ding, M.A. Gritsenko, E.A. Kawaler, M. Thiagarajan, Y. Dou, W. Liu, D. Cui Zhou, M. Mesri, Q. Gao, S.H. Payne, B. Wen, L.B. Wang, C.R. Kinsinger, Y. Wu, D.A. Levine, R.D. Smith, M.J. Ellis, K.V. Ruggles, H. Rodriguez, K.D. Rodland, B. Zhang, D. Fenyo and T. Liu. Baylor College of Medicine, Houston, TX, USA, Washington University School of Medicine in St. Louis, St. Louis, MO, USA, Pacific Northwest National Laboratory, Richland, WA, USA, New York University, New York, NY, USA, Frederick National Laboratory for Cancer Research, Frederick, MD, USA, Baylor College of Medicine, Houston, TX, USA, NYU Langone Medical Center, New York, NY, USA, National Cancer Institute, Bethesda, MD, USA, Brigham Young University, Provo, UT, USA, NYU Langone Health, New York, NY, USA

Objective: To better understand uterine cancer using an integrated, high-throughput strategy that evaluates patterns of protein expression, post-translational modification (PTM), somatic mutations, copy number variation (CNV), and patterns of protein-coding and noncoding RNA expression in parallel.

Method: State-of-the-art platforms for mass spectrometry, next-generation sequencing, and bioinformatics were used to comprehensively profile carefully annotated specimens of endometrial cancer and matched adjacent and nonmatched normal tissue. Normals were histologically assessed for their relative composition of endometrium and myometrium. Microsatellite instability (MSI) was categorized as high or low based on whole exome sequencing and patterns of genomic methylation. Clinical demographics, including tumor histology and patient comorbid conditions, were verified across multiple source sites.

Results: Use of mass spectrometry consistently identified ~11,000 distinct proteins for each cancer (n = 101) and normal specimen (n = 40) in the discovery dataset (matched endometrium low, n = 25; nonmatched endometrium high normal cores, n = 9; and matched pure myometrium, n = 6). These data reveal unique patterns of proteomic biomarkers and neoantigen expression that differ significantly between cancer histotypes and normals. Cancer-associated protein expression is driven, at
least partly, by distinct patterns of mutations and genomic CNV. Our data also reveal novel patterns of circular RNA associated with disruptions in protein expression that vary by uterine cancer histotype. Last, proteogenomic integration reveals previously unrecognized mechanisms potentially responsible for modulating immune responses in MSI-H uterine cancers. Ongoing work includes integrating patterns of microRNA expression, protein phosphorylation, and acetylation into our analyses.

**Conclusion:** Comprehensive proteogenomic analyses have revealed novel patterns of protein, PTM, and circular RNA expression associated with uterine cancer. These observations will be discussed, emphasizing the novel metabolic and immunologic susceptibilities we have identified.

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**1229 - Poster Session**

The contribution of adipocyte reservoirs towards ovarian cancer growth in time and site-specific manner


Karmanos Cancer Center/Wayne State University, Detroit, MI, USA

**Henry Ford Health System, Detroit, MI, USA**

**Henry Ford Hospital, Detroit, MI, USA**

**Objective:** Free fatty acids derived from omentum adipocytes have been shown to meet the energy demands of rapidly proliferating epithelial ovarian cancer (EOC) cells. We have previously shown that EOC progresses aggressively in high-fat diet (HFD)-fed obese mice, highlighting the importance of overall adipocyte reserves in promoting EOC progression. Since major adipose reservoirs exist at multiple body sites (omentum, retroperitoneal, subcutaneous, visceral, and gonadal), the aim of the study is to determine the contribution of individual adipocyte reserves in promoting EOC growth in time and site-specific manner.

**Method:** Eighty female B6 mice were fed either HFD or a regular diet (RD). Post 5 weeks, mouse EOC ID8 (5 million cells/mouse) was injected intraperitoneally. Tumor growth was monitored by in situ luciferases-guided imaging. Sets of mice were sacrificed at days 0, 20, 40, and 60. Individual adipocyte reserves were isolated, weighed, and processed for microscopic analysis.

**Results:** The HFD-fed mice displayed increased EOC burden compared to RD-fed mice ($P < 0.001$). The starting ratio of total adipose to body weight was higher in HFD mice compared to RD mice ($P < 0.01$) but declined with time as tumor progressed. The decline in adipose/body weight ratio was more pronounced in HFD mice than in RD mice at every timepoint studied. Individual microscopic analysis of each adipose reserve (omentum, retroperitoneal, subcutaneous, visceral, and gonadal) revealed the HFD group lost more adipose mass at each site compared to RD mice, even at the early timepoint of 20 days ($P < 0.01$).

**Conclusion:** Our study suggests that EOC cells can acquire free fatty acids from various host adipocyte reserves, regardless of the location. In addition, the presence of excess adiposity may be a crucial factor in the mechanism of proliferation and spread of EOC.

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**1230 - Poster Session**

Becoming a BET inhibitor 'sommelier': Identifying the best combinations for ovarian cancer

**C.J. LaFargue, A. Villar-Prados, C. Ivan, J. Strovel and A.K. Sood.**

The University of Texas MD Anderson Cancer Center, Houston, TX, USA

University of Puerto Rico, San Juan, PR, USA

ConverGene, Cambridge, MD, USA

**Objective:** To identify combination strategies using Bromodomain and Extra-Terminal Domain (BET) inhibitors in a mechanism-driven fashion to maximize antitumor activity, and to determine the efficacy of BET inhibitor combinations in preclinical ovarian cancer mouse models.

**Method:** We used a novel, previously uncharacterized pan-BET inhibitor, CN210, for all in vitro (MTT, apoptosis, reverse phase protein array, RPPA) analysis and in vivo (orthotopic mouse model) experiments. Statistical analyses of in vitro and in vivo experiments were performed using a 1- or 2-way analysis of variance (ANOVA) with $P < 0.05$ considered significant. For the RPPA data, differential expression between control and CN210 for each cell line was determined by $P < 0.05$ obtained from the moderated $t$ statistic from LIMMA package.
**Results:** Eight ovarian cancer cell lines were screened using MTT assays with CN210 to determine the most and least sensitive. HeyA8 and OVCAR8 ip1 displayed the greatest degree of sensitivity, whereas OVCAR4 and OVCAR5 were the most resistant. Concordantly, no significant increase in apoptotic cells was seen after CN210 treatment in either the OVCAR4 or OVCAR5 cell lines. We next examined the previously reported synergistic combination of olaparib and BETi. HeyA8, OVCAR8 ip1, and OVCAR5 all showed a synergistic increase in apoptosis after combination CN210/olaparib treatment versus olaparib or CN210 alone (*P* < 0.001). Applying our findings to an in vivo model using OVCAR5 revealed a nonsignificant trend towards decreased tumor weight and nodules in the combination treatment group compared to control. RPPA analysis was then performed on all four cell lines after CN210 treatment. Each cell line showed an over-expression of CDKN1A, PTEN, and PARP1 (significant in 2/4 lines) and a decreased expression of Connexin-43. Interestingly, both resistant cell lines had upregulation of RAD51 and p-CHEK1 (significant in 3/4 lines), whereas both sensitive ones had downregulation of these two proteins.

**Conclusion:** Resistance to BET inhibition in ovarian cancer may be related to increased RAD51 and p-CHEK1 expression. These findings have potential implications for future rational usage of BET inhibitors.

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**1231 - Poster Session**

**CD3+ and CD8+ tumor-infiltrating lymphocytes (TILs) as markers of improved prognosis in high-grade serous ovarian cancer**


**Objective:** Tumor-infiltrating lymphocytes (TILs) are the host immune response against cancer cells and have been determined to play a role in ovarian cancer outcomes. The quantification of TIL levels has yet to be developed into a clinical scoring system. The aim of this study was to assess CD3+/CD8+ TIL levels as a predictor of high-grade serous ovarian cancer (HGSOC) prognosis.

**Method:** Patients diagnosed with HGSOC between 2007 and 2017 were identified. Immunohistochemical staining for intratumoral lymphocytes CD3+/CD8+ was performed on ovarian whole tumor sections and three 2.2-mm-diameter hotspots equivalent to a 10X high-power field on selected cases. TILs were measured using HALO™ imaging software. The Cutoff Finder software tool was applied to determine cutoff points. Unpaired *t* tests were used to compare TIL groups based on FIGO staging and CA-125 levels. Kaplan-Meier curves were used to compare PFS (as time to first recurrence) with log rank testing.

**Results:** A total of 48 HGSOC patients were identified for this pilot study. Median time of follow-up was 46 months (range 16–130 months). Mean age was 65 years (range 41–91 years). Using whole tumor staining, average CD3+/CD8+ levels were found to be 1.9-fold greater in stage 1–2 disease compared to stage 3–4 (*P* = 0.01). Using 10X hotspots, average CD3+ and CD8+ levels were 1.7-fold and 2.9-fold greater in patients with CA-125 levels <500 at presentation compared to CA-125 levels >500 (*P* = 0.04). Cutoff values for high TIL counts were determined to be CD3+ >1800 and CD8+ >735. High TIL levels demonstrated improved PFS (CD3+, HR = 2.03, *P* = 0.04; CD8+, HR = 2.04, *P* = 0.04). See **Figure 1**.

**Conclusion:** High levels of CD3+ and CD8+ were associated with lower stage, decreased CA-125 levels, and improved PFS among HGSOC patients. This pilot study suggests that 10X hotspot cutoff values of CD3+ >1800 and CD8+ >735 can be used for risk stratification in HGSOC patients. This method warrants further investigation as a universal method for tumor TIL assessment.
Identification of unique genomic alterations in extramammary Paget's disease

T. Kilts\textsuperscript{a}, S. Zarei\textsuperscript{b}, Y. Wu\textsuperscript{c}, Q. Zhang\textsuperscript{c}, K. Halling\textsuperscript{a}, J.N. Bakkum-Gamez\textsuperscript{a}, B.R. Kipp\textsuperscript{c} and B.A. Cliby\textsuperscript{a}.

\textsuperscript{a}Mayo Clinic, Rochester, MN, USA, \textsuperscript{b}Cleveland Clinic, Cleveland, OH, USA, \textsuperscript{c}Mayo Clinic College of Medicine, Rochester, MN, USA

Objective: Extramammary Paget's disease (EMPD) is a rare neoplasm with high rates of recurrence; treatment is largely confined to morbid, large perineal resections. There is minimal research into the molecular and genetic alterations associated with EMPD. We sought to identify genomic alterations that could lead to alternative therapy options.

Method: EMPD patients with archival tissue were identified after Institutional Review Board approval. Formalin-fixed paraffin-embedded specimens were microdissected and nucleic acids extracted for whole genome copy number variation (CNV) assessment using chromosomal Microarray (Oncoscan, Affymetrix) and next-generation sequencing (NGS) on a oncogene-targeted panel. Patient clinical data were recorded from electronical medical records.

Results: Tumors from 27 EMPD cases were identified ($n = 17$ female, $n = 10$ males) that had adequate tissue for analyses. Of the cohort, 6 (22\%) were found to harbor invasive EMPD, and the remainder were noninvasive. Across all 27 samples we observed large chromosomal abnormalities. Copy number gains were observed at chromosome 17q21 and chromosome 6p22 in the majority of cases. Loss of heterozygosity (LOH) was present at chromosome 11q22-23 and chromosome 9p21 with frequency of 67\%. Copy number loss was seen with 67\% frequency in chromosome 9p21. Interestingly, all patients with invasive EMPD showed LOH at chromosome 11q22-24 and chromosome 15q14-15, versus 19\% and 15\%, respectively, for noninvasive EMPD. Initial results from NGS revealed a large number ($n = 357$) of rare variants (MAF $< 0.001$) with Cosmic ID; genes with high case frequency include PIK3CA (44\%), TP 53 (28\%), and EGFR (24\%). See Figure 1.

Conclusion: This is one of the first studies to characterize somatic genomic alterations in patients with EMPD in an effort to identify targetable pathways to develop novel therapeutic approaches. We report unique gene alterations and copy number variants, including alterations that are specifically associated with invasive disease. Next steps include further analysis to identify whether any of these mutations are targetable.
1233 - Poster Session

Long noncoding RNA SNHG6 promotes cell proliferation and migration through sponging mir-4465 in ovarian clear cell carcinoma

Y. Wu. Fudan University Cancer Center, Shanghai, China

Objective: Dysregulation of SNHG6 plays a critical oncogenic role and facilitates tumorigenesis in human cancers. However, little information is available about the expression pattern of SNHG6 in ovarian clear cell carcinoma (OCCC). The contributions of this long noncoding RNA (IncRNA) to tumorigenesis and progression of OCCC also remains unclear. This study investigates the pivotal role of SNHG6 in OCCC.

Method: To investigate the clinical significance of SNHG6, we analyzed its expression levels in 48 OCCC samples and 44 normal ovarian tissues from Fudan University Shanghai Cancer Center. Functional assays, including the CCK8, colony formation, wound healing, and Transwell assays, were used to determine the oncogenic role of SNHG6 in human OCCC progression. Furthermore, subcellular fractionation and Dual-Luciferase Reporter Assays were used to determine the mechanism of SNHG6 in OCCC progression. Animal experiments were used to determine the role of SNHG6 in OCCC tumorigenicity and metastasis in vivo.

Results: In this study, we showed that SNHG6 expression was abnormally upregulated in OCCC tissues compared with unpaired normal ovarian tissues. High SNHG6 expression was correlated with vascular invasion, distant metastasis, and poor survival. Further functional experiments demonstrated that knockdown of SNHG6 in OCCC cells inhibited cell proliferation, migration, and invasion in vitro as well as tumor growth in vivo. Moreover, SNHG6 functioned as a competitive endogenous RNA (ceRNA), effectively becoming sponge for miR-4465 and thereby modulating the expression of Enhancer of zeste homolog 2 (EZH2).

Conclusion: Our data suggest that SNHG6 was a novel molecule involved in OCCC progression, and targeting the ceRNA network involving SNHG6 may be used as a treatment strategy against OCCC.
How does microbiome change with chemotherapy? Using an *in vivo* model of uterine cancer to assess changes in gut microbiome.

C. de Haydu, V. Ramakrishnan, Y. Ban, L. Zhang, M.P. Schlumbrecht, S. Roy and S. Ramakrishnan. *University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, University of Minnesota, Minneapolis, MN, USA*

**Objective:** Recent studies have suggested interactions between microbiome and cancer therapeutics. In addition to direct cytotoxicity, chemo-induced changes in microbiome may play a significant role in disease outcomes. Our objective was to evaluate the efficacy of therapeutic agents in a mouse model of human endometrial cancer (EC) and their effect on tumor growth and gut microbiome.

**Method:** An EC cell line, HTB-112 (ATCC), was injected subcutaneously into female, athymic mice. After 1 week, mice were randomized and treated with 1 or a combination of 3 chemotherapies, carboplatin (C), paclitaxel (T), and a new investigational agent, Minnelide (M). Mice were treated for 4 weeks with either single-agent C, T, M, or combination C/T, C/M, T/M, or C/T/M. Mice were euthanized and tumors weighed. Fecal samples were collected prior to establishing tumors and weekly after. Microbial DNA was isolated from fecal samples and processed (Qiagen) for sequencing 16S rRNA gene, variable region 4 (University of Minnesota, Genomics Center). Diversity between groups was calculated using Bray-Curtis dissimilarity.

**Results:** Tumors from mice treated with M, or C/M, or T/M were significantly smaller than tumors treated with single-agent C or T (both, $P < 0.0005$) or with C/T ($P < 0.02$). There was no significant difference between single-agent M, C/M, or T/M. Triplet therapy C/T/M treated tumors were significantly smaller than all other treatments ($P < 0.05$). Untreated controls with tumor were compared to treatment groups. Both single-agent C and T changed beta diversity of fecal microbial composition significantly ($P = 0.02$ for both), as did the combination of C/T ($P = 0.04$), and tumors were larger. Monotherapy with M or in doublet, C/M or T/M, did not significantly change the microbial beta diversity ($P > 0.05$), and tumors were smaller. In taxonomic analyses, M-treated tumors were smaller and retained a greater percentage of Firmicutes. C or T alone or C/T lost Firmicutes and increased Bacteroides relative abundance (*Figure 1*).

**Conclusion:** We used a mouse model of EC with 3 chemotherapies and compared chemotherapeutic efficacy and changes in microbiome. There was a correlation with increasing Bacteroides species abundance and increased tumor size. Interestingly, C treatment showed no significant change in tumor size and correlated with the emergence of Verrucomicrobia. Further studies are underway to delineate the role of the microbiome observed.

![Phylum Composition by Treatments](image_url)

**Fig. 1.**
Pim1 promotes cell proliferation and regulates glycolysis via interaction with c-MYC in ovarian cancer
Y. Wu. Fudan University Cancer Center, Shanghai, China

Objective: Ovarian cancer (OC) is the leading cause of death among women with gynecologic malignancies. Recent studies have highlighted the role of Pim1, which belongs to a group of constitutively activated serine/threonine kinases, in cancer development. However, the effect of Pim1 in ovarian cancer is largely unclear.

Method: The protein expression of Pim1 was verified from the human protein atlas (www.proteinatlas.org), as well as ovarian cancer cell lines, and its association with survival was then analyzed by bioinformatic analysis. CCK-8 assay and colony formation were used to measure cell proliferation. In order to evaluate the mechanism of Pim1 in high-grade serous ovarian cancer (HGSOC), extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) and lactate analysis were performed to find that Pim1 maintains Warburg effect via c-Myc-glycolysis signaling axis. In vivo subcutaneous xenograft inoculation was also performed to certify its role.

Results: We present the first evidence that silencing or over-expressing Pim1 can suppress or promote, respectively, OC cell proliferation. Furthermore, we demonstrate that upregulation of Pim1 significantly enhanced glycolysis in OC cells. In vivo experiments further confirmed that knockdown of Pim1 inhibits the growth of tumors derived from the A2780 cell line. To search for the underlying molecular mechanism, we examined the effect of Pim1 on c-Myc, a pivotal gene in glycolysis, and observed that Pim1-mediated phosphorylation of c-Myc activated the expression of glycolysis-associated key genes such as PGK1 and LDHA. Moreover, we found that the Pim1 inhibitor SMI4a induced chemosensitization to cisplatin. Clinically, Pim1 was also over-expressed in ovarian cancer and correlated with poor overall survival by bioinformatics analysis.

Conclusion: Together, these results suggest that Pim1 contributes to proliferation and glycolysis in OC via interaction with c-Myc and may serve as a potential target in the treatment of OC patients.

Developing a clinically relevant ovarian cancer model for use as a platform to test novel immunotherapies that incorporates surgical cytoreduction
C.B. Morse\textsuperscript{a}, K.G. Anderson\textsuperscript{b}, B.M. Bates\textsuperscript{b}, E.Y. Chiu\textsuperscript{b}, N.M. Garcia\textsuperscript{b} and P.D. Greenberg\textsuperscript{b}. \textsuperscript{a}University of Washington Medical Center, Seattle, WA, USA, \textsuperscript{b}Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Objective: We are developing an immunotherapy with engineered T cells targeting mesothelin (MSLN), a protein selectively over-expressed in ovarian cancer. We have previously shown that CD8\textsuperscript{+} T cells engineered with a MSLN-specific T cell receptor (TCR\textsubscript{MSLN}) kill ovarian cancer cells in vitro, and that TCR\textsubscript{MSLN} T cells transferred into mice with advanced-stage metastatic disease reduce tumor burden and prolong survival. We have now developed a novel ovarian cancer mouse model in which mice develop metastatic ovarian cancer following orthotopic tumor injection and are then treated with surgical cytoreduction followed by T cell therapy.

Method: Murine ID8 ovarian cancer cells were transduced with an enhanced luciferase (eLuc) construct to permit imaging of microscopic tumors; 1 × 10\textsuperscript{6} tumor cells were injected beneath the ovarian bursa of C57Bl/6 mice. At 6 and 10 weeks after orthotopic injection, after detection of metastases, mice underwent hysterectomy and bilateral salpingo-oophorectomy to remove all macroscopic disease. Survival was compared between no-surgery, 6-week surgery, and 10-week surgery cohorts. Immunohistochemistry (IHC) was performed on primary and metastatic tumors.

Results: eLuc-transduced ID8 cells were brighter than cells transduced with standard luciferase, enabling in vivo visualization of microscopic intra-abdominal metastases in mice that developed large primary ovarian tumors following orthotopic injection. Primary surgical cytoreduction yielded minimal residual disease in all mice. Metastatic sites of disease following orthotopic injection resembled human ovarian cancer. IHC showed no difference in staining for CD3, CD8, CD31, CD45R, CD68, or FoxP3, between primary tumors and metastases. Early surgical cytoreduction 6 weeks after orthotopic injection prolonged survival compared to either no-surgery or delayed surgical cytoreduction at 10 weeks.

Conclusion: Adoptive transfer of high-affinity TCR\textsubscript{MSLN} T cells improves survival in mice with advanced-stage ovarian cancer. In a clinically relevant model, early surgical cytoreduction leads to improved survival. However, extended survival among all surgically treated cohorts limited our ability to efficiently characterize the function, persistence, and therapeutic activity of TCR\textsubscript{MSLN} T cells in this model.
Discovery and validation of novel DNA methylation markers for the detection of endometrial cancer: Selection by methylome-wide analysis


**Objective:** DNA methylation is an early event in endometrial cancer (EC) development and may have utility in early detection. We conducted a whole methylome search followed by validation on independent tissues to identify discriminant EC-specific methylated DNA marker (MDM) candidates suitable for downstream clinical application.

**Method:** For discovery, DNA from 113 frozen tissues — 16 grade 1/2 endometrioid (G1/2E), 16 grade 3 endometrioid (G3E), 11 serous, 11 clear cell ECs, 15 uterine MMMTs, 44 benign endometrial (BE) tissues (14 proliferative, 12 atrophic, 18 disordered proliferative), 70 formalin-fixed paraffin-embedded (FFPE) cervical cancers (CC) (36 squamous cell, 34 adenocarcinomas), and 18 buffy coats from cancer-free females — underwent reduced representation bisulfite sequencing (RRBS) to identify differentially methylated regions (DMRs). Candidate MDM selection from DMRs was based on receiver operating characteristic (ROC) discrimination, methylation fold change, and background methylation. Candidates were retested using methylation-specific PCR (MSP) to confirm performance. Blinded biological validation was performed using MSP on independent EC (141), BE (79), and CC (50) FFPE tissue sets representing all discovery set histologies.

**Results:** From RRBS discovery, 37 candidate MDMs met filtering criteria. On biological validation, multiple MDMs showed marked methylation fold changes (10 to >1,000) across all EC histologies versus BE. A 3-MDM panel (EMX2OS, NBPF8, SFMBT2) discriminated overall EC from BE (97% specificity, 97% sensitivity, and AUC 0.98, **Figure 1**). Some MDMs discriminated clear cell from BE and all other EC histologies (MDFI, GDF7, SEPTIN9, EEFIA2), and C5orf52 discriminated endometrioid (G1/2E, G3E) from BE and all other EC histologies. A 6-MDM panel (ABCB1, NXPH1, Max.chr10, ITPKA, LRRC41, C5orf52) discriminated between EC and CC with 99% specificity.

**Conclusion:** Whole methylome sequencing, stringent filtering criteria, and biological validation yielded outstanding candidate MDMs for EC. Some MDMs discriminate all EC histologies from BE with comparably high sensitivity, while others accurately distinguish among histologies. Given high discrimination and ease of assay, such MDMs merit further exploration for clinical application as early detection markers.

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**1238 - Poster Session**

**Serum exosome profiling reveals distinct phosphorylation biosignatures in cervical cancer: A pilot study**

D.M. Roque, C. Fan, G.G. Rao, M. MacKenzie, I. Alexandrov and J. Reader. "The University of Maryland School of Medicine, Baltimore, MD, USA, "ActivSignal, LLC, Belmont, MA, USA"

**Objective:** Exosomes are functional vesicles secreted by normal and tumor cells that may modulate the tumor microenvironment to influence metastasis and invasion. In cervical cancer, recurrent disease continues to represent a significant cause of morbidity and mortality. Exosomal signaling has not been well-characterized in cervical cancer.
**Method:** Serum and clinicopathologic characteristics were prospectively collected from cervical cancer patients and benign controls from a single urban tertiary institution. The exosome fraction was isolated from 100 μL aliquots and analyzed by a proprietary ActivSignal IPAD assay to identify a phosphorylation biosignature based on 66 human proteins representing ≥20 canonical signaling pathways in one reaction. The technology allows detection of targets with high specificity/sensitivity because of the combination of 2 distinct antibodies per target. Signal was normalized to median values defined across benign controls. Descriptive statistics and t tests were employed.

**Results:** A total of 81 cases (5,346 data points) were examined, including 26 cervical cancers (Figure 1a) and 55 benign controls (Figure 1b). Among cancer cases, mean follow-up interval was 437 (range 50–936) days. Mean age was 47 ± 14 years, and race was characterized as black (54%), white (38%), Asian (4%), or Hispanic (4%) (Figure 1c). At the time of initial diagnosis, an average of 15.9% ± 7.3% and 16.1% ± 8.7% of targets were found to be activated or suppressed, respectively. Relative to control, cervical cancer cases demonstrated (1) increased cleaved PARP, pSMAD2, glypican1 (TCF1), (2) decreased p-NUMB, p-Hsp27, p-STAT3, p-IRS1, p-Lck, p-c-kit, and (3) dichotomous expression of p-mTOR, p-Zap70, p-Stat5, p-EGFR. Phospho-mTOR was differentially expressed in adenocarcinoma versus squamous cell carcinoma (12.5 ± 15.4 vs 2.4 ± 5.04, \(P = 0.02\)). There was a trend towards (1) greater pNUMB expression in patients dead of disease/alive with disease (0.9 ± 0.6) versus alive without disease (0.6 ± 0.2) (\(P = 0.07\)) at last follow-up, and (2) lower Hsp70 expression in patients who had received radiation and/or chemotherapy (0.85 ± 0.26) versus those who were treatment-naïve (0.98 ± 0.08) (\(P = 0.08\)).

**Conclusions:** Exosomal serum profiling is feasible and may have prognostic potential and therapeutic implications. Larger studies are needed, particularly for diseases such as cervical cancer, which lack reliable serum markers of active disease and early recurrence.

**Fig. 1.** (a) cervical cancer exosome profiles (b) control exosome profiles (c) cervical cancer patient characteristics. NS-not specified; SCC-squamous cell carcinoma; SD-stable diseases; PR-partial response; CR-complete response; PD-progressive disease; d-days; NED-no evidence of disease, AWD-alive with disease; DOD-dead of disease; EBRT-external beam radiation therapy; chemosn-chemosensitization.
**Method:** RNA-sequencing was performed on 12 HGSOC tumor pairs pre- and post-NACT (24 total). Differential expression analysis of Wnt pathway signaling and T cell infiltration was performed on these samples and on RNA-seq data from the Ovarian Cancer Genome Atlas (TCGA). T cell infiltration was assessed using a “T cell inflamed” signature previously described in melanoma. Semiquantitative analysis was performed on immunohistochemistry (IHC) results to evaluate tumor infiltrating CD8 T lymphocytes (TILs) and β-catenin expression in 9/12 patients. Results were compared between platinum-sensitive and -resistant patients.

**Results:** Data gathered from TCGA showed an inverse correlation between canonical Wnt pathway gene upregulation and T cell infiltration in all patients, but it was statistically significant only in platinum-sensitive patients. Similarly, we found this inverse correlation in our 12 patients both per- and post-NACT, although the strongest correlation was pretreatment ($P = 0.049$). Consistent with prior studies showing improved outcomes with higher TIL to regulatory T cell (Treg) ratios, platinum-sensitive patients were more likely to have a CD8:Treg ratio greater than 1 ($P < 0.05$). Resistant patients had more of an increase in Tregs and a decrease in dendritic cells following NACT. β-catenin expression remained similar pre- and post-NACT. Although there was not a strong correlation between the trends of CD8 infiltration and β-catenin staining post-NACT, an inverse relationship, with β-catenin decreasing and CD8 increasing, was found in 2 patients.

**Conclusion:** An inverse correlation was found between Wnt signaling and T cell infiltration in HGSOC patients who received NACT and from TCGA. More investigation is needed for further insight into the mechanism that the Wnt pathway plays in immunomodulation in HGSOC.

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**1240 - Poster Session**

**The identification and validation of exosome proteins as biomarkers for high-grade serous ovarian cancer**


*The Ohio State University, James Cancer Hospital, Columbus, OH, USA, The Ohio State University Medical Center, Columbus, OH, USA, Cedars-Sinai Medical Center, Los Angeles, CA, USA, Georgia Regents University, Augusta, GA, USA*

**Objective:** The objective of this study was to identify and validate exosomal protein signatures that can be used for the early detection of high-grade serous ovarian cancer (HGSOC).

**Method:** We hypothesize that origin-based exosomal protein signatures could serve as more specific biomarkers for the early detection of HGSOC using throughput technologies. We isolated exosomes from ovarian cancer cell lines and their normal counterparts, and serum samples from patients with and without HGSOC using Exo-quick (System Biosciences, California), ultra-centrifugation, and a microfluidics chip. The vesicle concentration and size were determined using nanoparticle tracking analyzer and TEM. Mass spectrophotometry (1D-LC-MS/MS) and IPA were then used to identify the exosomal protein profiles that are differentially upregulated between normal ovarian and fallopian tube epithelial cell lines (OSE, FTSECs) versus cancer cell lines (OVCAR-8), and benign versus HGSOC patient serum samples. The top proteins identified based on their statistical significance were further validated using Western blot and protein array in whole serum and serum exosomes to determine the specificity and reliability of exosomal proteins as potential biomarkers.

**Results:** LC-MS/MS identified over 25 exosomal proteins that are differentially expressed in HGSOC compared to normal cell lines. Further validation in patient serum samples identified multiple proteins that are differentially expressed in exosomes compared to whole serum, between benign versus cancer specimens, and among stages of HGSOC. For example, there were statistically significant differences in the exosomal expression of FAS between benign versus early-stage HGSOC ($P = 0.039$), although expression in early-stage compared to advanced-stage HGSOC samples was not significant ($P = 0.85$). There were no significant differences in FAS protein expression between any groups in whole serum. AGRIN expression was significantly different between benign versus early-stage disease in whole serum ($P = 0.018$), and between early-stage versus advanced-stage HGSOC within exosomes ($P = 0.045$).

**Conclusion:** We identified several exosomal protein signatures that could serve as biomarkers for HGSOC, which when used in isolation or combination with serum testing could offer increased specificity compared to whole serum testing alone.

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**1241 - Poster Session**

**Evaluation of WNT/β-catenin pathway inhibitor CGX-1321 in a syngeneic ovarian cancer mouse model**

B.T. Mott, W. Goldsberry, A.A. Katre, N. Goel, S. Meza-Perez, T. Randall and R.C. Arend. *University of Alabama at Birmingham, Birmingham, AL, USA*
**Objective:** We sought to understand the effect of the Wnt/β-catenin pathway inhibitor CGX-1321 alone and in combination with paclitaxel on tumorigenesis and T-cell exclusion in a syngeneic ID8 tumor model in mice.

**Method:** There were $7 \times 10^6$ ID8 cells injected into the peritoneum of C57BL/6 mice and allowed to grow for 28 days. Groups of seven mice were randomized into treatment arms including vehicle control, CGX-1321, paclitaxel, and combination of CGX-1321 and paclitaxel. Mice receiving CGX-1321 (1 mg/kg) or vehicle received appropriate formulation once daily by oral gavage. Paclitaxel was given via intraperitoneal injection (5 mg/kg, 3 days on, 3 days off). After 14 days of treatment, mice were sacrificed, and omentums were harvested for analysis by flow cytometry. Tissue was processed for flow cytometric analysis of Tregs, CD8$^+$ and CD4$^+$ T-cells, and dendritic cells, and immune checkpoint markers PD-1, CTLA-4, and FOXP3. Statistical analysis was done in GraphPad Prism.

**Results:** Administration of CGX-1321 alone inhibited tumor growth, as evidenced by omentum weight, while reducing expression of PD-1, although not significantly, and paradoxically increasing CTLA-4 expression. There was a trend toward an increase in Tregs, and in CD103$^+$ dendritic cells, but a slight decrease in CD8$^+$ cells; however, these effects did not reach significance. Paclitaxel alone also reduced tumor burden and had similar effects on T cells and immune markers, except for a decrease in CD103$^+$ dendritic cells. Combining CGX-1321 with paclitaxel further reduced tumor growth and prolonged survival but had no additional effect on the T cell profile.

**Conclusion:** This study indicates that inhibition of the Wnt/β-catenin pathway using CGX-1321 combined with administration of paclitaxel significantly reduced tumor burden in a syngeneic mouse model. Further investigation is required to fully understand any potential effect on T cell function.

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**1242 - Poster Session**

**Hormonal receptor expression and clinical outcome in ovarian high-grade serous carcinoma**

S. George, R. Sowamber, L. Dodds, S.E. Jordan, I. Paudel, M. Huang, A. Pinto, M.P. Schlumbrecht, P. Shaw and B.M. Slomovitz

*University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, University of Miami Miller School of Medicine, Miami, FL, USA*

**Objective:** Ovarian high-grade serous carcinoma (HGSC) is genetically unstable and rapidly growing and diagnosed at advanced stages. Immunohistochemical profiles have demonstrated differential expression of estrogen receptor alpha (ER) and progesterone receptor (PR) in HGSC. Our objective was to investigate the ER and PR in HGSC and its precursor lesions and to assess the influence of ER/PR subtype on OS and ER/PR-driven pathogenesis in HGSC.

**Method:** Data were derived from a cohort of archival HGSC tissue with advanced-stage and adjuvant platinum-based chemotherapy ($n = 386$) and a cohort of serous tubal intraepithelial carcinoma (STIC, $n = 14$). Gene set enrichment analyses (GSEA) was performed using mRNA gene expression profiles based on ER/PR expression in tumors (Affymetrix U133, $n = 45$). Log rank (Mantel-Cox) analysis was used to calculate OS and PFS.

**Results:** ER is maintained in serous tubal intraepithelial lesions (STIC) while PR is lost; 71% of HGSC are ER$^+$ and 29% ER$^-$. ER expression alone was not associated with a significant OS ($P = 0.406$) and PFS ($P = 0.473$) advantage, while PR$^+$ displayed significant OS advantages at both the 5% cutoff (60.1 months, 95% CI 49.1–71.3, vs 44 months, 95% CI 37.6–52.1, $P = 0.008$) and the 10% cutoff (60.3 months, 95% CI 48.5–72.2 vs 47.8 months, 95% CI 40.3–55.2, $P = 0.019$). Clinical outcome assessment on ER/PR status showed ER$^+$/PR$^-$ (5% cutoff expression, 51% of cohort) patients had significantly lower OS (41.7 months, 95% CI 35.0–48.4) relative to ER$^-$/PR$^+$ (63.1 months, 95% CI 35.6–90.6, $P = 0.041$). GSEA analyses demonstrated upregulation of meiotic recombination ($P = 0.00$, NES = 2.15), RNA polymerase I transcription ($P = 0.00$, NES = 2.14), double strand break repair ($P = 0.00$, NES = 1.86), and Fanconi pathways ($P = 0.00$, NES = 1.84) in ER$^-$/PR$^+$ tumors. Upregulation of interferon alpha, beta ($P = 0.0$, NES = 2.12) gamma signaling ($P = 0.0018$, NES = 1.77) and antigen presentation pathways ($P = 0.0$, NES = 2.12) was identified in the worse survival group, ER$^+$/PR$^-$. Hormone receptor status in HGSC is heterogeneous. PR receptor loss occurs during tumor evolution between normal FTE and STIC. Progesterone receptor expression confers improved OS driven by an increase in mitotic activity and suppression in interferon beta and gamma signaling.

**Conclusion:**
Objective: *MLH1* gene methylation is the main cause for sporadic microsatellite instability-high (MSI-H) endometrial cancer and is one of the most common molecular changes seen in endometrial cancer. It is well established that environmental influences such as nutritional state can have an impact on gene methylation. We hypothesized that environmental factors were associated with *MLH1*-methylated endometrial cancers.

Method: A cohort of patients with sporadic microsatellite-stable (MSS) and *MLH1*-methylated MSI-H sporadic endometrial tumors was retrospectively identified following the usual clinical evaluation for Lynch syndrome. Patients with suspected Lynch syndrome based on this initial screening were excluded. Clinical and pathology characteristics were identified by review of the medical record and were compared across groups using comparative statistics.

Results: A total of 463 patients were included; 349 (75%) of tumors were MSS, and 114 (25%) were sporadic *MLH1*-methylated, MSI-high. Patients with MLH1-methylated tumors were significantly older than those with MSS tumors (65 vs 58 years, *P* < 0.001). *MLH1*-methylated tumors were more often grade 3 (14% vs 5%, *P* < 0.001) and more often had lymphatic/vascular space invasion (LVSI) (42% vs 27%, *P* = 0.003). There were no differences in race, BMI, histology, or myometrial invasion across groups. Further analyses of environmental factors were performed after stratifying endometrioid tumors into low (grades 1–2) and high grade (grade 3). Patients with low-grade, *MLH1*-methylated, MSI-high tumors were significantly older at diagnosis (65 vs 57 years, *P* < 0.001), but had no difference in mean BMI. Alternatively, patients with high-grade, *MLH1*-methylated, MSI-high tumors had significantly higher BMIs (36 vs 28 kg/m², *P* = 0.02), but no difference in mean age. See Table 1.

Conclusion: The relationship of endometrioid grade with environmental characteristics is complex. While causality cannot be certain, these data suggest that the environmental impact of obesity may promote *MLH1* methylation, which may be linked with increased prevalence of grade 3 disease and LVSI. A provocative hypothesis moving forward is that weight loss could induce a “molecular switch” to alter the histologic and molecular characteristics of an endometrial tumor.
Table 1.

| Objective: Somatic CTNNB1 mutations have been associated with worse recurrence-free survival (RFS) in low-grade, early-stage endometrial cancer patients. We hypothesized that the use of current adjuvant therapy strategies would improve survival outcomes in CTNNB1-mutant early-stage endometrial cancer patients. |
| Method: Patients with stage I endometrioid endometrial cancer who received care at our institution were included in this study. Demographic and clinical information was obtained by review of the electronic medical record. CTNNB1 mutation status was determined using either next-generation sequencing panels or focused Sanger sequencing of exon 3 of the CTNNB1 gene. Comparative statistics were used to compare baseline characteristics, and Kaplan-Meier product limit estimator was used to determine RFS. |
Results: A total of 253 stage I endometrial cancer patients were identified. Of these, 45 (18%) had CTNNB1 mutations. In patients with low-risk endometrial cancer (no LVSI, no or superficial myometrial invasion less than 50% myometrial thickness, grade 1–2) who did not receive adjuvant therapy, CTNNB1 mutation status was not associated with significantly worse RFS (8.1 vs 11.3 years, \( P = 0.64 \)). However, in patients with deep myometrial invasion and/or LVSI with any histologic grade (n = 71), the presence of a CTNNB1 mutation was associated with shorter RFS (2.4 vs 8.5 years, \( P = 0.01 \)). Furthermore, those patients with somatic CTNNB1 mutations who did not receive adjuvant therapy demonstrated the worst RFS (Table 1).

Of the 7 patients with somatic CTNNB1 mutations who received adjuvant therapy, all received radiation (3 brachytherapy only, 2 pelvic radiation and brachytherapy).

Conclusion: In stage I endometrioid endometrial cancer patients with intermediate risk factors, treatment of patients whose tumors harbor CTNNB1 mutations resulted in improved RFS. Molecular characteristics including CTNNB1 mutation status should be incorporated into adjuvant therapy treatment algorithms. Prospective trials such as PORTEC4a can help elucidate which adjuvant therapies are most beneficial.

Table 1.

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1245 - Poster Session
Gut microbial diversity and genus-level differences identified in cervical cancer patients versus age and BMI matched healthy controls
T.T. Simsa, L.E. Colberta, J. Zheng2, K.L. Hoffmana, L.M. Ramondettaa, A.A. Jazaeri2, M. Frumovitza, A. Jhingrana, K.M. Schmeler2, C.R. Daniel-MacDougalla and A.H. Kloppa. "The University of Texas MD Anderson Cancer Center, Houston, TX, USA, bBaylor College of Medicine, Houston, TX, USA

Objective: The gut microbiome is proposed to alter host immunity, affecting cancer risk and treatment outcomes in various malignancies. The impact of the gut microbiome on cervical cancer risk and progression has not been reported. The aim of this study was to characterize variations in fecal or gut microbiome between women with locally advanced cervical cancer and healthy controls.

Method: We characterized the 16S rDNA fecal microbiome in 43 cervical cancer patients and 68 healthy female controls. Controls, comparable in regard to age and BMI, were derived from the medical center catchment area. Shannon diversity index (SDI) was used to evaluate alpha (within sample) diversity. Beta (between sample) diversity was examined using principal coordinate analysis (PCoA) of weighted Unifrac distances. Relative abundance of specific operational taxonomic units (OTUs) and genera was compared across samples using Mann Whitney \( U \) test with FDR-adjusted \( P \) values and linear discriminant analysis effect size (LEfSe). Because of observed variations in diversity with age, associations were assessed by age group strata (>45 vs ≤45 years).

Results: In the age 45 years and older group, patients with cervical cancer had higher \( \alpha \)-diversity than healthy controls (\( P = 0.0022 \)), but no differences were observed among the under 45 years age group. Overall \( \beta \)-diversity or microbiota community composition (weighted Unifrac, \( P = 0.001 \)) significantly differed between cervical cancer patients and controls. Based on age- and BMI-adjusted LEfSe analysis, multiple taxa were significantly associated with cervical cancer versus control status. Ezakiella, Porphyromonas, and Dialister were significantly enriched in cervical cancer samples, while Bacteroides, Alistipes, and members of the Lachnospiracea family were significantly enriched in controls (\( P < 0.05 \), LDA score >3). See Figure 1.

Conclusion: Our study demonstrates distinct differences in gut microbiota diversity and composition between cervical cancer patients and controls. Differential associations within the gut microbiome of older versus younger women may reflect
etiologic/clinical differences in these two groups. These findings provide rationale for further study of the gut microbiome in cervical cancer.

**Fig. 1.** A) Alpha Diversity, as assessed by Shannon Diversity in cervical cancer patient’s vs. controls, stratified by age group (45 y/o). B) LEfSe analysis adjusted for age and BMI strata demonstrates significant compositional differences across a range of taxa in cervical cancer patients (green) vs. controls (red). Only genera meeting a linear discriminant analysis score threshold >3 and \( p<0.05 \) are shown. C) Beta diversity, as assessed by weighted UniFrac, demonstrates significant compositional differences at the community level in cervical cancer patients vs. controls among both age groups.

1246 - Poster Session
Total abdominal ultra-rapid flash irradiation decreases gastrointestinal toxicity compared to conventional radiation
K. Levy\(^a\), M. Rafat\(^b\), K. Casey\(^c\) and E. Rankin\(^a\). "Stanford University School of Medicine, Stanford, CA, USA, "Vanderbilt University, Nashville, TN, USA, "Stanford University, Stanford, CA, USA

**Objective:** Total abdominal irradiation (TAI) in ovarian cancer treatment is limited due to gastrointestinal toxicity. Ultra-rapid FLASH irradiation spares normal tissues from toxic radiation effects, which suggests this may be an effective strategy to reduce complications of radiotherapy while maintaining antitumor control. We developed a FLASH irradiation system for mice using a linear accelerator that delivers large doses of radiation in a single beam in <500 ms. Conventional radiotherapy delivers a dose rate of 3–4 Gy/minute, while FLASH delivers a dose rate of >40 Gy/second. Our objective is to deliver TAI using FLASH, assess normal tissue toxicity, and evaluate the potential for tumor control in a mouse model of ovarian cancer.

**Method:** Female C57BL/6 mice received TAI using FLASH and conventional (CONV) radiation at 8.5 Gy, 10.5 Gy, and 12 Gy. Normal tissue toxicity was determined by measuring body weights, stool counts, laboratory analysis, histological analysis, and survival.

**Results:** Unirradiated controls and cohorts receiving FLASH-TAI or CONV-TAI at 8.5 Gy, 10.5 Gy, and 12 Gy were analyzed. At 5 days post-TAI, stool production was unchanged from controls in FLASH mice; however, stool production decreased by 50% after 8.5 Gy and 63% after 12 Gy in the CONV cohorts. FLASH preserves villus height in the duodenum and jejunum and protects against the formation of submucosal edema throughout the small intestine at 5 days post-TAI. In the survival analysis, all of the 12-Gy CONV mice died by 9 days post-TAI, whereas 75% of the 12-Gy FLASH mice were alive at 11 months. There
was no evidence of long-term hematopoietic toxicity or significant difference in weight in the surviving cohorts at 12 months post-TAI. Exploratory necropsy of surviving cohorts at 12 months post-TAI demonstrated secondary proximal duodenal adenocarcinomas in 25% of the aged CONV cohorts. These gastrointestinal tumors were not found in any of the aged unirradiated controls or FLASH cohorts.

**Conclusion:** These data demonstrate FLASH protects against death from TAI, improves the epithelial integrity and function of the small intestine following TAI compared to conventional radiation, and may have a protective effect against secondary gastrointestinal tumors from radiation in a preclinical model. Our discovery that FLASH is a safe strategy to deliver effective doses of total abdominal radiation potentially identifies a new opportunity to utilize FLASH-TAI for treatment of ovarian peritoneal metastases.

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**1247 - Poster Session**  
**Alterations of bone metabolism of patients with primary and platinum-sensitive recurrent tuboovarian carcinoma induced by platinum-based chemotherapy with and without bevacizumab**  

**Objective:** During the last two decades, survival rates of patients with tuboovarian carcinoma (TOC) have markedly improved, now highlighting the importance of late sequelae of antineoplastic treatment. Direct effects of chemotherapy on the bone metabolism of TOC patients are only poorly elucidated so far. The present translational project sought to gain detailed information on the influence of platinum-based chemotherapy with or without bevacizumab (Bev) on the expression of various bone markers in patients with primary or platinum-sensitive recurrent TOC.

**Method:** A total of 85 TOC patients receiving platinum-based chemotherapy apart from a clinical trial were analyzed; 16 patients also received Bev. The following bone markers were determined at baseline and prior to every subsequent chemotherapy cycle (C1-C6): C-terminal telopeptide of type I collagen (ICTP) as a marker of osteoclast function, N-terminal propeptide of type I collagen (P1NP) as a marker of osteoblast function, and alkaline phosphatase (AP). Results for C2-6 were calculated as percentage of baseline values prior to C1. Changes of bone markers over time were analyzed using repeated measures ANOVA with \( P < 0.05 \) indicating statistical significance for all statistical analyses.

**Results:** A total of 350 chemotherapy cycles without and 87 with Bev were evaluated. In both groups of patients, ICTP showed a constant decline beyond C2 to 76% of the baseline value without and 56% of the baseline value with Bev at C6. For chemotherapy alone, P1NP decreased immediately after C1 showing a plateau effect beyond C3 with 85% of the baseline level at minimum. For chemotherapy with Bev, P1NP values declined during the whole course of chemotherapy reaching 66% of the baseline level at C6 without any plateau effect. Adding Bev to chemotherapy resulted in a significantly stronger effect on both parameters (ICTP, \( P = 0.043 \); P1NP, \( P = 0.002 \)). For AP, no significant changes were detected.

**Conclusion:** Platinum-based chemotherapy for primary and platinum-sensitive recurrent TOC resulted in a significant inhibition of osteoblast and (secondarily) osteoclast activity. This is the first study demonstrating that addition of Bev is likely to both increase and accelerate the negative effect of platinum-based chemotherapy on bone metabolism of patients with TOC. Prospective clinical trials adding osteoprotective agents to chemotherapy for TOC are thus strongly recommended.

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**1248 - Poster Session**  
**Understanding the impact of chemotherapy on the immune landscape of high-grade serous ovarian cancer (HGSOC)**  
K. LaVignea, J. Benhamidaa, J. Youngb, O. Zivanovicc, D.S. Chi1, A. Snydera and T. Hollmanna. *aMemorial Sloan Kettering Cancer Center, New York, NY, USA, bTexas Tech University Health Sciences Center, School of Medicine, Lubbock, TX, USA*

**Objective:** The purpose of our study is to quantitatively and spatially characterize the expression of repressive and stimulatory immune cell proteins across immune cells and to compare the density of immune cell populations before and after chemotherapy.

**Method:** A total of 48 paired tumors were identified from patients with high-grade serous ovarian cancer (HGSOC). Nine patients had adequate tissue samples available before and after treatment for analysis. Samples were acquired prior to neoadjuvant chemotherapy (NACT) and at interval debulking surgery. Each patient had three 7-color multiplex staining panels performed on pre- and post-therapy samples to assess effector T cells (Ki-67, CD8, PD-1, FoxP3, LAG3, AE1/AE3), macrophages (CD68, CD3, C3aR, PDL1, IDO, AE1/AE3), and regulatory T cells (CD3, CD8, GITR, ICOS, FoxP3, AE1/AE3).
Multiplex stained slides were imaged using the Vectra Multispectral Imaging System (Perkin Elmer). Cell segmentation and signal thresholding were performed using the Indica Labs Halo image analysis platform. Data analysis was done in R, and hierarchical clustering was performed using Euclidean distance and average linkage.

**Results:** There is a small overall increase in CD8+ T cells following chemotherapy. The targetable T cell exhaustion markers PD-1 and lag3 were seen in CD4 and CD8 T cell populations both before and after chemotherapy without significant changes. ICOS co-expression is seen in the CD3+ population, with higher expression in the nonregulatory T cell population (CD3+FoxP3-). Minimal expression of GITR is seen on the T cell populations. When comparing changes in the pre- and post-treatment biopsies, hierarchical clustering shows a subset of patients with an increase in CD8+PD1-LAG3-Mib- T cells and another population with a decrease in CD68+C3aR+ macrophages following chemotherapy. BRCA status correlates to a subset of patients with increased PDL1+ expression following NACT. See Figure 1.

**Conclusion:** Chemotherapy does not cause uniform change in immune cell populations overall, but does cause changes in subsets of patients. Increases in PD-L1 expression among BRCA+ patients following NACT could provide a rationale for checkpoint blockade at the time of NACT. ICOS is seen preferentially expressed in the nonregulatory T cell population. This could justify the rational use of ICOS agonism in the treatment of HGSOC.

Fig. 1.
1249 - Poster Session
Large-scale proteomic analysis of mechanisms of response to anti-angiogenesis therapy in CTNNB1-mutated endometrial cancers
E.A. Kawaler*, A.A. Bergerb, K.V. Rugglesc and D.A. Levinec. *New York University, New York, NY, USA, bNew York University School of Medicine, New York, NY, USA, cNYU Langone Medical Center, New York, NY, USA, dNYU Langone Health, New York, NY, USA

Objective: The aim of this study was to determine potential proteomic mechanisms by which activating CTNNB1 exon 3 mutations may drive angiogenesis in endometrial cancer (EC). CN-low and MSI endometrioid EC patients with these mutations tend to have poorer outcomes than wildtype (WT) patients. β-catenin is thought to increase VEGFA expression and tumor vascularity. Results from clinical trial GOG-86P suggested an improved outcome for patients with CTNNB1 mutations treated with bevacizumab (Bev), an antiangiogenic drug that targets VEGFA.

Method: We analyzed the portion of endometrial CPTAC data consisting of CN-low and MSI endometrioid tumors to build a profile of CTNNB1 somatic mutations, RNA expression, and β-catenin protein expression. We evaluated the association between VEGFA and β-catenin levels. We also identified differentially expressed proteins involved in β-catenin signaling.

Results: Of the 63 CN-low and MSI tumors, 18 (29%) had CTNNB1 exon 3 mutations and exhibited increased β-catenin protein levels (P < 0.01) without a significant change in CTNNB1 RNA expression. Although VEGFA RNA and protein levels were not significantly different between WT and CTNNB1-mutated tumors, we did identify increased protein levels of matrix metalloproteinases MMP2 and MMP7 (P < 0.01 for each), which are regulated through the Wnt/β-catenin signaling pathway and activate VEGFA.

Conclusion: We have shown in silico that CTNNB1 exon 3 mutations are consistently associated with increased β-catenin protein expression but not increased VEGFA expression. However, CTNNB1 mutations are associated with increased expression of MMP2 and MMP7, which regulate VEGFA activity. Ongoing in vitro studies will test the hypothesis that patients with activating CTNNB1 mutations have increased neoangiogenesis because of actions of increased MMPs. MMP regulation of VEGFA may lead to alternative splicing and cleavage rather than extensive modulation of overall VEGFA protein levels, explaining both the lack of VEGFA upregulation and the improved outcomes in the GOG-86P patients treated with Bev.

1250 - Poster Session
Impact of ethnicity and obesity on the uterine microbiome in women and mice with endometrial cancer

Objective: Obesity and race are known to have a negative impact on clinical outcomes in endometrial cancer (EC). We sought to evaluate the microbiota of murine and human ECs and to assess for variations by obesity and race status.

Method: Banked tumor specimens of patients undergoing hysterectomy for endometrioid and serous ECs were identified. Tumors were analyzed from African-American and Caucasian patients and stratified as obese (BMI ≥30 kg/m²) or nonobese (BMI <30 kg/m²). Endometrioid ECs from obese and nonobese LKB1fl/flp53fl/fl mice were also compared. The microbiota of the murine and human ECs were characterized by bacterial 16S rRNA high-throughput sequencing, and data were analyzed using MicrobiomeAnalyst.

Results: A total of 92 human EC specimens were evaluated. Of these, 21 were from African-American (23%) and 71 from Caucasian (77%) patients. Median age was 67.5 years. The majority of women were obese (n = 73, 79%). Tumor grade was evenly distributed with 31 grade 1 (34%), 25 grade 2 (27%), and 36 grade 3 (39%). When we analyzed by race, obesity status, and histology, we observed significant differences in EC microbiota composition. Firmicutes and actinobacteria phyla abundance was higher among endometrioid ECs in African-American women than that in Caucasian women (P < 0.001). Abundance of actinobacteria (P = 0.0062), bacteroidetes (P = 0.48), firmicutes (P = 0.003), and proteobacteria (P < 0.001) was increased in endometrioid ECs in obese versus nonobese women. When comparing endometrioid ECs from obese African-American versus obese Caucasian women, genus level abundance of brachybacterium (P = 0.009) and hyphomictobium (P < 0.001) were lower and flavobacterium (P = 0.26), geobacillus (P < 0.001), ralstonia (P < 0.001), and stenotrophomonas (P = 0.007) were higher. Abundance of firmicutes-differentiated endometrioid versus serous ECs (P < 0.008). Overlap was seen in obesity-associated microbiota between mice and women that included Delftia and Pseudomonas.
Conclusion: Distinct microbiota profiles were found between ECs of obese and nonobese African-American and Caucasian women, with obesity-associated microbiota shared between EC-afflicted mice and women. Better understanding of the interrelationship of obesity and race on the EC microbiota may provide critical insight into the disparate clinical outcomes between African-American and Caucasian women with EC.

1251 - Poster Session
Endometriotic milieu enhances proliferation of ovarian cells and might cause malignant transformation
N. Bou Zgheib, M. Parsons, A. Huck and N. Santanam. *Marshall University School of Medicine, Huntington, WV, USA, †Marshall University, Huntington, WV, USA

Objective: Peritoneal fluid (PF) from women with endometriosis causes gene changes in ovarian cells and might lead to cancer transformation. Factors leading to this link between endometriosis and risk to ovarian cancer are still unclear. We sought to investigate the effect of endometriotic peritoneal fluid (endoPF) on proliferation and transformation of ovarian cancer cells.

Method: After Institutional Review Board approval, PF was collected from patients with and without endometriosis undergoing gynecological surgery. Human clear cell carcinoma cells (TOV-21G), normal ovarian epithelial cell line (IOSE 364), and ovarian endometrioid adenocarcinoma cell line (A2780/CP70) were treated with different volumes of normal and endoPF, and proliferation was measured using an MTT assay after 48 or 96 hours. A Human Cancer Inflammation and Immunity Crosstalk RT²Profiler PCR Array was used to assess gene variation in the ovarian cells treated with 1 or 10% PF or endoPF and compared against cells treated with just media. Expression data were subject to background correction and normalization using the RMA algorithm implemented in Affymetrix Expression Console. Genes differentially expressed between control PF and endoPF treated cells were subject to pathway analysis.

Results: TOV-21G cells treated with various percentages of control PF and endoPF during 48- and 96-hour periods showed a differential proliferation pattern. Moreover, there was a time-dependent increase in proliferation of TOV-21G cells with a more prominent (>2-fold) proliferation in cells treated with endoPF compared to control PF at similar concentrations. RT² Human Cancer Array results from IOSE, A2780/CP70, and TOV-21G cells treated with control and endoPF showed significant increase in several cancer related genes CCL20, CXCL5, CXCR4, HIF1A, HLA-B, KITLG, SPP1, TNF. The TOV-21G cells treated with endoPF had the highest induction of these genes. These genes include significant representation of the CXCR4-CXCL12 axis molecular signaling pathway.

Conclusion: Our results, taken together, show that PF from women with endometriosis causes a proliferation of ovarian cells and might play a role in malignant transformation. The role of endoPF will need to be further explored in future studies to determine what factors are involved in growth promotion and the role of the CXCR4-CXCL12 axis.

1252 - Poster Session
Preparing for the unexpected: Panel-based testing of patients with uterine carcinoma reveals actionable variants in non-canonical genes

Objective: A new paradigm is emerging for genetic testing of patients with carcinoma of the uterus (UC). With next-generation sequencing (NGS), clinicians can choose to test only a limited number of genes such as the five Lynch syndrome (LS) genes involved in mismatch repair and PTEN, or a more comprehensive panel of cancer genes, for no additional cost. The clinical utility of genes such as the LS genes and PTEN is established. National Comprehensive Cancer Network (NCCN) guidelines, however, indicate that additional genes not typically associated with UC are also actionable for prevention of other malignancies. We report data on the diagnostic yield in UC patients using a comprehensive multigene panel of 80+ genes and the implications for clinical management.

Method: We studied 6,582 consecutive patients with UC who were referred for testing at Invitae. Genomic DNA variants were identified using an NGS-based hereditary cancer panel of up to 83 genes; panel size was determined by the ordering clinician. Patients’ medical histories were obtained from test forms and were de-identified for this analysis.

Results: A Pathogenic or Likely Pathogenic (P/LP) variant was identified in 1,031 (15%) patients. Of the mutation carriers, 54% had a P/LP variant in PTEN or the LS genes, while 39% had a P/LP variant in other cancer-risk genes, including ATM,
BRCA1, BRCA2, BRIP1, CHEK2, PALB2, TP53, and others (excluding MUTYH heterozygotes). The clinical utility of these germline P/LP variants includes 32% with clinical trial eligibility, 52% with eligibility for FDA-approved therapies, >90% with management recommendations based on NCCN guidelines, and cascade testing of at-risk family members.

Conclusion: Multigene panel testing identified P/LP variants in genes with published management recommendations that would have been missed by a targeted UC gene panel. Over 80% of patients with P/LP germline variants were potentially eligible for precision therapeutic intervention based in part on their germline test results. These data highlight the benefit of comprehensive gene panels for the evaluation of UC and the impact these results can have on cancer intervention, surveillance, and family variant cascade testing protocols.

1253 - Poster Session
ARID1A: A new synthetic lethality partner to PARP inhibitors in the treatment of ovarian clear cell cancer  
V.A. Yakovlev, S.A. Sullivan, L.A. Rubinsak, E.C. Fields and S.M. Temkin. Virginia Commonwealth University, Richmond, VA, USA

Objective: ARID1A is a tumor suppressor gene mutated in >50% of ovarian clear-cell carcinomas (OCCC). Mutated or downregulated ARID1A significantly compromises homologous recombination repair (HRR) of DNA double-strand breaks. We hypothesize that treatment with PARP inhibitors (PARPi) will activate synthetic lethality (SL) in OCCC with ARID1A mutations and sensitize them to DNA-damaging agents (DDA) such as radiation therapy.

Method: Wildtype ARID1A ovarian cancer cell lines (OVCA-429, CAOV-3) and OCCC cell line with mutant ARID1A (TOV-21G) were treated with PARPi: ABT-888 (10 mM) or olaparib (1 mM) and subjected to clonogenic assay with radiation doses 0, 2, 4, 6, and 8 Gy. In OVCA-429 and CAOV-3 cell lines, ARID1A expression was inhibited by 100 nM of siRNA by transfection approach (QIAGEN). DNA HRR activity was measured by DR-GFP repair assay. PI3K inhibitor LY294002 (Sigma) was used in 10 mM concentration.

Results: TOV-21G showed significantly lower level of DNA HRR compared to OVCA-429 and CAOV-3 cell lines. Downregulation of ARID1A expression in OVCA-429 and CAOV-3 by transfection dramatically reduced DNA HRR activity in both cell lines (0.24 ± 0.035-fold and 0.16 ± 0.028-fold, respectively, P < 0.001). Clonogenic assay revealed that only the TOV-21G cell line demonstrated effect of SL in response to treatment with PARPi; survival fractions for ABT-888 and olaparib treatment were 0.36 ± 0.061 (P < 0.001) and 0.2 ± 0.017, respectively (P < 0.0001), compared with nontreated control. The addition of radiation significantly enhanced the activity of PARPi in ARID1A-deficient cells: survival fractions for combinations of ABT-888+2Gy and Olaparib+2Gy were 0.041 ± 0.0045 (P < 0.0001) and 0.018 ± 0.0043 (P < 0.0001), respectively, compared with subsequent PARPi treatment with no radiation (see Figure 1). Pretreatment with PI3K inhibitor LY294002 restored DNA HRR in ARID1A-mutant or -depleted cell lines and attenuated effect of SL in TOV-21G cell line treated with PARPi with or without radiation (see Figure 1).

Conclusion: Mutation and inactivation of ARID1A significantly attenuates DNA HRR through the PI3K-dependent way. Synergy with radiation therapy was observed. Applying PARPi for activation of SL and sensitization to DDA is a promising treatment approach for OCCC with ARID1A mutation.
The prevent ovarian cancer program (POCP): Identification of ovarian cancer-associated mutations in self-referring women from low-risk families


Objective: The aim of this study was to perform comprehensive germline testing and genetic counselling in women with a first-degree relative (FDR) who died from ovarian high-grade serous carcinoma (HGSC) but did not receive BRCA1/2 genetic testing.

Method: Potential participants self-identified in response to an ongoing educational campaign in Ontario Canada, followed by eligibility screening, confirmation of diagnosis, panel sequencing for BRCA1/2 and other established/emerging hereditary cancer genes, and pre- and post-test genetic counselling. Participants indicated whether they prefer to receive results for BRCA1/2 only or for additional panel genes. Clinical follow-up and risk-reducing surgery are facilitated based on genetic test results.

Results: Since the Prevent Ovarian Cancer Program website was launched in May 2015, 742 women from across Ontario have registered and 409 have officially enrolled following confirmation of diagnosis in their deceased FDR. Median age at consent was 53 years (range 24–80 years); 70% reported only 1 case of HGSC in the family and 94% did not meet provincial testing criteria based on risk estimation models. Of those participants who completed pre-test counselling, 94% pursued genetic testing, and 88% indicated that they would like to receive results for all panel genes. Panel-based genetic testing has been completed on blood samples from 373 unaffected participants from 325 families, with an overall pathogenic mutation rate of 10%. Of 13 participants with pathogenic mutations in BRCA1/2, RAD51C, or BRI1, 7 (54%) reported only 1 case of HGSC in the family and 12 (92%) would not be eligible for provincial testing. Pathogenic mutations were observed most frequently in participants <age 50 years, but were detected up to 70 years of age. Mutation rates were highest for participants with an FDR diagnosed at a younger age (18% for <50 years vs 7% for 70+ years). Preliminary analysis of tumor samples from corresponding deceased FDRs has revealed the presence of the same mutation in 5/8 (63%) of cases tested to date.
**Conclusion:** The Prevent Ovarian Cancer Program is successfully targeting a population of women who may be at increased risk for HGSOC, and cancer-predisposing mutations have been identified in women who would not otherwise be tested.

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**1255 - Poster Session**

**Loss of heterozygosity among short-term ovarian cancer survivors with germline BRCA1/2 mutations**

J. Fehniger, F. Dao, N. Olvera, D. Gerber and D.A. Levine. NYU Langone Health, New York, NY, USA

**Objective:** Ovarian cancer patients with germline BRCA1/2 mutations (gBRCAmut) often have improved survival compared to patients without mutations. We characterized the molecular features of tumors from gBRCAmut patients with short-term compared to longer term survival.

**Method:** DNA was extracted from FFPE tumor and normal samples collected at the time of surgery for gBRCAmut high-grade serous ovarian cancer (HGSOC) patients from a single institution. Short-term survivors (STS) were defined as those having a PFS <18 months and compared with longer term survivors (LTS) who had a PFS >36 months. gBRCAmut were confirmed using Sanger sequencing and targeted next-generation sequencing (NGS) of a panel of over 500 cancer-relevant genes. Fragment analysis was performed to identify loss of heterozygosity (LOH) for patients with frameshift mutations. Molecular data were correlated with clinicopathologic characteristics.

**Results:** Of the 16 patients with sufficient tumor available for this study, 9 were STS and 7 LTS, with median PFS of 16 (range 10–18) and 57 (range 43–92) months, respectively. There were no differences in age at diagnosis, stage, rates of neoadjuvant chemotherapy, and optimal cytoreduction between STS and LTS. Somatic TP53 mutations were identified in all 15 patients who underwent targeted NGS. Of 11 patients with evaluable LOH data, LOH was present in 6/7 (86%) STS and 4/4 (100%) LTS. Among STS, additional mutations were detected in the RB (2), HRD (4), and PI3K/RAS (4) pathways more frequently than LTS (RB, 1; HRD, 1; and PI3K/RAS, 1). The 1 tumor without LOH was from a BRCA2 gmut patient who developed recurrent disease 11 months after diagnosis.

**Conclusion:** Among a small cohort of gBRCAmut patients with HGSOC, no differences in rates of TP53 mut, LOH, or other somatic mutations were found to account for short-term compared to longer term survival. LOH was absent in 1 patient with poor STS, and larger sample sizes may help to determine the contribution of LOH to tumor behavior in HGSOC patients with gBRCAmut.

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**1256 - Poster Session**

**Streamlined next-generation sequencing panel provides comprehensive molecular assessment of mismatch repair deficiency in endometrial and non-serous ovarian cancer**


1. University Health Network, Princess Margaret Hospital, Toronto, ON, Canada, 2Sunnybrook Cancer Center/University of Toronto, Toronto, ON, Canada, 3University of Toronto, Toronto, ON, Canada, 4Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

**Objective:** The aim of this study was to determine the molecular determinants of mismatch repair (MMR) deficiency in endometrial (EC) and nonserous, nonmucinous ovarian carcinomas (OC) using a one-stop integrative next-generation sequencing (NGS) panel.

**Method:** Women with newly diagnosed EC and nonserous/nonmucinous OC were recruited at 3 cancer centers in Ontario, Canada, between 2015 and 2018 in a prospective study. Whole blood was collected, and tumors were reflexively assessed for MMR protein expression by immunohistochemistry. Clinical genetic testing was offered to women with MMR-deficient (MMRd) tumors or a family history of Lynch syndrome-associated cancers. Tumor DNA was extracted from macromilled MMRd cases and MMR-intact (MMRi) controls following pathology review. Matched tumor-normal samples were run on a custom NGS panel to identify germline and somatic mutations, copy number variants, rearrangements, and promoter methylation in MMR and associated genes.

**Results:** We recruited a total of 886 participants, including 670 EC, 185 OC, and 31 synchronous cases of EC/OC; of these, 161 EC (24%), 18 OC (9.7%), and 11 synchronous (35.5%) cases were MMRd. We have completed NGS panel analysis for 24 EC cases to date, including 22 MMRd and 2 MMRi. An explanation for the observed MMR phenotype was found in 21/22 (95%) deficient cases, including 12/12 MLH1−/PMS2− (10 somatic methylation, 2 bi-allelic somatic mutation), 2/2 PMS2− (1 germline...
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mutation, 1 bi-allelic somatic mutation), 2/2 MSH6− (germline mutations) and 4/5 MSH2−/MSH6− (2 germline mutation, 2 bi-allelic somatic mutation). A case deficient for all 4 MMR proteins harbored a germline pathogenic MSH2 mutation, a germline PMS2 deletion, and somatic MLH1 methylation. Concordance between clinical and research panel sequencing results was 91%. Previously reported somatic pathogenic POLE mutations (P286R, V411L, L424V, S297F) were identified in 4/24 (17%) cases. Somatic pathogenic TP53 mutations were also observed in 4 cases; these were distinct from POLE-mutant cases and were limited to those with MMR loss.

**Conclusion:** Use of our custom NGS panel allows for the streamlined assessment of hereditary and somatic causes of MMR deficiency in gynecologic cancer, and reveals coexistence of MMR loss and POLE and/or TP53 mutation in some EC cases.

1257 - Poster Session

**AXL in metastatic ovarian cancer tumors is a targetable biomarker associated with chemoresistance and poor prognosis**

M.M. Mullen\(^a\), J.M. Quinn\(^b\), M. Greenwade\(^b\), G. Opara\(^a\), H. Beck-Noia\(^a\), I.S. Hagemann\(^a\), A.R. Hagemann\(^a\), L.M. Kuroki\(^a\), C.K. McCourt\(^a\), P.H. Thaker\(^a\), M.A. Powell\(^a\), D.G. Mutch\(^a\) and K.C. Fuh\(^a\). \(^a\)Washington University School of Medicine in St. Louis, St. Louis, MO, USA, \(^b\)The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, \(^c\)Women & Infants Hospital, Brown University, Providence, RI, USA

**Objective:** The aim of this study was to determine the association between AXL expression in primary and metastatic tumor samples and clinical outcomes, in order to establish a predictive and prognostic biomarker in ovarian cancer patients

**Method:** A tissue microarray was constructed with primary and metastatic tumors from patients with high-grade ovarian cancer collected at the time of debulking surgery. Each case was represented by up to 2 tumors depending on the presence and size of metastatic disease. Immunohistochemistry was used to measure AXL expression in tumor and associated stromal tissue. Chemoresistance was defined as recurrence within 6 months of treatment. Clinical data were collected from the electronic medical record.

**Results:** A total of 214 tumor samples were included from 139 patients: 122 primary and 92 metastatic sites, contributing to 85 matched samples. The majority of patients had stage III–IV disease (79%) and high-grade serous histology (78%) and did not receive neoadjuvant chemotherapy (88%). Fifty-four percent of patients had no gross residual disease, and 30% were optimally debulked to <1 cm of disease. Residual disease after cytoreductive surgery (HR = 3.26, 95% CI 1.50–7.06) and high AXL expression in metastatic tumor samples (HR = 3.65, 95% CI 1.00–13.30) were predictive of chemoresistance. Accordingly, high versus low AXL expression in metastases was associated with a decreased platinum-free interval (PFI, 5.92 vs 15.9 months, \(P = 0.03\)) as well as decreased PFS (11.6 vs 18.8 months, \(P = 0.02\)). Multivariate analyses demonstrated AXL expression in metastatic tumors was also associated with decreased OS (\(P = 0.04\)). Specifically, patients with OS <3 years had significantly more AXL expression in their metastases than those with OS >5 years (\(P < 0.001\)). Increased AXL expression in primary tumor samples was predictive of metastatic disease or stage III–IV disease (\(P = 0.002\)) but was not associated with survival.

**Conclusion:** AXL expression in metastatic sites compared to primary ovarian tumor predicts poor response to chemotherapy and decreased survival. Based on these data, AXL should be further characterized as a predictive and prognostic biomarker. Metastatic tumor may also be the preferred sample for validation of other biomarkers.

1258 - Poster Session

**The function of matrix metalloproteinase 1 in ovarian cancer**

C. Hobbs\(^a\), Z. Huang\(^b\), S. Murphy\(^b\) and A. Berchuck\(^b\). \(^a\)Duke University School of Medicine, Durham, NC, USA, \(^b\)Duke University Medical Center, Durham, NC, USA

**Objective:** It is known that an acidic tumor microenvironment is favorable for cancer cell metastasis largely because of the dysregulation of extracellular matrix (ECM) proteins. Furthermore, we have previously demonstrated that recurrent ovarian cancer (OC) has a higher expression of matrix metalloproteinase 1 (MMP1) when compared with the primary OC tumor from the same patients. The objectives of this study were to investigate the function of MMP1 in OC and to determine whether MMP1 expression changes with varying pH and how these changes affect proliferation and invasiveness in OC.
Method: OC cells (CAOV2) were stably transduced with MMP1-specific shRNA or a control, nonsilencing shRNA using a lentiviral system. shRNA MMP1 knockdown in T293 cells was used to produce conditioned medium with low expression of MMP1. Cell proliferation, invasion, and chemosensitivity were evaluated with MMP1 knockdown OC cells and with OC cells cultured in conditioned medium with low expression of MMP1. OC cells cultured in acidic, basic, and neutral pH medium were evaluated for expression of MMP1, proliferation, and invasion.

Results: OC cells with knockdown expression of MMP1 were less proliferative ($P = 1.08^{-5}$) and more chemosensitive ($P = 0.032$), and showed decreased invasion compared to control cells, although the changes in invasion were not statistically significant ($P = 0.22$). Paradoxically, OC cells cultured in conditioned medium with low expression of MMP1 showed increased invasion ($P = 0.018$) and decreased chemosensitivity ($P = 2.3^{-4}$). OC cells cultured in acidic conditions (pH = 6.2) showed elevated expression of MMP1 ($P = 0.017$) accompanied by increased invasion ($P = 0.004$).

Conclusion: Our results suggest that there are striking differences in OC cell aggressiveness based on the source of MMP1, with diminished extracellular MMP1 associated with a more aggressive phenotype. Likewise, more acidic media also promoted aggressive behavior while enhancing intracellular MMP1 transcript levels. These data open the door for further investigation of the functional differences between MMP1 expressed within cancer cells and MMP1 present in the tumor microenvironment and the feasibility of therapeutic targeting of MMP1.

1259 - Poster Session
Focal adhesion kinase (FAK) may predict poor prognosis in endometrioid but not serous endometrial cancer
K.N. Taylor, M.T. McHale, D. Stupack and S.C. Plaxe. UCSD Rebecca and John Moores Cancer Center, La Jolla, CA, USA

Objective: FAK is a cytoplasmic tyrosine kinase that promotes tumor cell survival and invasion, with high protein levels linked to poor prognosis in endometrial cancer. The objective of this study was to evaluate whether FAK copy number alterations (CNAs), specifically amplifications, offered prognostic value beyond standard histopathology.

Method: Data were obtained from The Cancer Genome Atlas (TCGA) sequencing of uterine corpus endometrial carcinoma patient tumor pairs. The provisional dataset of 548 tumors was analyzed for CNAs in the FAK gene (PTK2) and for outcomes in a cohort of 242 patients with both CNA and mutational data. The TCGA PanCancer Atlas of 529 tumors was queried to determine an association between FAK CNAs and TCGA subtypes in endometrial cancer patients. The Fisher exact test was used to determine associations of genomic alterations. PFS and OS were determined using the Kaplan-Meier method and the log rank test.

Results: In the PanCancer Atlas cohort, the majority of patients (56%) were classified as copy-number high, whereas only seven patients (4%) were POLE ultramutated and 28 demonstrated microsatellite instability (16%). In the provisional dataset, there was no allelic loss of PTK2 by GISTIC. Sixty-eight patients (28%) displayed a gain of at least 1 copy of PTK2 by GISTIC. Among these, 43 patients (63%) had serous tumors, and most patients were stage I. Amplification of FAK demonstrated significant co-occurrence with TP53 mutation (log OR = 1.805, $P < 0.001$) and was mutually exclusive with PTEN mutation (log OR = $-1.232$, $P < 0.001$). PTK2 amplification was associated with decreased PFS ($P = 0.04$) and a trend toward decreased OS ($P = 0.09$). Surprisingly, PTK2 amplification suggested poor prognosis in the endometrioid group, with a trend toward decreased PFS and OS ($P = 0.06$ and $P = 0.09$, respectively), but not in patients with serous disease (see Figure 1).

Conclusion: The prognostic value of genomic alterations over histologic classification is increasingly recognized, particularly in endometrial cancer. Here we demonstrate that PTK2 amplification may uniquely identify a subset of patients with favorable histology but worse prognosis. As FAK is an actionable target, this finding could eventually lead to a novel treatment paradigm for some patients and warrants further study.
Fig. 1. Kaplan-Meier curves for progression-free survival (PFS) and overall survival (OS). Red line denotes samples with FAK copy number amplifications. Blue line denotes all other samples. FAK amplification trended toward with significantly worse PFS (p=0.066) and OS (p=0.092) in endometrioid tumors (Panels A and B, respectively). FAK amplification did not alter PFS (p=0.802) or OS (p=0.799) among serous tumors (Panels C and D, respectively).

1260 - Poster Session

**BRCA1/2** heterozygous truncating mutations lead to phenotypic changes in CRISPR/Cas9 mutated fallopian tube secretory epithelial cells


Womens Cancer Program/Cedars-Sinai Medical Center, Los Angeles, CA, USA, Cedars-Sinai Medical Center, Los Angeles, CA, USA

**Objective:** We sought to understand the phenotypic effects of different **BRCA1** and **BRCA2** truncating mutations in p53-mutated fallopian tube secretory epithelial cells (FT282).

**Method:** Cas9 was over-expressed in p53-mutated FT282 for efficient CRISPR/Cas9-mediated gene editing. Western blot confirmed ectopic mutant p53 and Cas9 expression. CRISPR/Cas9 was used to create truncating mutations in breast cancer cluster regions (BCCR) and ovarian cancer cluster regions (OCCR) in both **BRCA1** and **BRCA2** genes. OR10A4 (olfactory) gene knockout was the control. T7 endonuclease I assay confirmed mutations at targeted PAM sites. Immunofluorescence and flow cytometry (FC) analysis of γH2AX levels determined baseline level of DNA damage. All cell lines were clonally derived. We used DNA cloning and Sanger sequencing to identify clones with truncating mutations. qRT-PCR and FC analyses were used to evaluate **BRCA1/2** expression. Proliferation and drug sensitivity assays were used to characterize phenotypic effects of each mutation.

**Results:** Only heterozygous truncating mutations in **BRCA1** OCCR, **BRCA2** BCCR, and **BRCA2** OCCR regions survived selection. Interestingly, **BRCA1** BCCR clones did not survive, regardless of mutation type. Only OR10A4 survived with homozygous out-
127

of-frame (OOF) mutation. FC analyses of yH2AX revealed that cells with higher DNA damage had lower expression of BRCA1/2. All BRCA1/2 mutations led to non-sense-mediated decay. FC analyses confirmed that BRCA1 OCCR mutants decreased BRCA1 protein levels. Heterozygous BRCA1 OCCR and BRCA2 BCCR mutations led to diminished growth compared to control. BRCA2 OCCR OOF growth was the same as control. All BRCA1/2-mutated cells demonstrated resistance to olaparib (Table 1).

**Conclusion:** Heterozygous BRCA1/2 mutants demonstrated differences in growth rates. BCCR mutations had more severe phenotypic effects in both BRCA1 and BRCA2 genes. OCCR mutations had survival advantage, compared to BCCR mutations. This may explain epidemiological observations that different risks of breast versus ovarian cancer depend on mutation location. Diminished growth was likely secondary to genetic instability. Some alternative splice isoforms in BRCA1 have demonstrated therapeutic resistance to PARP inhibition, which might explain decreased olaparib sensitivity in our developed cells.

<table>
<thead>
<tr>
<th>BRCA1/2 Mutation</th>
<th>Sequencing</th>
<th>Nonsense Mediated Decay?</th>
<th>Diminished Growth Compared to Control?</th>
<th>Olaparib [IC50]</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR10A4 Control Cl. 4</td>
<td>Homozygous 8 base pair deletion</td>
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<td>N/A</td>
<td>13.2</td>
</tr>
<tr>
<td>BRCA1 OCCR Cl. 3</td>
<td>Heterozygous 1bp insertion (Out of Frame) 9bp deletion (In Frame)</td>
<td>Yes</td>
<td>Yes*</td>
<td>146.2</td>
</tr>
<tr>
<td>BRCA1 OCCR Cl. 4</td>
<td>Heterozygous 1bp insertion (Out of Frame) 9bp deletion (In Frame)</td>
<td>Yes</td>
<td>Yes*</td>
<td>216.8</td>
</tr>
<tr>
<td>BRCA1 BCCR</td>
<td>No clones survived this mutation</td>
<td>XXX</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>BRCA2 BCCR Cl. 4</td>
<td>Heterozygous Wild Type 12bp deletion (In Frame)</td>
<td>Yes</td>
<td>Yes, though not statistically significant</td>
<td>158.5</td>
</tr>
<tr>
<td>BRCA2 BCCR Cl. 5</td>
<td>Heterozygous Wild Type 2bp deletion (Out of Frame)</td>
<td>Yes</td>
<td>Yes*</td>
<td>44.3</td>
</tr>
<tr>
<td>BRCA2 OCCR Cl. 4</td>
<td>Heterozygous 21bp deletion (In Frame) 47bp deletion (Out of Frame)</td>
<td>Yes</td>
<td>No</td>
<td>41.8</td>
</tr>
</tbody>
</table>

* p < 0.05 using student’s t-test

Fig. 1. BRCA Mutation Results

1301 - Poster Session
Positive association between CD3Z hypermethylation and cervical cancer
National Cancer Center Korea, Goyang-si, South Korea, Gachon University Gil Medical Center, Incheon, South Korea

**Objective:** The aim of the present study is to investigate whether the CD3Z hypermethylation in whole blood differs in normal, cervical intraepithelial neoplasia (CIN)1, CIN2/3, and cervical cancer subjects, and to determine the association between CD3Z hypermethylation and CIN1, CIN2/3, and cervical cancer.

**Method:** The data consisted of blood samples from 114 normal, 120 CIN1, 49 CIN2/3, and 32 cervical cancer patients. Microarray analysis was applied to screen the CD3Z hypermethylation epigenetic marks in blood DNA samples. The association between CD3Z hypermethylation and cervical diseases was assessed using logistic regression analysis. The area under the receiver operation characteristics curve (ROC) was used in the biomarker evaluation.

**Results:** Our results showed the methylation levels were significantly higher in cervical cancer (P = 0.001) patients compared with those in normal subjects. After multivariate adjustment, the highest tertile of CD3Z hypermethylation was significantly associated with cervical cancer (OR = 17.7, 95% CI 3.51–89.0) compared with the lowest tertile group. Furthermore, ROC analysis showed DNA methylation in cervical cancer (0.727) differed more than CIN1 (0.595) and CIN2/3 (0.594) compared with that in normal subjects. See Figure 1.
**Conclusion:** CD3Z hypermethylation concentration (highest tertile) in blood showed a positive association with cervical cancer. This study suggests that detection of CD3Z hypermethylation in blood also may be useful as a biomarker for diagnosis, treatment, and prognosis of cervical cancer.

![Fig. 1. Median (interquartile range) of CD3Z hypermethylation distribution values in normal, CIN1, CIN2/3 and cervical cancer subjects (CX). Kruskal-Wallis test was used. * P < 0.05, *** P < 0.001](image)

**1302 - Poster Session**

The identification of genetic mutations associated with prolonged survival in ovarian serous cystadenocarcinoma using The Cancer Genome Atlas

A. Kohuta, M.C. Earnhardt, J.M. Patel, T. Orfanelli, M. Song, E. Girda, A. Buckley De Meritens, R.D. Stephenson, A. Leiser and L. Rodriguez-Rodriguez. aRobert Wood Johnson Medical School, New Brunswick, NJ, USA, bIcahn School of Medicine at Mount Sinai, New York, NY, USA, cRutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA

**Objective:** We sought to explore what somatic mutations are associated with prolonged survival in patients with high-grade ovarian serous cystadenocarcinoma using The Cancer Genome Atlas (TCGA) database.

**Method:** Genetic data for high-grade ovarian serous cystadenocarcinoma specimens analyzed in the TCGA was accessed using the cBioPortal for Cancer Genomics. Prolonged OS was defined as greater than or equal to the third quartile of those contained in the study population. Multivariate logistic regression was used to develop a model predictive for prolonged OS.

**Results:** A total of 318 patients with complete genetic sequencing of their tumor specimens were identified; 3,660 total gene mutations were included in the multivariate analysis. The mean OS for the entire study population was 35 months with the third quartile possessing a mean OS of >49 months. The following gene mutations were found to be statistically significant for prolonged OS (mean OS in months, OR, Pvalue): DPP10 (65.7, 21.2, 0.008), DOCK2 (58.1, 21, 0.009), GOLGA4 (52.4, 20.4,
Conclusion: TCGA has fostered tremendous advancements toward understanding the molecular basis of ovarian cancer. Advances in genetic technology and analytical strategies, in combination with large cohorts for genetic study, like TGCA, have formed a new body of information about the genetic and molecular basis of ovarian cancer. Combining patient-specific clinical features with genomic data may allow for individually tailored prognoses and therapeutic approaches. Our study permits this focus by defining mutations associated with prolonged survival.

1303 - Poster Session
Distinct early changes in the fallopian tubes of BRCA mutation carriers
Y. Raza, B. Trabert, B. Taylor-Harding, B.Y. Karlan and S. Orsulic. aWomens Cancer Program/Cedars-Sinai Medical Center, Los Angeles, CA, USA, bNational Cancer Institute, Bethesda, MD, USA, cCedars-Sinai Medical Center, Los Angeles, CA, USA

Objective: A poor understanding of the initial events in ovarian cancer significantly hampers our efforts toward early ovarian cancer detection and prevention. Specifically, the morphological and molecular events that create a permissive microenvironment for cancer are unknown. Germline BRCA1 mutations are associated with an increased risk of ovarian cancer as well as an early onset of cancerous transformation of secretory epithelial cells in the fallopian tubes. These may be related to earlier development of a precancer niche in BRCA1 mutation carriers. The events that lead to secretory cell transformation are unknown. Our goal was to identify potential precancerous niches in the human fallopian tubes.

Method: Normal fallopian tube sections of 30 BRCA1/2 mutation carriers (10 BRCA1, 19 BRCA2, and 1 BRCA1/BRCA2) and 27 age-matched noncarriers were stained with ASS1 (marker of secretory cells) and scored for runs of a single cell type (secretory or ciliated) uninterrupted by another cell type using the ImageJ software. An arbitrary cutoff of >100 μm was selected. The percentage of secretory or ciliated runs was calculated. Least squares means were utilized to compare means across groups.

Results: In premenopausal fallopian tubes, the secretory and ciliated cells were arranged in small clusters of 1–5 cells, while in postmenopausal tubes, the secretory and ciliated cells were flattened and formed long runs of dozens, and sometimes hundreds, of cells of the same type (Figure 1a). Fimbria contained the longest clusters. The results of our analyses showed that secretory cell runs correlate with postmenopausal status and that both secretory and ciliated cell runs correlate with age (Figure 1b). The ratio of percentage of secretory to ciliated cells was significantly increased in BRCA1 mutation carriers in comparison with noncarriers; this difference was more pronounced among postmenopausal women (Figure 1c).

Conclusion: Compared to noncarriers, BRCA mutation carriers have a higher ratio of percentage of secretory to ciliated cells and exhibit more frequent segregation of secretory and ciliated cell clusters. Whether this segregation creates a permissive microenvironment for cancer initiation and progression necessitates further investigation.
1304 - Poster Session
Ionizable lipid nanoparticles are effective at penetrating the core of epithelial ovarian cancer spheroids
O. Tala, T. Levy, S. Ramishetti, D. Landesman Milo and D. Peer. aE. Wolfson Medical Center, Holon, Israel, bTel Aviv University, Tel Aviv, Israel

Objective: Typically in epithelial ovarian carcinoma (EOC), malignant cells aggregate and survive as spheroid-like structures (spheroids). These spheroids possess a core of cancer stem-like cells that are responsible for tumor growth, recurrence, and chemoresistance. If these cells could be reached, chemotherapy or precision nanomedicine could be delivered directly and more efficiently and hence reduce the high recurrence rate. For that purpose, one must potentially attempt to maximally penetrate into the core of the spheroid in order to reach the inner stem-like cells layer. One of the promising delivery systems developed is the lipid nanoparticle (LNP) submicron-sized dispersions of ionizable lipids. These lipids improve circulation time and efficiently enter target cells, thus enabling effective delivery of therapeutic biological drugs, such as siRNA. Our goal was to grow three-dimensional spheroids, in order to mimic in vivo tumor microenvironment conditions, and develop an effective way to penetrate their core using LNPs.

Method: We grew spheroids composed of the NAR (NCI/ADR-Res) human ovarian adenocarcinoma cell line in stem-cell medium (SCM) in 96-well low attachment round bottom plates, which were incubated for 7 days at 37°C with 5% CO₂. We assembled different types of LNPs, composed of different types of ionizable lipids, encapsulating Cy5-siRNA. The 5-day spheroids were transfected with each type of LNP for 24 or 48 hours. The spheroids were then observed under a SP5 confocal microscope to assess the intensity and depth of penetration of spheroids by cy5-siRNA.

Results: By analyzing the three-dimensional structure of each spheroid and measuring the penetration depth of cy5-siRNA, transfection of spheroids with LNPs made of MC3 at a dose of 750 ng cy5-siRNA has shown the highest degree of penetration into the spheroid core.

Conclusion: We have demonstrated that MC3-containing LNPs are effective at penetrating the core of spheroids made of human EOC NAR cells. In the future, we plan to use this system to study gene knockdown effect in spheroid models of EOC, and to assess whether their use may render spheroids more penetrable to drugs and susceptible to treatment with chemotherapy.

1305 - Poster Session
CDK7 as a potential therapeutic target for ovarian cancer: Preclinical study
W.Y. Kim, J. Kim, M.S. Kim, S.Y. Jeong, E.S. Paik, Y.Y. Lee, C.H. Choi, T.J. Kim, B.G. Kim, D.S. Bae and J.W. Lee. Kangbuk St Mary's Hospital, Seoul, Korea, aKangbuk St Mary's Hospital, Seoul, Korea
Objective: Cyclin-dependent kinases (CDKs) are involved in temporal regulation of the cell cycle and transcription and play central roles in cancer development and metastasis. CDK7 activates cell cycle CDKs and is a member of the general transcription factor TFIIH. In this study, we evaluate the therapeutic effects of CDK7 inhibition in ovarian cancer using in vitro and in vivo models.

Method: We analyzed the clinical significance of CDK7 expression using The Cancer Genome Atlas (TCGA) data. Using CDK7 siRNA or covalent CDK7 inhibitor (THZ1), we performed cell proliferation, apoptosis, and effects of cell cycle analysis in ovarian cancer cell lines including using A2780, HeyA8, A2780-CP20, and RMG1. Based on in vitro results, we also performed in vivo experiments including cell line xenograft (A2780) and patient-derived xenografts (PDXs).

Results: Higher CDK7 expression is significantly associated with poor PFS of ovarian cancer patients in the analysis of TCGA data. CDK7 suppression with its siRNA or THZ1 could significantly decrease cell proliferation and increase apoptosis in ovarian cancer cells. Moreover, combination treatment with CDK7 inhibition and cisplatin increased cell proliferation in drug-resistant A2780-CP20 cells. When we performed the flow cytometric analysis to check the influence in cell cycle of CDK7 inhibition, we found that THZ1 triggered G0/G1 cell cycle arrest in a dose-dependent manner. In in vivo therapeutic experiments with cell line xenograft, CDK7 suppression with its siRNA or THZ1 could significantly decrease the tumor weight in A2780 and HeyA8 models. Moreover, we also found similar effects of this treatment in a PDX model with clear cell carcinoma.

Conclusion: These results showed that CDK7 suppression with its siRNA or THZ1 could significantly suppress ovarian cancer growth in in vitro and in vivo by triggering G0/G1 cell cycle arrest. Therefore, CDK7 might be a novel promising therapeutic target for ovarian cancer and will be explored in the near future for therapy of ovarian cancer.
and 10 stage IV. All patients received paclitaxel-carboplatin combination for 3 cycles. Twenty patients had complete debulking (no macroscopic residual disease), 18 had optimal (macroscopic disease <1 cm), and 7 suboptimal. Twenty-two patients also received bevacizumab as part of their treatment after IDS. Median follow-up was 30.9 months. CRS assessed at omentum predicted PFS when adjusted for age, stage, debulking status (complete, optimal, suboptimal), and post-IDS bevacizumab administration (mPFS CRS 1, 10.3 months, 95% CI 7.0–13.5; CRS 2, 13.9 months, 95% CI 12.9–15.0; CRS 3, 18.7 months, 95% CI 14.3–23.0). Lymphocytic invasion was associated with improved OS (log rank test, \( P = 0.007 \)) (Figure 1). Presence of necrosis and mitosis per HPF did not predict either PFS or OS. BRCA status was known for 23 patients, and presence of BRCA1/2 mutation was strongly correlated with lymphocytic infiltration (\( P = 0.019 \)) but not CRS (\( P = 0.787 \)).

**Conclusion:** Our study demonstrates the prognostic significance of lymphocytic infiltration in IDS specimens. It also confirms the predictive value of CRS in EOC patients treated with NACT and IDS. It is of interest that BRCA1/2 mutation status was not related to CRS.

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1307 - Poster Session

**The functional role and clinical significance of long non-coding RNA Xist in cervical cancer**

S.H. Lee\(^a\), S.W. Kim\(^b\), E.J. Nam\(^b\), J.S. Park\(^a\), J.W. Kim\(^b\) and Y.T. Kim\(^b\).

\(^a\)Yonsei University Wonju College of Medicine, Wonju, South Korea, \(^b\)Yonsei University College of Medicine, Seoul, South Korea

**Objective:** Long noncoding RNA (lncRNA) X inactivate-specific transcript (Xist) has been verified as an oncogenic gene in several human malignant tumors, and its dysregulation was associated with tumor initiation. In the present study, we examined Xist expression levels in patients with cervical cancer and determined the relationships between Xist expression and clinicopathological factors.

**Method:** Xist expression was determined in cervical cancer tissues (\( n = 81 \)) and corresponding normal tissues (\( n = 22 \)) by using real-time polymerase chain reaction, and its correlation with clinical parameters and prognosis were analyzed. To determine the role of Xist in cell proliferation, migration, and invasion, RNA interference was used to knock down Xist expression in cervical cancer cell lines.

**Results:** Xist expression significantly improved 5-year OS rates (19.5 and 27.2 months, respectively, log rank test \( P = 0.009 \)). Univariate analysis showed that high Xist expression was an independent prognostic factor of overall survival (HR = 0.320, \( P = 0.031 \)). We also investigated the biofunctional consequences of Xist overexpression in vitro using Cell Counting Kit-8, colony formation wound healing migration, and Matrigel invasion assays. The results showed that Xist overexpression enhanced cell proliferation, migration, and invasion in vitro. See Figure 1.

**Conclusion:** The expression of Xist is associated with overall survival rates and tumorigenesis. These findings indicated that Xist has the potential to become a predictor for the prognosis of cervical squamous cell carcinoma.

**Fig. 1.** Relative Xist expression and its clinical significance Kaplan-Meier overall survival curves of the patients with ovary cancer and different levels of Xist (log-rank test; \( p = 0.009 \)).
1308 - Poster Session
ONC201 induces the unfolded protein response (UPR) in high- and low-grade ovarian carcinoma cell lines and leads to cell death regardless of platinum sensitivity

M. Rummana, V. Prabhub, J. Allenb and I. Winer, 1Karmanos Cancer Center/Wayne State University, Detroit, MI, USA, bOncoceutics, Inc., Philadelphia, PA, USA, cWayne State University, Detroit, MI, USA

Objective: Treatment of both platinum-resistant high-grade (HG) and all low-grade (LG) ovarian cancers (OVCA) poses significant challenges as neither respond to conventional chemotherapy, leading to morbidity and mortality. Identification of novel agents that can overcome chemoresistance is therefore critical. Previously, we have demonstrated that OVCA has upregulated unfolded protein response (UPR) and that targeting cellular processes leading to upregulation of UPR leads to cell death. ONC201 is a first-in-class, orally bioavailable inhibitor of DRD2 that has demonstrated anticancer activity and was found to induce UPR in other systems. Given its unique properties, we hypothesized ONC201 would overcome resistance in both HG and LG OVCA.

Method: Cisplatin-sensitive and -resistant HG OVCA and three primary LG OVCA cell lines were studied. Cell viability was determined using MTT assay. Cell migration was studied using wound healing assay. Apoptosis and cell cycle analyses were investigated using flow cytometry. Analysis of pathway inhibition was performed by Western blot. mRNA expression of UPR-related genes was measured by qPCR. In vivo studies were completed utilizing axillary xenograft models. Co-testing with conventional chemotherapy was performed to study synergy.

Results: ONC201 significantly inhibited cell viability and migration in a dose-dependent manner with IC_{50}s from 1-20 µM for both cisplatin-sensitive and -resistant HG and LG OVCA cell lines at 48 hours. ONC201 increased apoptosis and S-phase arrest with increased levels of cleaved PARP, BIM protein expression. ONC201 leads to upregulation of the apoptotic arm of the UPR, specifically CHOP and ATF3. PI3/AKT/mTOR pathway was also downregulated. In vivo studies demonstrated single-agent, once weekly dosing of ONC201 decreased xenograft size by 40% while activating the UPR compared to vehicle. ONC201 demonstrated significant synergy in combination with both paclitaxel and cisplatin in a highly resistant platinum OVCA cell line (OV433R).

Conclusion: Our findings demonstrate that ONC201 can effectively overcome chemoresistance in both HG and LG OVCA cells by blocking prosurvival pathways and inducing the apoptotic arm of the UPR. This is a promising therapeutic agent in OVCA treatment and should be considered for clinical translation.

1309 - Poster Session
GM-CSF increases myeloid-derived suppressor cells infiltration after anti-VEGF therapy in ovarian cancer

K. Abiko, N. Horikawa, R. Murakami, K. Yamaguchi, J. Hamanishi, T. Baba and M. Mandai. Kyoto University Graduate School of Medicine, Kyoto, Japan

Objective: Myeloid-derived suppressor cells (MDSCs) in ovarian cancer suppress antitumor functions of cytotoxic T lymphocytes and are associated with unfavorable prognosis. Recently, anti-VEGF antibody has been used to treat advanced ovarian cancer, but most cases eventually exhibit resistance to anti-VEGF antibody. Herein, we focused on the alteration of tumor immunity after antiangiogenic therapy. We aimed to elucidate the mechanisms of MDSCs infiltration after antiangiogenic therapy to overcome resistance to anti-VEGF therapy in ovarian cancer.

Method: HM-1, a mouse ovarian cancer cell line, was inoculated to immunocompetent syngeneic mice. Anti-VEGF antibody was administered, and tumor-infiltrating lymphocytes and MDSCs were assessed by flow cytometry and immunohistochemistry. Expression microarray and cytokine array of the mouse tumor treated with anti-VEGF antibody were also assessed. GM-CSF expression in the tumor and hypoxic cultured cells was confirmed by Western blot analysis. Chemotaxis of MDSCs was measured with or without tumor-conditioned medium and anti-GM-CSF antibody. Anti-VEGF antibody and anti-GM-CSF antibody were administered to the mouse ovarian cancer model.

Results: Administration of anti-VEGF antibody delayed HM-1 tumor growth, but the tumors eventually grew, indicating resistance to anti-VEGF therapy. In anti-VEGF-resistant tumors, infiltration of MDSCs was prominent, and CD8-positive lymphocytes were decreased (P < 0.05). Expression microarray analysis revealed significant upregulation of genes belonging to HIF-1 and NF-κB pathways (P < 0.005). Cytokine array demonstrated upregulation of GM-CSF in the anti-VEGF-treated tumors. By Western blot analysis, GM-CSF was confirmed to be upregulated in the ovarian cancer cells cultured in hypoxic
condition. Hypoxic tumor-conditioned medium increased the migration of MDSCs in double-chamber chemotaxis assay, and anti-GM-CSF antibody abrogated this effect. Administration of anti-GM-CSF antibody increased the treatment effect of anti-VEGF antibody in mouse ovarian cancer model ($P < 0.05$). See Figure 1.

**Conclusion:** Anti-VEGF therapy induces tumor hypoxia and upregulation of GM-CSF expression, which recruits MDSCs and inhibits tumor immunity. Targeting GM-CSF or MDSCs could overcome the resistance to anti-VEGF therapy.

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**1310 - Poster Session**

**Dual anti-HER2 therapy in HER2+ uterine and ovarian carcinomas: Durable effect with combined therapy**


"Cleveland Clinic, Cleveland, OH, USA, bThe Cleveland Clinic Foundation, Cleveland, OH, USA"

**Objective:** HER2 over-expression/amplification occurs in 11%-30% of ovarian (OC) or endometrial (EC) cancer. HER2 is an attractive target especially with potent new molecules including irreversible tyrosine kinase inhibitors like neratinib and antibody drug conjugates like trastuzumab emtansine (T-DM1). Anti-HER2 monotherapy with trastuzumab resulted in limited responses presumably because of alterations in HER2 that evade monoclonal antibodies and compensatory feedback mechanisms that circumvent treatment. The objectives of this preclinical study were to evaluate the efficacy with dual anti-HER2 therapy compared to monotherapy in HER2+ OC and EC.

**Method:** We examined the efficacy of neratinib alone and in combination with T-DM1, trastuzumab, or trastuzumab and paclitaxel in HER2+ OC and EC using HER2+ ovarian (SKOV3 and CCLM1) and uterine serous (ARK1 and ARK2) cell lines. Preclinical in vivo efficacy experiments were done using the ARK1 and SK-OV3 cell line-derived xenograft (CDX) model. The other CDX models are still ongoing. Downstream signaling pathways were assessed using Western blot. An experimental group size of 8 tumors per group was used with a power of 85% and $P < 0.05$.

**Results:** We determined the IC$_{50}$ of these drug combinations in SKOV3, CCLM1 (ovarian cell lines), and ARK1 and ARK2 (uterine serous cell lines) in vitro by dose response curve using cell titer glow assays. In vitro, the combination of neratinib with T-DM1, neratinib with trastuzumab, and neratinib and trastuzumab/paclitaxel performed better than corresponding monotherapy. In vivo, each of the three dual anti-HER2 therapy regimens in xenografts derived from HER2+ and CCNE1-amplified and PIK3CA-mutated serous cancer significantly and synergistically reduced tumor growth compared to monotherapy. Downstream signaling data supported such synergistic activity. The most promising regimen was dual anti-HER2 therapy with neratinib and T-DM1, which led to complete eradication of tumors in mice with no evidence of regrowth for >120 days and continued even after discontinuing therapy (45 days). Downstream signaling data supported this synergistic activity.

**Conclusion:** Dual anti-HER2 therapy with neratinib and T-DM1, trastuzumab, or trastuzumab/paclitaxel may represent a potential therapeutic option for HER2+ OC and EC patients. The most effective regimen was combined therapy with neratinib and T-DM1. These data are being replicated in other HER2+ OC and EC models.

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**1311 - Poster Session**

**Passenger fusion genes are correlated to antitumor effect of anti-PD-1 antibody nivolumab for ovarian cancer**

J. Hamanishi, R. Murakamii, T. Baba, K. Yamaguchi, K. Abiko and M. Mandai. "Kyoto University, Kyoto, Japan, bKyoto University Graduate School of Medicine, Kyoto, Japan, cNational Hospital Organization Kyoto Medical Center, Kyoto, Japan"
Objective: Immune checkpoint PD-1 signal blockade provides significant clinical efficacy and durable response for several cancer patients. However, it is crucial to identify a biomarker to predict the response to PD-1 signal blockade. Herein we analyzed the somatic mutanomes and transcriptomes of tumor samples from ovarian cancer patients treated with nivolumab to identify potential biomarkers of antitumor response.

Method: We previously reported a phase II clinical trial for resistant ovarian cancer with nivolumab (UMIN000005714) and showed a disease control rate of 45% including 2 complete responders. To estimate the somatic mutation burden (TMB) of tumor samples, the number of nonsynonymous single nucleotide variants (nsSNVs), insertions, and deletions of genes was analyzed by whole exome sequencing of formalin-fixed paraffin-embedded tumor tissues. Next, to evaluate whole transcriptome of these samples, we performed an RNAseq analysis and detected several fusion genes in some patients. We evaluated the correlation between clinical antitumor response for nivolumab treatment with the numbers of somatic mutations or transcriptomic alignments containing gene fusions.

Results: Sixteen tumor samples (7 responders and 9 nonresponders) for whole exome sequencing and 17 samples (7 responders and 10 nonresponders) for RNA sequencing were available. Contrary to expectations generated by previously reported papers on melanoma or lung cancers, the levels of TMB including nsSNVs, insertions, and deletions of genes were not significantly correlated to antitumor response. However, more than 2 fusion genes were detected (mean 6.3, range 0–15) in 6 of 7 responders, while 8 of 10 nonresponders did not have any fusion genes and the remaining nonresponders had only 1 fusion gene each (mean 0.2, range 0–1). Therefore an antitumor response to nivolumab was strongly correlated to the number of fusion genes in ovarian cancer ($P = 0.0003$, sensitivity 86%, 6/7; specificity 100% 10/10).

Conclusion: This study, to our knowledge, is the first to describe passenger fusion genes of tumors and might provide a clinically useful and novel predictive biomarker of antitumor response to anti-PD-1/PD-L1 antibody therapy for ovarian cancer.

1312 - Poster Session
Identification of mediators of chemoresistance in a heterogeneous tumor model of ovarian cancer

Objective: The purpose of this study was to identify the pathways that small populations within a heterogeneous tumor utilize to survive primary chemotherapy.

Method: Under Institutional Review Board and IACUC approvals, high-grade serous ovarian cancer (HGSOC) omental tumors from 16 patients were obtained and implanted subcutaneously in the flanks of SCID mice, grown, and harvested at humane endpoints. Tumor was divided, with one portion preserved in RNAlater as “untreated” tumor and part implanted in a new generation of mice. Once tumors had grown to 0.5–1 cm³, mice were treated with maximum tolerated dose (MTD) of carboplatin (75 mg/kg) and paclitaxel (10 mg/kg) for 4 weekly treatments. Residual tumor was harvested as “4wk MTD treated.” Tumor that was residual or recurred within 6 months was propagated to a new generation of mice, expanded, and retreated with carbo/taxol. Tumors growing after chemotherapy were harvested as “resistant” tumor. RNA sequencing was performed followed by differential gene expression analysis using Limma-voom and subsequent pathway interrogations (KEGG, Reactome) from gene set enrichment analysis (GSEA).

Results: Pathway analysis following RNA sequencing showed multiple pathways differentially regulated between untreated and resistant PDX models. Ribosome and spliceosome pathways were top hits with an FDR of 2.12−8 and 7.53−6, respectively. Within the ribosome cluster, RPSA, RPS2, and RPS15a ($P = 5.55−7, 1.38−6$, and $6.43−5$, respectively) were all found to be differentially expressed in resistant tumor. In the spliceosome cluster, RBM17 and DDX5 were significantly increased. While resistant models appeared to have ribosome and spliceosome machinery upregulated, acutely treated models had protein ER processing and splicing upregulation but no enrichment of ribosomal proteins.

Conclusion: Using PDX models of untreated, treated, and resistant tumors allows for identification of differentially expressed transcripts and pathway alterations that may contribute to chemoresistance. Targeting these genes and pathways may allow killing of the final microscopic portion of tumor after primary therapy, allowing durable cures.
1313 - Poster Session
Mechanistic basis for synergy between SMAC-mimetic birinapant and chemotherapeutic agents: Insights for clinical development
D.M. Anderson, K.P. Zelig, K.P. Bunch, L. Hernandez and C.M. Annunziata. Walter Reed National Military Medical Center, Bethesda, MD, USA, National Cancer Institute, Bethesda, MD, USA

Objective: The purpose of this study was to determine the means of synergy between birinapant and selected drugs, focusing on the NF-kB pathway, with the goal of optimizing strategies for clinical application.

Method: Docetaxel and panobinostat were selected out of a 2,000-drug screen as 2 drugs most synergistic in combination with birinapant. NF-kB activity was measured in cell lines OVCAR8 and OVCAR3 transduced with an NF-kB luciferase reporter. Cells were exposed to docetaxel or panobinostat alone and in combination with birinapant, with and without TNF, a known activator of NF-kB signaling. Luminescence was quantified by Promega Luciferase Assay and normalized to XTT-PMS cellular viability assay. Caspase 3/7, 8, and 9 activities were evaluated under the same experimental conditions using Promega Caspase Glo assay. Secreted cytokines IL-6, IL-8, and TNF were determined using the Human ProInflammatory-4 II Tissue Culture Kit. The combination of docetaxel and birinapant was evaluated in vivo in a mouse survival model of immunocompromised nude mice with intraperitoneal OVCAR 8 inoculation.

Results: Birinapant decreased NF-kB activity induced by TNF, as expected. Docetaxel consistently decreased NF-kB activity; panobinostat increased NF-kB, and birinapant blocked this rise. Caspase 3/7, 8, and 9 activities (indicating common, extrinsic, or intrinsic apoptosis, respectively) were significantly increased when birinapant was added to each drug in the presence of TNF. The addition of birinapant induced TNF secretion, as did both panobinostat and docetaxel in the cytokine assay. Combination docetaxel and birinapant improved OS of mice compared to either agent alone.

Conclusion: Birinapant enhances apoptotic cell death in HGSOC cell lines in combination with docetaxel or panobinostat. NF-kB signaling may be integral to synergy with birinapant, although for opposite reasons. The increase in TNF production may augment apoptotic signaling while NF-kB is blocked, switching TNF from a prosurvival stimulus to an apoptosis-inducing signal. These two combinations show promise for clinical development, and future clinical trials will include biomarkers to measure tumor-specific NF-kB activity, TNF secretion, and caspase cleavage.

1314 - Poster Session
BRIP1 mutation does not confer sensitivity to PARP inhibition
A. Castaneda, C. Moyer, J.L. Gillespie, R. Doberstein, F.J. Backes, D.E. Cohn and P.J. Goodfellow. The Ohio State University, Columbus, OH, USA, The Ohio State University Medical Center, Columbus, OH, USA

Objective: PARP inhibitors (PARPi) were recently FDA-approved for treatment of ovarian cancer (OC) patients who have mutations in the BRCA1/2 genes. PARPi therapy is effective in patients with homologous recombination repair (HRR) defects. BRIP1 (BRCA1 interacting protein 1) is the third most common OC susceptibility gene and is hypothesized to play a role in HRR. With increased use of gene panels, BRIP1 status has potential to influence choice of treatments. Although it is hypothesized that BRIP1 mutation confers sensitivity to PARPi, the effects of PARPi in cancer cells lacking BRIP1 are largely unknown. The objective of this study is to assess the sensitivity of BRIP1 deficient cells to PARPi in vitro.

Method: HeLa (cervical cancer) and HEK 293 (kidney) cells were genetically engineered to create isogenic lines homozygous or heterozygous for BRIP1 mutations. Cells were treated with 3 PARPi (olaparib, rucaparib, or ME0328, a PARP3 inhibitor) and the effects on cell viability determined. The BRCA1 mutant SUM-149 cell line served as a control for PARPi sensitivity. The effect of PARPi on cell viability was measured using the crystal violet clonogenic assay. Experiments were performed in triplicate with 2 independent clones representative of BRIP1 genotypes. Results for biologic replicates were combined calculated (GraphPad Prism statistical software).

Results: Rucaparib and olaparib showed the expected effects on viability for BRCA1 mutant SUM-149 cells, with IC50s of 1.0 μM and 1.5 μM, respectively (50% inhibitory concentration). Sensitivity in the isogenic HeLa clones was variable and independent of BRIP1 status. Overall, HeLa clones were approximately 7-fold more resistant to PARPi than SUM-149 cells. The PARP3 inhibitor had no effect on SUM-149 or HeLa cells at the highest concentration tested (10 μM). Studies are ongoing in the isogenic HEK 293 cells, as well as studies to assess the effects of combined cisplatin/PARPi treatment.
Conclusion: \textit{BRIP1} deficiency does not confer sensitivity to PARPi in vitro. This finding suggests OC patients with \textit{BRIP1} defects are unlikely to see the same benefits from PARPi as patients with \textit{BRCA1/2} mutations. Further study of PARPi in patients with \textit{BRIP1} mutations should be considered before routine recommendation of PARPi treatment for \textit{BRIP1} mutant OC is adopted.

1315 - Poster Session
Combined therapy with HER2 and CDK4/6 inhibitors in HER2+ uterine and ovarian carcinomas: Synergistic effect with combined therapy
H. Mahdi\textsuperscript{a}, M. Hasipek\textsuperscript{b}, Y. Guan\textsuperscript{b}, D. Grabowski\textsuperscript{b}, H.Q. Al-Sudani\textsuperscript{b}, Y. Parker\textsuperscript{b}, A. Boyd\textsuperscript{b}, P.G. Rose\textsuperscript{b}, D. Lindner\textsuperscript{b} and B.K. Jha\textsuperscript{b}.
\textsuperscript{a}Cleveland Clinic, Cleveland, OH, USA, \textsuperscript{b}The Cleveland Clinic Foundation, Cleveland, OH, USA

**Objective:** HER2 over-expression/amplification occurs in 11%–30% of ovarian (OC) or endometrial cancer (EC) cases. HER2 is an attractive target especially with new potent strategies to inhibit HER2 functions including irreversible tyrosine kinase inhibitors (TKI) like neratinib. Neratinib has many attractive features including being irreversible, pan-HER receptor TKI with high selectivity and affinity toward HER2. Neratinib has shown efficacy against HER2 amplification/over-expression, with HER2 intracellular or extracellular domain mutations, or truncated HER2 (p95HER2). Cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors are another class of drugs with potential synergy with anti-HER2 therapy. The objective of this preclinical study was to evaluate the efficacy and signaling pathways altered with neratinib combined with the CDK4/6 inhibitor abemaciclib compared to monotherapy in HER2+ OC and EC.

**Method:** We examined the efficacy of neratinib alone and in combination with abemaciclib in HER2+ OC and EC using HER2+ ovarian (SKOV3 and CCLM1) and uterine serous (ARK1 and ARK2) cell lines. Preclinical in vivo efficacy experiments were done using the ARK1 cell-line derived xenograft (CDX) model. Downstream signaling pathways were assessed using Western blot. An experimental group size of 8 animals per group was used with a power of 85% and \(P < 0.05\).

**Results:** IC\textsubscript{50} of this drug combination in SKOV3 and CCLM1 (HER2+ ovarian cell lines) and ARK1 and ARK2 (uterine serous cell lines) in vitro were determined by dose response curve using cell titer glow assays. In vitro, the combination of neratinib with abemaciclib performed better than monotherapy. Neratinib monotherapy was active, but abemaciclib alone had limited activity. Significant synergistic effect in vitro was noted when neratinib was combined with abemaciclib. In vivo neratinib combined with abemaciclib was significantly more effective than single-agent treatment in decreasing tumor growth in xenograft model of HER2+, CCNE1-amplified, and PIK3CA-mutated serous cancer model.

**Conclusion:** Anti-HER2 therapy with neratinib combined with CDK4/6 inhibitor abemaciclib may represent a novel therapeutic option for HER2+ OC and EC patients. These data are being replicated in other HER2+ OC and EC models with and without alteration in CDK pathway.

1316 - Poster Session
Comparative exosomal protein profiling to identify key signaling pathways in high-grade serous ovarian cancer
K.D.P. Dorayappan\textsuperscript{a}, B.Q. Smith\textsuperscript{b}, M.D.S. Lightfoot\textsuperscript{b}, M.M. Flannery\textsuperscript{c}, D.E. Cohn\textsuperscript{b} and S. Karuppaiyah\textsuperscript{a}.
\textsuperscript{a}The Ohio State University Medical Center, Columbus, OH, USA, \textsuperscript{b}The Ohio State University, James Cancer Hospital, Columbus, OH, USA, \textsuperscript{c}The Ohio State University, Columbus, OH, USA

**Objective:** The aim of this study was to evaluate the exosome proteome to identify upregulated signaling pathways and potential candidates for biomarker and therapeutic targets in high-grade serous ovarian cancer (HGSOC).

**Method:** Exosomes were isolated using a microfluidic chip developed at our institution for the economic and rapid isolation of serum exosomes. We used mass spectrometry (1D-LC-MS/MS) for label-free quantification of protein profiles in the exosomes isolated from normal ovarian epithelial cells, cancer cell lines, and patient serum samples. Raw MS data were searched with the ProteoWizard platform containing the open source software program MyriMatch, and the output files were passed to the IDPicker for protein inference and assembly. To discover changes in the proteins across study groups, we used a multispec platform. The filtered count list was trimmed mean normalized, and a modified exact test determined DE as defined by a Benjamini-Hochberg multitest corrected \(P\) value, or \(q\) value threshold, \(<0.05\). Raw spectral counts were adjusted to center, normalized, and clustered across the arrays and genes using the average linkage function of the Cluster 3.0 software and visualized using the Java Tree View software. We used IPA to identify upregulated signaling pathways in HGSOC and prioritize potential candidates for further validation studies based on their statistical significance and disease relevance.
Results: We isolated and characterized a pure population of exosomes using our microfluidics chip based on specific surface markers EpCAM and CD9/CD63. 1D-LCMS/MS analysis of exosomes isolated from FTSEC, OSE, and OVCAR8 cells (n = 5) led to the identification of 988 total protein groups across all samples (FDR = 2.6%). Hierarchical clustering analysis showed upregulated protein clusters in HGSOC exosomes. PANTHER Classification System showed that these proteins were involved in integrin and inflammation signaling pathways. IPA predicted the activation of an HGF-specific cytokine signaling pathway.

Conclusion: The successful isolation of exosomes using our microfluidics device is a major step forward in clinical translation. Our study offers mechanistic insights as to the molecules involved in key signaling pathways in HGSOC including HGF, and its downstream effector STAT-3, as putative targets for therapy.

1317 - Poster Session
Characterization of tumor origin for high-grade serous ovarian carcinoma in three transgenic mouse models
M. Roberts, V. Sodi, C. Wu, K. Cho and D. Connolly. aFox Chase Cancer Center, Philadelphia, PA, USA, bThe University of Michigan Hospitals, Ann Arbor, MI, USA

Objective: Accumulated evidence shows most ovarian high-grade serous carcinomas (HGSC) originate in fallopian tube. We previously described a transgenic mouse model, MISIIR-TAg-DR26, that develops spontaneous ovarian carcinomas similar to HSGC. Gene expression analyses of tumors revealed expression of PAX8, OVGP1, and FOXJ1, suggesting that tumors may arise in the oviduct. We developed two additional transgenic lines, DR12 and DG61, which develop HGSC. Our aim was to characterize tumor histology and expression of protein biomarkers to understand the origin of HGSC in these models.

Method: Mice were bred, and reproductive tracts collected at specified ages and reviewed by a pathologist. Immunohistochemical (IHC) staining of FFPE tumor sections was performed with antibodies recognizing proteins specific for reproductive tract epithelium (CK8, PAX8, and FOXJ1), granulosa cells (α-inhibin), and tumor (TAg). Staining was analyzed by automated imaging; the intensity and extent of staining were quantified; and H scores were computed for each antigen. To further explore oviductal tumor origin, a lineage-tracing approach was used in which mice from each line were crossed to OVGP1-iCreTAM, ROSA26-LSL-eYFP mice in which eYFP is inducibly expressed in oviduct.

Results: Tumor histology and biomarker expression confirm morphology similar to HGSC. There is prominent expression of TAg, CK8, and PAX8, moderate levels of FOXJ1, and absence of α-inhibin in all lines. Two distinct patterns of tumor development were observed. DR26 mice developed neoplastic lesions in the oviduct and hilum, which appear to migrate to ovary and develop into large tumors. DG61 and DR12 developed neoplastic oviductal lesions that expand locally, with occasional progression to ovary. Tamoxifen-inducible expression of eYFP in oviducts has been confirmed, and lineage-tracing analysis of tumors in DR26 and DG61 mice is underway.

Conclusion: Tumors from all three lines appear to originate, at least in part, from the oviduct. The consistent development of spontaneous oviductal tumors in these lines makes these models highly relevant in tumor biology in which there is strong evidence for tubal origins of HGSC in women. A deeper understanding of ovarian cancer origin and ovary as a site of metastasis is monumental to identification of targets for therapeutic intervention.

1318 - Poster Session
Identification of a novel mechanism of survival in epithelial ovarian cancer
N.M. Fletcher, A.K. Harper, R. Fan, I.K. Singh, H. Deirawan, I.G. Tsolakian, J. Maclean, J.D. Naaman, S. Bandyopadhyay, R. Ali-Fehmi, R.T. Morris and G.M. Saed. aWayne State University School of Medicine, Detroit, MI, USA, bKarmanos Cancer Center/Wayne State University, Detroit, MI, USA, cWayne State University, Detroit, MI, USA, dJohn Carroll University, Cleveland, OH, USA, eMichigan State University, East Lansing, MI, USA

Objective: We were the first to report that chemo-sensitive and -resistant epithelial ovarian cancer (EOC) cells produce myeloperoxidase (MPO), which is critical to their survival. The objective of this study is to determine the mechanism by which MPO protects EOC cells from apoptosis. Here we identified an integrin, αVβ1, that is uniquely expressed by EOC cells and serves as a specific ligand to MPO to control this mechanism.

Method: Formalin-fixed paraffin-embedded sections of high-grade ovarian serous carcinoma were deparaffinized. Heat-mediated antigen retrieval with cell conditioning was performed. Sections were incubated with integrin αV antibody (1:100 dilution, Santa Cruz Biotechnology) for 1 hour at room temperature. Optimization for β1 immunohistochemistry is underway.
The complex was visualized using ultraview universal DAB detection kit (Ventana Medical Systems). Surface expression of integrin subunits αV and β1 as a heterodimer, MPO binding in human EOC cell lines (A2780, MDAH-2774, SKOV-3), and their docetaxel or cisplatin-resistant counterparts and macrophages (EL-1) were determined by flow cytometry and proximity assay, respectively. Cytotoxicity of integrin αV or β1 antibodies (0.5 or 1.5 μg/mL) was assessed by MTT Cell Proliferation Assay. Apoptosis was assessed by Tunnel assay. Protein expression was evaluated with independent t tests. One-way ANOVA followed by Tukey post hoc tests with Bonferroni correction was performed for cytotoxicity comparisons, P < 0.05.

Results: Subunits αV and β1 integrins were shown to be expressed in human EOC tissue. These subunits were expressed as a heterodimer in EOC cells, with significantly higher expression in chemoresistant cells. There was no detectable expression of the heterodimer in macrophages. In addition, MPO was shown to bind the αVβ1 heterodimer. Interruption of this binding by αV or β1 antibodies significantly induced cytotoxicity and apoptosis in both chemo-sensitive and -resistant EOC cells. Neither antibody was cytotoxic to macrophages.

Conclusion: Here we identify a unique integrin that binds MPO and serves as a survival mechanism. Interruption of this binding has potential therapeutic impact in selectively killing ovarian tumor cells.

1319 - Poster Session
Targeting ERBB family genomic alterations in gynecological malignancies
L. Gay, J.C. Schink, J.D. Wright, S.B. Lele, P.C. Mayor, K. Odunsi, A. Hemmerich, N. Ngo, A.A. Secord, J.Y. Hou, G.E. Konecny, A.D. Santi and J.A. Elvin. aFoundation Medicine, Inc., Cambridge, MA, USA, bCancer Treatment Centers of America, Chicago, IL, USA, cColumbia University, New York, NY, USA, dRoswell Park Cancer Institute, Buffalo, NY, USA, eDuke University School of Medicine, Durham, NC, USA, fNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, gUniversity of California, Los Angeles, Los Angeles, CA, USA, hYale University School of Medicine, New Haven, CT, USA

Objective: HER2 or EGFR activation is a targetable oncogenic mechanism in breast, gastroesophageal, lung, and colorectal carcinomas (CA). The National Comprehensive Cancer Network (NCCN) now recommends carboplatin/paclitaxel/trastuzumab for women with advanced HER2+ uterine serous carcinoma (USC). We evaluated genomic alterations (GA) in ERBB family genes (EGFR, ERBB2, ERBB3, ERBB4) for 14,692 comprehensive genomic profiles (CGP) of both common and rare gynecological malignancies (GM).

Method: CGP of 14,692 advanced GM FFPE specimens by hybridization capture of up to 406 cancer-related genes and for some RNA sequencing of 265 genes was performed. Evaluated GA include base substitutions, small indels, amplification (AMP) or loss, and rearrangements (RE). Tumor mutational burden (TMB, mutations/Mb) was determined on ~1.1 Mbp of sequenced DNA. For some samples, genomic loss of heterozygosity (gLOH) and microsatellite instability (MSI) was evaluated.

Results: Of 14,692 GM, ovarian-type serous carcinomas (OSC) (n = 6,847) or endometrial adenocarcinomas (aCA) (n = 3,618) predominated. A total of 1,343 (9.1%) GM had ≥1 oncogenic GA in an ERBB gene, and 119 (0.8%) had ≥2 ERBB GA. A large fraction of USC (22.5%) or clear cell (14.9%) aCA, cervical aCA (17.3%), mucinous (15.9%) or clear cell (13.4%) ovarian CA, and uterine carcinosarcomas (12.0%) were ERBB++. Fewer (4.3%–7.1%) primary OSC were ERBB++. ERBB2 (HER2) AMP was by far the most common ERBB GA. Distribution of ERBB GA was as follows: ERBB2 6.1% (n = 893, AMP 50.7%, n = 681), ERBB3 1.6% (n = 239, AMP 7.2%, n = 97), EGFR 1.2% (n = 183, AMP 5.7%, n = 77), and ERBB4 0.7% (n = 103, AMP 3.9%, n = 52). Oncogenic RE, fusions, and splice site GA were observed in both ERBB2 (n = 16) and EGFR (n = 7), including the oncogenic variant EGFRvIII. Although ERBB2 AMP is concordant with HER2+ IHC/FISH, 187/1343 (13.9%) ERBB2+ GM harbored targetable, oncogenic non-AMP ERBB2 GA that would not be detected by FISH or IHC, including well-characterized GA: A775_G776insYVMA (n = 13), S310Y/F (n = 33), and V842I (n = 30). Co-occurring GA were frequent in GM, and some, such as PIK3CA (31.4%, range 26.2%–33.0%), are associated with anti-HER2 therapy resistance in other tumor types.

Conclusion: Nearly 9% of gynecologic tumors harbor potentially targetable GA in an ERBB gene, but 49.3% of these would not be identified by HER2 IHC or FISH, despite potentially conferring sensitivity to anti-ERBB treatment. An ERBB+ basket trial for gynecologic malignancies to investigate the efficacy of HER2- or EGFR-targeted therapies and impact of co-occurring GA appears warranted.

1320 - Poster Session
Selected genetic variation between endometrial endometrioid adenocarcinomas (EEA) and normal controls can be developed as minimally invasive screening markers for cancer development and recurrence
Objective: We hypothesize that endometrial endometroid adenocarcinomas (EEA) have unique genetic variants that can be used to create an early cancer diagnostic tool. Our goal is to identify variants that are unique to EEA that can be developed into screening markers for minimally invasive assays.

Method: RNA sequencing (RNA-seq) of 62 EEA cases from our tumor bank was performed and compared with 123,136 normal controls from the Genome Aggregation Database (gnomAD). Case control analysis to identify genetic variants with different allele frequencies \((P < 10^{-7})\) between the groups using variant effect predictor software (VEP) from Ensembl was performed. In addition, genetic variation present only in the majority of EEA cases (>99%) but not present in the gnomAD data was selected for analysis. Finally, all resulting variants were filtered based on the predicted consequence of the variants on protein function.

Results: (1) Out of 157,908 variants present in both EEA cases and gnomAD controls, only 676 variants had different allele frequencies between both groups meeting the threshold \((P < 10^{-7})\). These variants were observed in 8 genes: \(AP2A2, MUC6, SIRT3, POLRMT, AC004449.1, PTBP1, FOXD4,\) and \(CBWD1.\) (2) Out of 11,845,998 unique variants identified only in EEA cases, 227,671 were observed in >99% of cancer cases. These variants encompassed more than 17,000 different genes. We then filtered those variants based on their predicted effect on the resulting protein. Filtering accepted variants in the 5' UTR, variants that would cause a frameshift, a missense translation, or a premature stop, coding sequence variants, and variants affecting a splice donor or splice acceptor. This filtering reduced the sample to 738 variants within 608 genes.

Conclusion: Considering genetic variants that are either (1) different between EEA cases and normal controls from a large diverse database or (2) a unique set of variants only detected in EEA cases results in a substantial pool of unique genetic variants that have the potential to be used as a cancer diagnostic tool. Since these variants can be detected in cell-free DNA, screening in both peripheral blood and/or vaginal smears is a viable option.

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1321 - Poster Session

**Whole genome CRISPR/Cas9 screen identifies established and novel genes required for ovarian cancer dissemination**


*University of Colorado, Denver, Denver, CO, USA*

Objective: Many high-grade serous ovarian cancers (HGSOC) arise from the exfoliation of transformed cells from fallopian tube fimbria, indicating that these cells must survive in suspension to disseminate. Our aim was to identify novel genes and pathways critical for HGSOC dissemination.

Method: We performed CRISPR/Cas9 whole genome screen of HGSOC cells grown in adherent and suspension settings. Principal component and differential guide RNA (gRNA) expression analyses, as well as KEGG pathway and gene ontology analysis, were utilized. We then examined the transcriptome of cells grown in adherent and suspension via RNA-sequencing. Known databases (Protein Atlas, STRING, The Cancer Genome Atlas, TCGA) were utilized to refine the candidate gene list. We validated a subset of genes using small hairpin RNA (shRNA) knockdown and cell viability studies.

Results: CRISPR/Cas9 screen of HGSOC cells grown in adherent compared to suspension settings identified 15,636 differentially expressed gRNAs (adj \(P < 0.05\)), representing 11,572 genes, of which 2,206 had ≥2 targeting gRNAs with similar directionality, suggesting greater significance. RNA-seq analysis of cells grown in adherent compared to suspension identified 804 differentially regulated genes \((P < 0.0001)\). CRISPR/Cas9 and RNA-seq analysis overlap found 108
genes, representing a 1.55-fold enrichment. KEGG pathway analysis of the 108 genes revealed enriched pathways including dorsoventral axis formation (NOTCH signaling), TGFbeta signaling, and calcium signaling. Cross-referencing TCGA found 8 of these genes were correlated with OS. Utilizing The Protein Atlas we identified 13 genes predominantly expressed in ovarian cancer for further validation and elucidation of their role in anoikis. All 13 genes were significantly upregulated in suspension. Specifically, knockdown of CASC4, a known proto-oncogene, significantly inhibited suspension growth of HGSOC cells. See Figure 1.

**Conclusion:** NOTCH and TGFbeta were identified by our approach, which are known regulators of anoikis, increasing the confidence in our experimental design. More importantly, we identified novel genes and pathways that may play a role in anoikis escape. For instance, beyond being upregulated in 20% of HGSOC, nothing is known of CASC4's role in promoting HGSOC dissemination. This endeavor highlights potential new markers involved in HGSOC dissemination.

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**Fig. 1.** STRING Protein-Protein network analysis and kMeans clustering of the 108 top genes identified three distinct protein-protein interaction clusters: NOTCH, TGFbeta, and ErbB receptor signaling, receptor ligand interactions, and intracellular signaling.

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**1322 - Poster Session**

**Understanding and diagnosing endometrial cancer using MULTI-organ microbial taxonomic signatures**


**Objective:** The incidence of endometrial cancer (EC) has increased worldwide in recent years. The gastrointestinal (GI) microbiome influences peripheral inflammation, the immune system, as well as estrogen metabolism. An increase in peripheral inflammation, immune system suppression, and increased levels of estrogen play significant roles in the development of EC. Therefore, it is necessary to study the effects of the microbiome on the development of EC; however, this has yet to be explored. We hypothesize there is a unique microbial and/or immunological signature associated with EC that could be utilized for screening and for optimizing treatment strategies.

**Method:** This pilot study consented 30 women scheduled for surgery with Southern Illinois University Gynecology/Oncology division because of a positive endometrial biopsy. Samples (blood, urine, and vaginal/rectal swabs) were collected on the day of surgery (DOS) and during a postoperative (PO) visit within 2 months of surgery. Subjects also completed a standardized questionnaire to evaluate factors (e.g., diet, sexual practices, hygiene) that may affect one's microbiome. DNA from urine and vaginal/rectal swabs was sequenced to assess archaeal/bacterial and fungal community composition using the 16S rRNA gene and ITS2 gene region, respectively. Peripheral blood mononuclear cells (PBMCs) were extracted, and flow cytometry analyses were performed to identify immunosuppressive (regulatory T cells, Tregs) and inflammatory (Th17) T cell populations. Tregs were defined as CD4+CD25+FOXP3+ (natural, nTregs) or CD4+CD25-FOXP3+ (inducible, iTregs). Th17 were defined as CD4+CD25-RORγt. Immune profiles were analyzed using the Mann-Whitney U test in GraphPad Prism to calculate differences in cell populations.

**Results:** Overall, distinct archaeal/bacterial and fungal communities associated with the GI, urine, and vaginal samples were found. In general, taxa diversity was greatest in the gut, and lower in the urine and vaginal samples. EC patients showed an increase in Th17 cells both on the DOS and at the PO visit.

**Conclusion:** This project will generate the substantial groundwork to accomplish our long-term goal of earlier detection and personalized treatment strategies for EC. Developing a tool to determine the presence, severity, and prognosis of EC will have a significant influence on management.

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**1323 - Poster Session**

**Shared tumor antigens in uterine cancers with microsatellite instability: Putative targets for immunotherapeutic approaches**

T. Orfanelli, V. Roudko, C. Cimen Bozkus, B.D. Greenbaum, S.V. Blank and N. Bhardwaj. Icahn School of Medicine at Mount Sinai, New York, NY, USA
**Objective:** In the era of immunogenic neoantigen vaccines that arise from tumor-specific genomic alterations, we sought to identify highly frequent shared immunogenic tumor epitopes among a cohort of patients from The Cancer Genome Atlas (TCGA) with uterine cancer (UC) positive for microsatellite instability (MSI-H).

**Method:** A cohort of 75 patients with MSI-H UC was identified on the TCGA using computational analysis. To assess immunogenicity of selected neopeptides, we stimulated T cells in vitro by overlapping long peptides spanning each neopeptide. Enzyme-linked immunospot assay (ELISPOT) and intracellular staining were used to determine T cell responses.

**Results:** We identified 9 highly frequent, prevalent peptides, encoding MHC-I epitopes that originated from frameshift mutations in patients with MSI-H UC. Specifically, the epitopes derived from those 9 shared endometrial peptides were predicted to target ~80% of all uterine patient HLAome. The average frequency of the original 9 frameshifts in each tumor was estimated at ~40% rate, indicating a wide presence of those mutations in patients’ tumors. Moreover, the frameshift load did not affect gene expression, as revealed by transcriptome analysis. T cell stimulation assays using peripheral blood mononuclear cells (PBMCs) isolated from healthy donors and patients with uterine cancer were used to test the immunogenicity of the 9 common frameshift peptides. Majority of peptides induced CD8+ T cell responses, as determined by TNF-alpha and IFN-gamma production. T cell responses were observed in the majority of patients.

**Conclusion:** Selected endometrial shared frameshift peptides appear to be clonal and prevalent in MSI-H patients and may be valuable to target for a shared antigen cancer vaccine. We developed a computational pipeline to predict the most frequent and shared peptides across patients with MSI-H UC.

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1324 - Poster Session

A novel NSAID derivative for ovarian cancer chemoprevention in the hen model

L. Madeira da Silva, W. Berry, X. Chen, Y. Maxuutenko, G.A. Piazza and JM. Scalici. Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, Auburn University, Auburn, AL, USA

**Objective:** Preventive strategies for epithelial ovarian cancer (EOC) are underexplored but desperately needed. The hen model of EOC is a spontaneous disease model ideal for the study of disease prevention. NSAIDs have preventive potential, but toxicity has limited their study and utility as chemopreventives, primarily as a result of COX enzyme inhibition. We propose that limiting COX inhibition minimizes their toxicity but preserves the antitumor mechanism through inhibition of PDE10 and that a novel derivative, MCI-030, accomplishes this goal. This report aims to establish the effective dose, distribution, and toxicity profile of a novel COX-independent NSAID derivative, MCI-030, in the hen model.

**Method:** Thirty 2-year-old hens were divided into three cohorts (control, Sulindac, and MCI-030) and treated daily with their respective oral agent. One hen in each cohort underwent treatment escalation weekly at 100% until evidence of clinical toxicity was noted. The cohorts were then expanded to 3 hens, and the remainder of the study was conducted in a 3+3 design with the last cohort of hens treated at the suspected MTD. Tissue biopsies—GI, renal, liver and oviduct—were obtained to assess drug levels and toxicity.

**Results:** Initial doses were based on prior PK/PD data in hens of MCI-030 and Sulindac. Over 12 weeks of treatment and dose escalation, clinical toxicity was noted in both the MCI-030 and the Sulindac cohorts, although hens tolerated a higher dose of MCI-030 (1,680 ppm) than Sulindac (675 ppm). Two deaths were noted in the Sulindac group, while there were none in the MCI-030 cohort. Notable toxicity included decreased oral intake, weight loss, and decreased egg production. The toxicity of MCI-030 resolved after a short treatment hold and dose reduction. Plasma and tissue levels of MCI-030 suggest absorption in the oviduct occurs above the projected IC50 of MCI-030.

**Conclusion:** Our results suggest that MCI-030 is both more potent and less toxic than traditional NSAIDs, such as Sulindac, accumulates in the fallopian tube, and therefore holds valid potential as a chemoprevention agent.

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1325 - Poster Session

Discovery and characterization of long non-coding RNA-derived peptides in ovarian cancer

C.S. Liu, S. Gadad, V. Malladi, T. Nandu and J.S. Lea. The University of Texas Southwestern Medical Center, Dallas, TX, USA
Objective: Noncoding RNAs make up over 80% of the human transcriptome, and recent evidence suggests that noncoding RNAs have a major biological role in cellular development, physiology, and pathologies. Several human long noncoding RNAs (lncRNAs) have been characterized in cancer with both oncogenic and tumor suppressor functions. In ovarian cancer, lncRNAs have been associated with cell proliferation, metastasis, platinum resistance, and OS. Recent ribosomal profiling has suggested that lncRNAs can produce short peptides with potential biological functions in a variety of diseases. We hypothesized that some lncRNAs may have coding potential and produce peptides that are biologically relevant in ovarian cancer.

Method: We developed a computational genomics pipeline to identify potential lncRNA-derived peptides from ovarian cancer cells. Whole-cell extraction protein was obtained from ovarian cancer cell lines and analyzed using mass spectrometry. Peptide fragments were aligned to known annotated proteins and predicted proteins from the open reading frames of annotated lncRNAs. The results were filtered to identify peptides uniquely attributable to predicted lncRNA open reading frames. We used the cell lines OVCAR4 and HCC5044, which are representative of platinum-treated and treatment-naïve high-grade serous ovarian cancer. RNA sequencing was used to correlate lncRNA gene expression.

Results: We identified 1,304 unique potential lncRNA-derived peptides from 3 replicates of mass spectrometry; 245 were found in both cell lines. A total of 626 were attributed exclusively to a single lncRNA transcript, and these were ranked according to a scoring system based on mass spectrometry results. Five of the top-scoring lncRNA-derived peptides have high-fidelity sequence homology to proteins with nucleotide-binding potential, including nonhistone chromosomal proteins, core histone proteins, and a long interspersed nucleotide element-1 retrotransposon. The sequence homology was similar at the RNA transcript level. See Figure 1.

Conclusion: Our results suggest that a subset of lncRNAs may have coding potential and can produce proteins homologous to nuclear protein-coding genes. Our novel computational pipeline can be utilized to identify lncRNAs with the potential to serve as biomarkers and therapeutic targets in cancer.

1326 - Poster Session
Short-term organoid culture for drug sensitivity testing in high-grade serous ovarian cancer
K. Gotimer, H. Chen, G.S. Leiserowitz and L.H. Smith. aUC Davis Medical Center, Sacramento, CA, USA, bUC Davis Comprehensive Cancer Center, Sacramento, CA, USA, cUC Davis School of Medicine, Sacramento, CA, USA
**Objective:** It is hypothesized that multicellular spheroids (MCS) found in high-grade serous ovarian cancer (HGSOC) malignant effusions contain cells with stem cell-like properties. The objective of this study is to develop a short-duration culture in conditions selected to support organoid growth to be used as a platform for empiric drug sensitivity testing.

**Method:** Effusion specimens from patients with HGSOC were collected. MCS were recovered from fluid, cultured, and recovered after 3 days of growth (D0). MCS were then resuspended and distributed into 96 well plates. On D1, drugs at single concentrations that approximate maximum plasma concentrations found when used in the therapeutic setting or control media were added to each well. Targeted agents included mocetinostat, trametinib, LY294402, AZD5363, BBI503, MK1775, sorafenib, APR246, CB5083, and napabucasin. On D6, luminescence viability assays were performed using CellTiterGlo. Luminescence and organoid area were calculated for control media wells. Average percentage inhibition for each drug was calculated and considered potentially clinically meaningful if ≥50%. IC50 titrations were performed on drugs with greatest inhibition.

**Results:** Twelve specimens from 6 individual subjects were included. Between D1 and D6, organoids demonstrated 147% growth by ATP content and 190% growth by mean area. Among standard agents, oxaliplatin was only marginally inhibitory, while aclitaxel was the most effective inhibitor. Among targeted agents, multiple drugs showed significant inhibitory effect (Figure 1). The IC50 was calculated for a subset of drugs.

**Conclusion:** Short-duration organoid culture of MCS from HGSOC effusions can be used as a platform for empiric drug sensitivity testing. Using this model as a pretreatment ex vivo assessment of a drug’s antitumor activity could be helpful in the selection of the most active agents for each patient.
treatments, with 3 patients demonstrating resistance to first-line therapy with platinum and paclitaxel. Best responses included 2 patients with partial response (PR): 12-month duration and an ongoing 8-month duration. Two patients had stable disease (SD) of 4-month duration each. Two additional patients had SD after 2 cycles. Interestingly, 3 patients with massive ascites had symptomatic resolution of the ascites, including 1 patient who had PD as best response. Expansion cohort results will be presented.

**Conclusion:** Paclitaxel in combination with SPL-108 is safe and well tolerated at the doses used. Four of 6 patients have shown prolonged PR and stable disease as well as clinical benefit from symptomatic ascites. Expansion cohort results are pending and will be presented.

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1328 - Poster Session

**Cowpea mosaic virus nanoparticles for the treatment of high grade serous ovarian cancer: A patient-derived xenograft study**

C. Dominick$, P. Joseph$, E. Ponting$, A.J. Armstrong, J. Nakayama, C.I. Nagel, K. Zanotti, S.E. Waggoner, N.F. Steinmetz and A. DiFeo. $University Hospitals Cleveland Medical Center, Cleveland, OH, USA, $Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH, USA

**Objective:** Epithelial ovarian cancer (EOC) is the most lethal gynecologic malignancy. Although surgery and chemotherapy improve survival, novel therapeutics are needed to improve outcomes for patients with EOC. It is known that plant virus-based nanoparticles can have anticancer properties in mouse-derived cell lines. However, the antitumoral activity of virus-like nanoparticles in a patient-derived xenograft (PDX) mouse model has not yet been studied in EOC. Therefore, our goal was to determine whether nanoparticles from cowpea mosaic virus (CPMV) can suppress tumor growth in a PDX model of high-grade serous ovarian cancer.

**Method:** Twenty female athymic nude mice underwent intraperitoneal injection of a luciferase-tagged patient-derived cell line of high-grade serous ovarian cancer. Intraperitoneal injection of luciferin provided a bioluminescence substrate. Bioluminescent images were captured by a PerkinElmer IVIS Spectrum, and tumor radiance (p/sec/cm$^2$/sr) was analyzed and quantified using Living Image software to monitor the development of tumor every 3 days. After 9 days, mice were randomized to weekly intraperitoneal treatment with CPMV versus phosphate buffered saline placebo based on tumor signal. Final imaging was obtained on day 21. Because of health concerns of the mice in the placebo group, all surviving mice were sacrificed on day 24. Postmortem examination was performed on each mouse to assess tumor weight and distribution. A Student t test was performed to compare average tumor bioluminescence and weight. A Fisher exact test was performed to compare tumor distribution.
Results: There was a significant difference in bioluminescence between CPMV-treated and placebo-treated mice at day 18 ($P = 0.025$) and at day 21 ($P = 0.0019$). The placebo-treated mice had significantly higher tumor weight upon study completion ($P = 0.03$). A significant difference in tumor distribution was noted with only 44.44% of the CPMV-treated mice demonstrating tumor burden beyond the pelvis, compared to 100% in the placebo group ($P = 0.0038$). See Figure 1.

Conclusion: Virus-like nanoparticles from CPMV suppress tumor growth and result in less disease beyond the pelvis in a high-grade serous ovarian cancer PDX model. These findings suggest that CPMV may represent a novel therapeutic option for the treatment of high-grade serous ovarian cancer.

1329 - Poster Session
Anticancer effect of CKD-602, a topoisomerase 1 inhibitor, against cervical cancer
S.Y. Hur Sr.a and Y.J. Choib.
aSeoul St. Mary's Hospital, College of Medicine, Catholic University, Seoul, South Korea, bSeoul St. Mary's Hospital, Seoul, South Korea

Objective: Cervical cancer is the third most common gynecological malignancy and responsible for 10%–15% of cancer-related deaths in women. However, only modest response rates with excessive toxicity were presented without improving survival rate. Therefore, novel therapeutic agents for cervical cancer are necessary. In this study, we aimed to investigate the anticancer effect of CKD-602, a topoisomerase 1 inhibitor, in cervical cancer.

Method: Two established human, immortalized, cervical cancer cell lines (CaSki and HeLa) were used in this study. We performed cell invasion assay in order to elucidate whether CKD-602 holds the character to inhibit cervical cancer cell (CaSki, Hela and Siha) invasion. Then, we identified the apoptotic cells by the Annexin V-FITC apoptosis detection kit. In order to elucidate whether CKD-602 has an effect upon cellcycle, we performed cell-cycle analysis. Tumor xenograft models were established by injecting female Balb/c nu mice (7–8 weeks) subcutaneously with CaSki cells ($4 \times 10^6$/head). CKD-602 was injected 4 times every 4 days, and tumor volume was checked until 16 days after the fourth CKD-602 injection.

Results: First we demonstrated CKD-602 has an inhibitory effect on cervical cancer cell survival, and it exerted apoptotic activity after 48 hours of treatment (control 5.5% and CKD-602 treated 29.2%, control 22.5% and CKD-602 treated 32.5%, in CaSki and HeLa, respectively). Second, we found that CKD-602 impairs the invasiveness of cervical cancer cells (CaSki 0.03% and HeLa 0.27% compared to control). Third, in cell-cycle analysis, we found the G2/M arrest in both cells (CaSki and HeLa). In the xenograft model, we also found that CKD-602 inhibited tumor growth. CKD-602 was injected when the tumor volume exceeded approximately 50 mm$^2$. On the post 16 days of the fourth treatment, the average tumor volume was evaluated, and we found 248 mm$^3$ for the control group and 123 mm$^3$ for the CKD-602 treated group.

Conclusion: We for the first time showed that CKD-602 has an anticancer effect against cervical cancer. This study supports future clinical trials of CKD-602 in cervical cancer.

1330 - Poster Session
NR4A1 inhibition as a novel strategy to sensitize homologous recombination-proficient ovarian cancer to PARP inhibitors
A. Beeghly-Fadiela, D. Khabeleb, M.A. Crispensc and A.J. Wilsonc.
aVanderbilt University School of Medicine, Nashville, TN, USA, bUniversity of Kansas Medical Center, Kansas City, KS, USA, cVanderbilt University Medical Center, Nashville, TN, USA

Objective: Ovarian tumors frequently retain proficiency in homologous recombination (HR) DNA repair, which is linked to resistance to poly ADP-ribose polymerase inhibitors (PARPi). Identifying new strategies to improve response to PARPi in women with HR-proficient ovarian cancer is a key clinical challenge. We previously demonstrated that nuclear orphan receptor NR4A1 has pro-tumor effects in ovarian cancer cells, but the prognostic value of NR4A1 expression in patient tumors was ill-defined. Our goals were to determine whether inhibiting NR4A1 reduces efficiency of HR in ovarian cancer cells, thereby enhancing sensitivity to PARPi, and to clarify the prognostic value of NR4A1 in patient tumors.

Method: In HR-proficient ovarian cancer cells (OVCAR-3, OVCAR-4, SKOV-3), we inhibited NR4A1 using the established antagonist C-DIM-pPHOH (C-DIM). Antitumor effects of C-DIM alone and in combination with PARPi olaparib or rucaparib were assessed in standard laboratory assays. NR4A1 was measured by immunohistochemistry in 203 formalin-fixed paraffin-embedded patient ovarian tumor samples with linked clinical data. Associations with patient overall and PFS were quantified with multivariate proportional hazards regression.
Results: NR4A1 inhibition reduced cell growth (sulforhodamine B assays) and HR efficiency (BRCA1 and RAD51 foci formation and DRGFP reporter activity), and stimulated markers of DNA damage (pH2AX) and apoptosis (cleaved PARP). Combination PARPi and C-DIM treatment induced synergistic growth inhibition, apoptosis, and DNA damage induction. In patient tumors, lower than median NR4A1 expression was more common among cases with later stage, higher grade, or platinum-resistant disease. After adjustment for prognostic covariates, higher NR4A1 expression was associated with more than two-fold significantly shorter PFS.

Conclusion: Shorter survival among ovarian cancer cases with higher NR4A1 expression is supported by evidence of reduced cell growth and increased apoptosis following NR4A1 inhibition, alone or combined with PARPi. Our findings provide rationale for NR4A1 inhibition as a novel therapeutic approach to sensitize HR-proficient ovarian tumors to PARPi, with the potential to benefit a large number of women with chemoresistant disease.

1331 - Poster Session
STAT3 promotes ovarian cancer growth and chemoresistance by modulating its energy metabolism
R. Rattana, V. Raja, T.E. Buekers, S. Hamid, M.A. Elshaikh, S. Giri and A.R. Munkarah. aHenry Ford Health System, Detroit, MI, USA, bHenry Ford Hospital, Detroit, MI, USA

Objective: STAT3 (signal transducer and activator of transcription 3) is associated with tumor progression, metastasis, and chemoresistance in ovarian cancer. High STAT3 expression is a predictor of poor prognosis in ovarian cancer patients. Recently STAT3 has been shown to modulate mitochondrial function to promote carcinogenesis. Our aim was to investigate whether mitochondrial STAT3 can modulate cellular metabolism of ovarian cancer cells and promote oncogenic abilities.

Method: STAT3-stable clones were generated in A2780 ovarian cancer cells, along with empty vector (pcDNA) clones. Proliferation was estimated by MTT and colony formation assays. Various clones were grown as xenografts in nude mice and treated with STAT3 inhibitor (STATTIC) via intraperitoneal injections. Seahorse XF Extracellular Flux analyzer was used to measure the bioenergetic phenotype by real-time measurements of glycolysis and mitochondrial oxidation using extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) as outputs, respectively.

Results: Induced expression of STAT3 in A2780 ovarian cancer cells caused increased proliferation (P < 0.01), colony formation (P < 0.001), and chemoresistance (P < 0.01) in vitro, and large ovarian tumors (P < 0.01) in vivo compared to parental/pcDNA controls. Bioenergetic profiling showed higher OCR and ECAR in clones expressing STAT3 (P < 0.01), suggesting their "metabolically active" phenotype compared to the metabolically less active phenotype of parental/pcDNA clones. STATTIC inhibited both nuclear and mitochondrial STAT3 and inhibited the proliferation of STAT3 over-expressing A2780 cells in vitro (P < 0.01) and in vivo (P < 0.01), reduced their chemoresistance (P < 0.05), and reversed their metabolically active state. In contrast, a selective inhibitor of nuclear STAT3, cryptotanshinone, was relatively less effective in reducing the chemoresistance and metabolic changes. Ascites-driven ovarian cancer cells from patients with chemoresistant ovarian cancer showed increased expression of mitochondrial-STAT3 compared to nuclear-STAT3.

Conclusion: Mitochondrial-STAT3 can induce metabolic changes in ovarian cancer cells and enhance their cellular fitness by promoting chemoresistance.

1332 - Poster Session
Role of MCP-1 in promoting adiposity-driven ovarian cancer
R. Rattana, T.E. Buekers, V. Raja, M. Hijazi, R.K. Hanna, S. Hamid, S. Giri and A.R. Munkarah. aHenry Ford Health System, Detroit, MI, USA, bHenry Ford Hospital, Detroit, MI, USA, cKarmanos Cancer Center/Wayne State University, Detroit, MI, USA

Objective: Ovarian cancer cells use fat from adipocytes to fuel their growth. We have shown that ovarian cancer cells exposed to adipocyte-conditioned media have an increased expression of monocyte chemotactrant protein-1 (MCP-1). MCP-1 aids in inflammatory response and increases adhesion and invasion of ovarian cancer cells. We showed that a high-fat diet induced aggressive ovarian cancer tumors in mice and produced increased amounts of MCP-1 and decreased expression of phosphorylated AMPK (amino monophosphate-activated kinase). In the current study we tested our hypothesis that MCP-1 promotes migration/invasion of ovarian cancer cells by promoting inflammatory immune response via inhibition of AMPK.

Method: ID8 ovarian cancer cells were treated with MCP-1, and effects on proliferation, migration, and invasion were assessed by MTT assay, scratch assay, and a migration/invasion assay, respectively. Western blots were performed to identify effects of
MCP-1 on phosphorylated AMPK (pAMPK). Preclinical efficacy of a MCP-1 neutralizing monoclonal antibody (mAb, 100 μg/bd kg wt thrice a week) was investigated in an immunocompetent syngeneic mouse ID8 ovarian cancer model on high-fat or regular diet. Tumor growth was monitored by in situ luciferase guided imaging and immunohistochemical markers, and immune response was assessed by flow cytometry.

**Results:** In vitro MCP-1 did not affect the ovarian cancer cell proliferation but increased the rate of cell migration \((P < 0.01)\) and invasion \((P < 0.05)\). MCP-1 reduced AMPK activity. Activation of AMPK by metformin reversed the increase seen in MCP-1 mediated migration and invasion \((P < 0.05)\). In vivo MCP-1 mAb treatment slowed the progression of ovarian cancer tumor growth and decreased the metastatic spread in mice as seen by decreased tumor burden \((P < 0.01)\) and Ki-67 \((P < 0.01)\). Neutralizing MCP-1 decreased the infiltration of tumor-associated macrophages and myeloid-derived suppressor cells \((P < 0.05)\), while it increased infiltration of T cells \((P < 0.05)\), with the effect being more pronounced in obese mice than in regular mice.

**Conclusion:** MCP-1 plays a crucial role in promoting ovarian cancer growth possibly by inhibition of AMPK, especially under conditions of increased adiposity.

**1333 - Poster Session**

**Inhibition of the Wnt/β-catenin pathway enhances anti-tumor immunity in ovarian cancer**


aUniversity of Alabama at Birmingham, Birmingham, AL, USA, bUniversity of California Riverside, Riverside, CA, USA, cThe University of Chicago Medicine, Chicago, IL, USA, dGenetics/Genomics, Huntsville, AL, USA

**Objective:** We sought to determine the effect of inhibition of the Wnt/β-catenin pathway with the small molecule WNT974 on antitumor immunity in human ovarian cancer ascites cells and in a syngeneic mouse model of ovarian cancer.

**Method:** Human ovarian cancer ascites cells were treated with WNT974, and RNAseq libraries were compared between responders and nonresponders to WNT974. C57BL/6 mice were injected subcutaneously (SC) or intraperitoneally (IP) with 7 × 10^6 ID8 mouse ovarian cancer cells. Mice were then treated with vehicle control, WNT974, paclitaxel, or a combination of the two drugs. SC tumors were measured with calipers, and tumors were harvested for NanoString® gene expression profiling. Mice with IP tumors were kept to evaluate survival or sacrificed after 14 days of treatment, and omental tumor weights and ascites volume were measured. Flow cytometry was used to evaluate the immune response in IP tumors. T cell repertoire was compared between groups.

**Results:** Gene expression profiling of human ovarian cancer ascites cells revealed distinct signatures in responders and nonresponders to WNT974, which strongly correlated with gene expression patterns related to T cell infiltration in The Cancer Genome Atlas analysis of ovarian cancer. Administration of WNT974 to mice implanted with syngeneic ovarian tumors inhibited tumor growth, prevented ascites formation, and prolonged survival. Treatment also increased the ratio of CD8+ T cells to T regulatory cells (Tregs) in tumors and enhanced the effector functions of infiltrating CD4+ and CD8+ T cells. Treatment decreased the expression of inhibitory receptors PD-1, CTLA-4, and TIM3 on CD8+ T cells. Combining WNT974 with paclitaxel further reduced tumor growth, prolonged survival, and expanded the T cell repertoire compared to either treatment alone.

**Conclusion:** These findings suggest that inhibiting the Wnt/β-catenin pathway may have a potent immunomodulatory effect in the treatment of ovarian cancer, particularly when combined with paclitaxel.

**1334 - Poster Session**

**Development and applicability of integrative tumor response assays for advanced epithelial ovarian cancer**


aUniversity of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea, bASAN Medical Center, Seoul, Korea, Republic of (South), cUniversity of Ulsan College of Medicine, ASAN Medical Center, Seoul, Korea, Republic of (South)

**Objective:** In platinum-resistant recurrent ovarian cancer patients, non-platinum-based agents are preferred. There is no clear guideline on which anticancer therapy must be chosen. Histoculture drug response assay (HDRA) is a test that evaluates chemosensitivity to a given chemotherapy agent in vitro before treatment is initiated, using tumor tissue obtained during
surgery to determine the appropriate drug of choice. However, with the pre-established HDRA method, only chemosensitivity to first-line therapies can be tested. To improve upon this issue, at our center, we pertinently applied an in vitro chemosensitive assay based on HDRA: the integrative tumor-response assay (ITRA, Patent No. 10-1046883, the Korean Intellectual Property Office, Seoul, Korea). Our study aimed to prospectively correlate clinical responses to second-line chemotherapy for recurrent epithelial ovarian cancer (EOC) with in vitro ITRA results.

**Method:** A total of 44 patients with advanced epithelial ovarian cancer (EOC) were prospectively enrolled between 2015 and 2017 at Asan Medical Center, Seoul, Korea. ITRA comprised two sequential histoculture drug response assays (HDRAs) of patients' tumor tissues. The first stage of ITRA was HDRA performed with first-line chemotherapy of paclitaxel/carboplatin, paclitaxel, and carboplatin. The second stage of ITRA was performed with tumor cells surviving after the first stage using second-line chemotherapy of topotecan, belotecan, gemcitabine, doxorubicin, ifosfamide, vinorelbine, and etoposide.

**Results:** Forty-four patients met this study's criteria. All patients underwent primary cytoreductive surgery. Among 44 patients, 18 (40.9%) patients completed second-line chemotherapy based on the ITRA results. Based on the results of ITRA, pegylated liposomal doxorubicin (PLD) was the most frequently used second-line chemotherapy agent in 18 patients, followed by camtobell. The objective response rate was 38.9%. Four patients (22.2%) showed complete response, and 3 (16.7%) had partial responses in target lesions (RECIST). Clinical benefit response rate was 50% including stable disease status of 2 patients (11.1%). The sensitivity of ITRA was 85.7% with a specificity of 18.2% and accuracy of 44.44%.

**Conclusion:** ITRA had acceptable applicability and may help choose second-line chemotherapy for advanced EOC patients.

**1335 - Poster Session**

**Development and characterization of a chimeric siRNA-aptamer with inhibitory activity in HER2/3+ cells**

H.Y. Liu and N.J. Maehle. **Medical College of Georgia, Augusta, GA, USA**

**Objective:** We have shown that resistance to HER2-targeted therapies is associated with an increase in the expression of other HER receptor family members (EGFR and HER3) in both breast and ovarian cancer cells. In this report we have developed a novel nucleic acid aptamer-siRNA chimera (H2EH3) that can target cells expressing EGFR/HER2/HER3 using a single molecule.

**Method:** Chimeras were generated through in vitro transcription. 2’ F-modified pyrimidines were incorporated into RNAs to increase resistance to nucleases. To evaluate biodistribution, tumor-bearing mice were intravenously administered with Cy5-labeled H2EH3. Female athymic mice were injected with BT474 tumor cells. Following the establishment of tumors (50 mm³), mice were administered H2EH3 (8 nmols) or controls every 3 days by intravenous injection for 4 weeks.

**Results:** To construct H2EH3, the 3’ terminus of an existing HER3 aptamer was fused with the antisense strand of EGFR siRNA (RNA1), and the 3’ terminus of HER2 aptamer was fused with the sense strand of EGFR siRNA (RNA2). Through in vitro transcription, 2 transcripts (RNA1 and RNA2) with 19-bp complementing sequences (sense and antisense strands of EGFR siRNA) were annealed to form a HER2 aptamer-EGFR siRNA-HER3 aptamer chimera (H2EH3). Cytotoxicity assays show that H2EH3 inhibits growth of HER2+ HER3+ cells but not HER2- and HER3- cells. Studies on cell cycle and apoptosis demonstrate that H2EH3 can cause G2/M arrest in 24 hours and trigger apoptosis at 72 hours in HER2+ HER3+ cells. To determine whether H2EH3 can be internalized into HER2+ HER3+ cells (a prerequisite for siRNA silencing), confocal microscopy with z stack was performed to visualize the subcellular localization of Cy5-H2EH3. Results show that Cy5-H2EH3 enters cells and is present in the cytoplasm after 12 hours of incubation. Protein expression assays demonstrated that H2EH3 significantly reduced EGFR, HER2, and HER3 expression and also upregulates several apoptotic proteins. Preclinical studies further demonstrate the tumor-targeting capability of this novel inhibitor in vivo.

**Conclusion:** These results demonstrate the construction of a novel chimeric molecule, H2EH3, that has the ability to simultaneously inhibit HER2+ HER3+ tumor cell growth in vitro and in vivo, while demonstrating limited toxicity in treated mice.

**1336 - Poster Session**

**Overexpression of HER2/HER3 and the clinical feature of ovarian cancer**

S. Kim, K.J. Ryu, S. Lee and J.Y. Song. **Korea University College of Medicine, Seoul, Korea, Republic of (South)**
Objective: Human epidermal growth factor receptor-2 (HER2) and -3 (HER3) belong to the epidermal growth factor receptor (EGFR) family of transmembrane receptor tyrosine kinases, which are responsible for cell survival and proliferation, but their role in ovarian cancer is not yet established. In this study, their status in specimens of epithelial ovarian cancer was determined with immunohistochemistry (IHC) and in situ hybridization (ISH) and was analyzed to determine the correlation with clinical features of ovarian cancer.

Method: Tissue microarrays (TMAs) were prepared from paraffin blocks of 105 ovarian tumor samples. HER2, HER3, PI3K, Akt, p-Akt, mTOR, p-mTOR, S6, and p-S6 expression levels were investigated using immunohistochemistry (IHC). HER2 and HER3 amplifications were determined using in situ hybridization (ISH). The correlation between HER2/3 expression and disease outcome of the patients including surgical outcome, progression-free survival (PFS), and overall survival (OS) was analyzed.

Results: HER2 positivity was 3.8% by IHC and 5.7% by ISH, whereas that of HER3 was 12.4% and 8.6%, respectively. HER2 status by either IHC or ISH was not related to PFS \((P = 0.128, P = 0.168, \text{respectively})\) and OS \((P = 0.245, P = 0.164, \text{respectively})\). However, the HER3 status determined using FISH was associated with poor PFS \((P = 0.035 \text{ on log rank test})\), which was a significant risk factor even after adjusting other possible risk factors in multivariate analysis \((HR = 2.377, 95\% \text{ CI 1.18–7.49, } P = 0.021)\). Expressions of Akt, p-mTOR, and S6 were also related with poor progression \((P = 0.008, P = 0.049, P = 0.014, \text{respectively})\).

Conclusion: HER3 is possibly an independent marker for poor prognosis in individuals with ovarian cancer, as the HER3 signalling pathway is distinct from that of HER2. The possibility of targeted therapy for patients with HER3 alteration in ovarian cancer should be evaluated.

1337 - Poster Session
Key immunological functions involved in the progression of epithelial ovarian serous carcinoma discovered by the gene ontology-based immunofunctionome analysis
C.C. Chang. Tri-service General Hospital, Taipie, Taiwan; National Defense Medical Center, Taipei, Taiwan

Objective: Serous carcinoma (SC) is the most common and lethal subtype of epithelial ovarian carcinoma; immunotherapy is a potential treatment for SC. However, the global immunological functions of SC as well as their change during the progression of SC have not been investigated in detail until now.

Method: We conducted a genome-wide integrative analysis to investigate the immunofunctionomes of SC at 4 tumor stages by quantifying the immunological functions defined by the Gene Ontology gene sets. DNA microarray gene expression profiles of 1,100 SCs and 136 normal ovarian tissue controls were downloaded from the Gene Expression Omnibus database and converted to the functionome. Then the immunofunctionomes were reconstructed by extracting the offspring from the functionome for the 4 SC staging groups.

Results: The key immunological functions extracted from immunofunctionomes with a series of filters revealed that the immunopathy of SC consisted of a group of deregulated functions with the core members including B cell activation and differentiation, regulation of leukocyte chemotaxis/cellular extravasation, antigen receptor-mediated signaling pathway, T helper-mediated immunity, and macrophage activation, and the auxiliary elements included leukocyte-mediated immunity, regulation of inflammatory response, T cell differentiation, mononuclear cell migration, megakaryocyte differentiation, complement activation and cytokine production.

Conclusion: These deregulated immunological functions reveal the candidates to target in immunotherapy.

1338 - Poster Session
Exosomal mir-219a-5p as a potential predictive biomarker for gestational trophoblastic neoplasia chemotherapy resistance
Y. Weng, X. Shen, X. Xie, X. Cheng, W. Lv and X. Wang. Women’s Hospital, School of Medicine, Zhejiang University, Zhejiang, China

Objective: Gestational trophoblastic neoplasia (GTN) is a group of malignant diseases derived from trophoblastic cells with abnormal proliferation and metastasis. The FIGO 2000 staging and risk factor scoring system has been globally used for
guiding management and predicting prognosis of GTN patients, but its accuracy still needs to be improved. It has been reported that exosomal molecules can be used as diagnostic and prognostic biomarkers in many types of tumors.

**Method:** Next-generation sequencing technique was performed to identify microRNAs profiles in exosomes from 10 methotrexate-sensitive and 10 methotrexate-resistant GTN low-risk patient plasma. The results were then validated by quantitative real-time PCR with 51 methotrexate-sensitive and 34 methotrexate-resistant GTN patients, and further analyzed by bioinformatics and statistical methods. Methotrexate-sensitive and -resistant cell lines were cultured. The expression of exosomal miRNA in culture medium was detected. Inhibitors or mimics of miRNA were transfected into cells, and the response of cells to methotrexate was detected.

**Results:** A total of 28 significantly downregulated and 1 significantly upregulated microRNAs were identified through sequencing, and only miR-219a-5p was statistically validated as downregulation on a large-scale sample subsequently. The discrimination of methotrexate-sensitive from methotrexate-resistant patients was demonstrated by a receiver operating curve (AUC = 0.723, P < 0.001, sensitivity 66.0%, specificity 81.3%). Decreased level of exosomal miR-219a-5p in GTN patient plasma was associated with poor response to methotrexate. Methotrexate-resistant cells showed lower exosomal miR-219a-5p level than methotrexate-sensitive cells. Enforced modulation of miR-219a-5p expression altered the response of cells to methotrexate.

**Conclusion:** Plasma exosomal miR-219a-5p is a potential biomarker for predicting methotrexate resistance in low-risk GTN patients.

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**1339 - Poster Session**  
**Synergistic anti-cancer effects of metformin and SGLT2 inhibitor with platinum-based chemotherapy against human endometrial carcinoma hec-1 and snu-1077 cells**  
J.S. Kim. KGOG / Gynecologic Oncology Center, Seoul, Korea, Republic of (South)

**Objective:** We investigated the anticancer effects of metformin and SGLT2 inhibitor either alone or in combination with cisplatin or carboplatin in Hec-1 and SNU-1077 human endometrial carcinoma cells.

**Method:** Cells with carboplatin or cisplatin treatment were used as control groups. To MTT assay, the cancer cell lines SNU-1077 and Hec-1 cultured in CO₂ incubator were centrifuged at 350 g for 5 minutes, then resuspended and counted by haemocytometer before replating in 96 well plates. The resuspended cells of 1.5 × 10⁴ cells/well were plated in 96 well plates and cultured for 24 hours in CO₂ incubator. The cultured cells in each well were supplemented with cisplatin, carboplatin, SGLT2 inhibitor, and metformin. The inhibition rate of cell growth (IR) was calculated using the equation IR (%) = (1− mean absorbance of treated wells ÷ mean absorbance of control wells) × 100. In both SNU-1077 and Hec-1 cells, a combination of 250 µg/ml SGLT2 inhibitor with 250 µg/ml metformin treatment for 48 hours showed a strong synergistic effect (combination index, CI, <0.5) in cell growth inhibition.

**Results:** Comparison of the IC₅₀ value of metformin and SGLT2 inhibitor individually demonstrated that the combination of metformin-SGLT2 inhibitor was more effective in preventing cell growth than each one of them (SNU-1077 plus carboplatin, 46%, 54% vs 59%, respectively; Hec-1 plus cisplatin, 48%, 57% vs 64%, respectively). In particular, SGLT2 inhibitor was more effective in preventing cell growth than metformin only (SNU-1077 plus cisplatin, 51% vs 35%; Hec-1 plus carboplatin, 54% vs 42%). The MTT test findings showed that the combination of metformin and SGLT2 inhibitor had high synergistic effects in killing cancer cells. In quantitative apoptosis studies, combination of metformin and SGLT2 inhibitor with carboplatin or cisplatin resulted in much stronger apoptotic death compared to each agent alone in both cell lines. SGLT2 inhibitor plus carboplatin combination showed stronger apoptotic effect than metformin plus carboplatin combination in SNU-1077 and Hec-1a cells. Metformin and SGLT2 inhibitor are synergistic antiproliferative effects to platinum-based chemotherapy in endometrial carcinoma. See **Figure 1**.

**Conclusion:** These results suggest a possible synergism between SGLT2 inhibitor and conventional cytotoxic agents for endometrial cancer treatment. Further work is needed to provide exact insight into the mechanisms involved in the elicited anticancer effects of the combination treatment of metformin and SGLT2 inhibitor.
Identification of autophagy related antitumor effect in cervical cancer
G.W. Lee, Y.B. Ko and H.J. Yoo. Chungnam National University Hospital, Daejeon, Korea, Republic of (South)

Objective: AMP-activated protein kinase (AMPK) is a highly conserved serine/threonine protein kinase and an essential mediator in maintaining cellular energy homeostasis. Recent studies suggested that AMPK is crucial for the activation of autophagy, which is an emerging target for the prevention and treatment of various cancers. The aim of this study was to explore the antitumor effects of AMPK-inducing agents in human cervical cancer cells.

Method: Human cervical cancer cell lines HeLa and SiHa were cultured. Autophagic cell death, intrinsic apoptosis and total apoptosis, and survival fraction were investigated after treatment with AMPK inducer.

Results: We found that AMPK-inducing agents including metformin, fenofibrate, or 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) decreased the cell viability of HeLa cells in a dose- and time-dependent manner. Treatment of AICAR or fenofibrate significantly activated the AMPK-signaling pathway, leading to subsequent induction of autophagy. However, pretreatment of autophagy-specific inhibitors markedly abrogated AICAR- or fenofibrate-mediated cytotoxic effects.

Conclusion: Collectively, our results suggested that the application of AMPK-inducing agents is a promising strategy for the prevention and treatment of cervical cancer and the activation of autophagy.

Fenofibrate induces G0/G1 phase cell cycle arrest in cervical cancer by targeting the AMPK/mtorc pathways
H.J. Yoo. Chungnam National University, Daejeon, South Korea

Objective: Fenofibrate is a commonly used drug for the treatment of diabetes. Accumulating evidence suggests that it exerts antitumor effects in several cancers, such as breast, liver, glioma, prostate, and pancreas. However, the underlying molecular mechanisms have not been clearly elucidated.

Method: The antitumor effects of fenofibrate were evaluated using human cervical cancer cell lines (HeLa) in vitro. Cell viability was assessed with CCK8, and cell proliferation was measured by Edu incorporation assay. Cell cycle distribution and apoptosis were examined by flow cytometry. Activation of AMPK and inhibition of mTORC1/C2 pathways were assessed by Western blot analysis.
**Results:** Fenofibrate effectively inhibited the proliferation of HeLa cell lines, an effect that was associated with G0/G1 cell cycle arrest but not apoptosis and the induction of autophagy. Fenofibrate activated AMPK and repressed both mTORC1 and mTORC2 signaling pathways in cervical cancer cells as well as downstream molecular signaling pathways, such as p-4EBP1 and p-AKT. AMPK activation resulted in direct phosphorylation and activation of tuberous sclerosis complex 2 (TSC2), leading to inhibition of the mammalian target of rapamycin (mTOR). In addition, fenofibrate inhibited cervical cancer cell growth in an AMPK-dependent manner.

**Conclusion:** Fenofibrate inhibits the proliferation of cervical cancer cells by cell cycle arrest. Our results suggest that the molecular mechanism involves dual repression of mTORC1 and mTORC2 pathways via AMPK activation. Our study provides a theoretical basis for the development of novel strategies for the treatment of cervical cancer using Fenofibrate as an already approved and safe drug.

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**1342 - Poster Session**

**Doxorubicin-loaded oligonucleotide conjugated gold nanoparticles: A promising drug delivery system for ovarian cancer**

S. Jeon, Y. Jang, J. Min, D. Kim and H. Jeon. Soonchunhyang Cheonan Hospital, Cheonan, Korea, Republic of (South)

**Objective:** A major cause of failure in the treatment of advanced ovarian cancer is chemoresistance. Gold nanoparticles (AuNPs) are promising drug delivery systems to overcome chemoresistance. Doxorubicin (DOX) is one of the representative cancer chemotherapeutic agents and is widely used by many researchers as a chemotherapy agent in the drug delivery system; however, there have been limited data on ovarian cancer research. Our aim was to compare cytotoxic effect between DOX and Doxorubicin-loaded oligonucleotides (ONTs) attached to gold nanoparticles (AuNPs) called DOA on ovarian cancer cell lines.

**Method:** We propose Doxorubicin-loaded oligonucleotides (ONTs) attached to gold nanoparticles (AuNPs) as a drug delivery system for cancer chemotherapy. We utilized AuNPs as drug delivery vehicle, which were synthesized by chemical reduction to be 13 nm diameter. Oligonucleotide-AuNPs present numerous binding sites for DOX, facilitating the delivery of DOX to cancer cells. Transmission electron microscope (TEM), fluorescence spectrometer, and MTT assay were done for characterization and for cell viability assay.

**Results:** We characterized Doxorubicin-loaded oligonucleotide conjugated gold nanoparticles (DOA) using TEM image of AuNPs. And 70% of DOX in solution could be bound to ONTs on AuNPs to become DOX-loaded AuNPs, and about 28% of loaded DOX was released from the as-prepared DOA. In MTT assay, significant reduction in the cell viability was detected in DOA-treated ovarian cancer cells (SKOV3, A2780, Hey A8) than DOX (P < 0.05).

**Conclusion:** Our results suggested that ONTs attached to AuNPs is an effective drug delivery system and DOA might be a beneficial strategy for chemoresistant patients with ovarian cancer. We plan to perform in vivo studies in the near future for verification of the results from our in vitro study.

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**1343 - Poster Session**

**Morpho-structural peculiarities of blood formed elements and clinic-pathological characteristics in women with uterine (Benign, Malignant) tumors in menopausal age**

N. Kotrikadze, L. Ramishvili, T. Tupinashvili, I. Nakashidze, M. Alibegashvili, M. Gordeziani and S. Ahmad. Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia, Batumi Shota Rustaveli State University, Batumi, Georgia, Florida Hospital Cancer Institute, Orlando, FL, USA

**Objective:** We sought to investigate ongoing alterations that reflect on the structural characteristics of blood-formed elements based on the hormonal imbalance and the ABO system antigens among menopausal women with uterine (benign and malignant) tumors.

**Method:** Blood specimens from women with benign (n = 15) and malignant (n = 15) uterine tumors and healthy menopausal women (control, n = 5) were used. ELISA kits were used for quantitative determination of hormones. The blood-formed elements ultrastructure observations were conducted by electronic microscope.
Results: Compared to control (33.8 ± 0.7 pg/mL), estradiol level was higher in benign (45.7 ± 0.9 pg/mL) and malignant (70.7 ± 3.7 pg/mL) cases (P < 0.001). A similar pattern was noted in testosterone levels (control, 0.38 ± 0.03 ng/mL; benign 0.55 ± 0.04 ng/mL, P < 0.01; malignant, 1.56 ± 0.14 ng/mL, P < 0.001) and was higher in malignant cases. In contrast, progesterone levels were decreased in the disease cases (control, 0.93 ± 0.05 ng/mL, benign, 0.44 ± 0.003 ng/mL, malignant, 0.31 ± 0.02 ng/mL, P < 0.001). The percentage ABO system antigens distributions were O(I), control, 60 ± 10.9, benign, 40 ± 10.2, malignant, 25 ± 10.2; A(II), control, 30 ± 10.2, benign, 55 ± 11.1, malignant, 70 ± 10.6; B(III), control, 5 ± 4.8, benign, 0 ± 0, malignant, 0 ± 0; and AB(IV), control, 5 ± 4.8, benign, 5 ± 4.8, malignant, 5 ± 4.8 percent. Assessments of morphologic structure of erythrocytes revealed numerous pathological form erythrocytes (poikilocytosis) as benign and also in case of malignant tumors, particularly target cell (codocytes), hamlet cell, teardrop cells (dacrocytes), sickle cells (drepanocytes) erythrocytes.

Conclusion: Using ELISA and transmembrane electron microscopy, our results demonstrate that in the malignant uterine tumor of menopausal women, quantitative/structural changes occur in blood-formed elements indicating ongoing alterations in hormonal imbalance. Assessing these changes in structural characteristics would be useful in examining uterine pathologies and subsequent treatment plans.

1344 - Poster Session
Yes-associated protein (YAP) silencing as a new therapeutic strategy for ovarian cancer
J.W. Roh¹, J. Kim² and H. Choi³, ¹Dongguk University Ilsan Hospital, Goyang, Korea, Republic of (South), ²Boramae Medical Center, Seoul Metropolitan Government Seoul National University, Seoul, Korea, Republic of (South), ³Chung-Ang University, Seoul, Korea, Republic of (South)

Objective: Yes-associated protein (YAP) is a key effector of the hippo tumor suppressive pathway, and its abnormal expression is associated with carcinogenesis and chemoresistance in a number of malignancies. There were no relevant data in ovarian cancer. We examined the biological roles of YAP and the therapeutic effect of YAP silencing using siRNA, dobutamine, single or combined.

Method: YAP expression was evaluated in clinical samples from patients with ovarian cancer, benign neoplasm, and controls, and also in normal or malignant ovarian cell lines (HOSE 0160, SKOV3, OVCAR3, A2780, HeyA8, and HeyA8-MDR). Biological roles of YAP and therapeutic effect of YAP silencing were examined using in vitro (cell viability, apoptosis, and invasion ability) and in vivo (orthotopic ovarian cancer models) assays. We examined the therapeutic effect of YAP silencing using YAP siRNA, dobutamine, and their combination in in vitro experiments. For in vivo experiments, YAP siRNA, dobutamine, and their combination-loaded PLGA nanoparticle were used for effective delivery.

Results: Nuclear YAP (nYAP) expression, active form, was increased in ovarian cancers compared to controls or benign neoplasm. HeyA8 and -MDR showed high nYAP and low cytosol phosphorylated-YAP (pYAP), but HOSE 0160, SKOV3, OVCAR3, and A2780 showed high nYAP and pYAP. HeyA8 or HeyA8-MDR cells were used as YAP-activated ovarian cancer models, and SKOV3 as a YAP-inactivated ovarian cancer model. YAP silencing with siRNA suppressed YAP expression and resulted in decreased cell viability and invasion ability, and increased apoptosis in HeyA8, and -MDR cells (P < 0.05) but not in SKOV3. Dobutamine-induced YAP inactivation by phosphorylation resulted in decreased cell viability, invasion ability, and increased chemosensitivity (significant reduction of paclitaxel IC50 in HeyA8-MDR) in YAP-activated cells, but not in YAP-inactivated cells. Additive effect of siRNA and dobutamine was observed in HeyA8 and -MDR in the in vitro experiment. In the in vivo model, YAP silencing using PLGA nanoparticle (YAP siRNA/PLGA or dobutamine/PLGA) showed antitumor effect in YAP-activated model (HeyA8 and -MDR) but not in YAP-inactivated model (SKOV3). However, no additive effect was observed when combination of YAP siRNA and dobutamine-loaded PLGA nanoparticle was used in the in vivo experiment. Dobutamine/PLGA showed the most prominent therapeutic effect (78% reduction of tumor weight, P = 0.0008) in the HeyA8 in vivo model.

Conclusion: These findings identify YAP silencing can be an attractive target to overcome YAP-activated ovarian cancer. Dobutamine/PLGA nanoparticle may be a possible new therapeutic strategy for YAP-activated ovarian cancer. Repeated preclinical trials and clinical trials will be needed in the future.

1345 - Poster Session
Differential assessments of blood lipids, lipid peroxidation, antioxidant status, and fatty acids in women with uterine tumors during menopausal period
N. Kotrikadze⁵, T. Tupinashvili⁶, L. Ramishvili⁵, M. Alibegashvili⁵, I. Nakashidze⁵, G. Nemsadze⁶, M. Gordeziani⁵, A. Khazaradze⁵,
Objective: The aim of this study was to study alterations in lipid spectrum, lipid peroxidation intensity, and fatty acid (FA) spectrum in the blood of women with benign and malignant uterine tumors during menopausal period.

Method: Blood samples from benign (myoma, $n = 15$) and malignant ($n = 15$) cases were collected, along with healthy menopausal cases (control, $n = 15$). Spectrophotometric methods assessed lipid spectrum composition, antioxidant enzyme activities, and lipid peroxidation intensity. Quantitative analyses of FA were performed by gas-liquid chromatography.

Results: Saturated FA in malignant cases decreased myristic acid (3-fold) and palmitic acid (~1.3-fold) compared to control, but increased stearic acid (1.13-fold). The decreased ratio between palmitic/stearic acids ($C_{16:0}/C_{18:0}$) by ~1.5 times was noted. Unsaturated FA in malignant cases showed a percentage decrease in oleic (2.9-fold), linolenic (1.5-fold), eicosatrienoic (3-fold), and arachidonic (1.3-fold) acid compared to control. The increased ratio between stearic/oleic acids ($C_{18:0}/C_{18:1}$) by 3.3 times was noted in malignant cases. Increase in lipid peroxidation intensification was associated with lipid spectrum composition (hyperlipidemia, disruption in the exchange rate of phospholipids). The negative correlation between lipid peroxidation intensity and phospholipids was $r = -0.96 \pm 0.04$. Total cholesterol was higher in malignant cases. Total amount and activities of superoxide dismutase (SOD), catalase (CAT) decreased in malignant cases. The negative correlation between total cholesterol and SOD, CAT activities was $r = -0.99 \pm 0.014$. Amine-containing phospholipids decreased, but choline-containing phospholipids increased with the severity of the disease.

Conclusion: Intensification of lipid peroxidation and alterations in lipid spectrum composition revealed hyperlipidemia, disruption of phospholipid exchange rate, and hypercholesterolemia. Thus, specific changes in these biochemical parameters can be useful in the differentiation of benign and malignant uterine tumors for menopausal women.

1346 - Poster Session
Monocytosis as a prognostic factor for survival in stage IB and IIA cervical cancer
H. Kim. Kosin University College of Medicine, Busan, Korea, Republic of (South)

Objective: We sought to measure hematologic parameters derived from the white blood cell (WBC) count and differential count (DC) as prognostic factors for survival in patients with stage IB and IIA cervical cancer.

Method: We retrospectively examined demographic, clinicopathologic, and laboratory parameters in a cohort of 233 patients with FIGO stage IB and IIA cervical cancer who underwent surgical resection. We further assessed the effects of the WBC count and DC-derived hematologic parameters on PFS and OS after controlling for other parameters.

Results: Patients were followed up for a median of 46.6 months (range 9–142 months). The Kaplan-Meier estimates of PFS and OS at 5 years were 88.5% and 92.3%, respectively. In a multivariate analysis, we identified the absolute monocyte count (AMC) ($HR = 11.78, P < 0.001$) and tumor size ($HR = 5.41, P = 0.003$) as the strongest prognostic factors affecting PFS. We also identified AMC ($HR = 23.29, P < 0.001$), tumor size ($HR = 5.27, P = 0.033$), and lymph node involvement ($HR = 3.90, P = 0.027$) as the strongest prognostic factors affecting OS. AMC remained prognostic with respect to PFS or OS in a Cox model that controlled for the neutrophil-lymphocyte ratio or lymphocyte-monocyte ratio, although neither ratio was a significant prognostic factor for survival.

Conclusion: Monocytosis and an increased tumor size were found to be independent prognostic factors affecting both PFS and OS in patients with stage IB and IIA cervical cancer.

1347 - Poster Session
Smoking: Inhibiting factor to regress abnormal cervical cytology
K.H. Han$^a$ and S.O. Hwang$^b$. $^a$Inha University School of Medicine, Incheon, Korea, Republic of (South), $^b$Inha University College of Medicine, Incheon, Korea, Republic of (South)

Objective: The aim of this study was to identify the effective factor on spontaneous regression for abnormal results of Pap test, atypical squamous cells of undetermined significance (ASC-US), and low-grade squamous intraepithelial lesions (LSILs).
**Method:** Between 2009 and 2014, a total of 46,233 healthy Korean women had a Pap test in the Seoul National University Hospital Healthcare System Gangnam Center. Among them, 872 women with ASC-US or LSIL had periodical Pap tests without additional treatment (ASC-US, \(n = 543\), 62.3%; LSIL, \(n = 329\), 37.7%). Regression time of abnormal cervical cytological findings was investigated with retrospective review for medical records. In addition, effective factors on spontaneous regression were evaluated with multiple regression analysis.

**Results:** The median follow-up period was 17.73 (range 1.1–104.9) months. In high-risk HPV infection, the number of women with LSIL was higher than that of women with ASC-US \((P = 0.044)\). Median regression time of abnormal cytological results was 12.95 months for ASC-US and 17.90 months for LSIL. Smoking history was the effective factor to inhibit spontaneous normalization of ASC-US and LSIL within 2 years by multiple regression analysis \((P = 0.018, \text{OR} = 0.423, 95\% \text{ CI} 0.208–0.860)\).

**Conclusion:** High-risk HPV infection was frequently found in women with LSIL than in women with ASC-US. Social experience of smoking was the inhibiting factor for spontaneous normalization of cervical cytological results.

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**1348 - Poster Session**

**Identification of a predictive model for chemo-response in epithelial ovarian cancer**

Y.C. Chiang. National Taiwan University Hospital Yunlin branch, Yunlin, Taiwan; National Taiwan University College of Medicine, Taipei, Taiwan

**Objective:** Epithelial ovarian cancer patients usually relapse after primary management. The promising targeted therapy, such as anti-angiogenesis antibodies and poly ADP-ribose polymerase inhibitors, are expensive. Cytotoxic chemotherapy remains the main treatment in developing countries. Determining how to predict the response of chemotherapy and identify which patients benefit from chemotherapy is important.

**Method:** We developed a predictive model of the chemo response using the cancer cell line encyclopaedia (CCLE) and then validated the model in The Cancer Genome Atlas (TCGA) and the GSE9891 dataset. Finally, we evaluated the feasibility of the model using ovarian cancer patients from our institute.

**Results:** The 10-gene predictive model demonstrated that the high-response group had a longer recurrence-free survival (RFS) \((\log \text{rank test, } P = 0.015 \text{ for TCGA, } P = 0.013 \text{ for GSE9891, and } P = 0.039 \text{ for NTUH})\) and OS \((\log \text{rank test, } P = 0.002 \text{ for TCGA and } P = 0.016 \text{ for NTUH})\). In a multivariate Cox hazard regression model, the predictive model \((\text{HR} = 0.644, 95\% \text{ CI } 0.436–0.952, P = 0.027)\) and residual tumor size < 1 cm \((\text{HR} = 0.312, 95\% \text{ CI } 0.170–0.573, P < 0.001)\) were significant factors for recurrence. The predictive model \((\text{HR} = 0.511, 95\% \text{ CI } 0.334–0.783, P = 0.002)\) and residual tumor size < 1 cm \((\text{HR} = 0.252, 95\% \text{ CI } 0.128–0.496, P < 0.001)\) were still significant factors for death. See **Figure 1**.

**Conclusion:** Our model predicted the chemo response in ovarian cancer patients. The patients of high-response group stratified by the model had good response and favorable prognosis. For the patients of medium- to low-response groups, introduction of other drugs or clinical trials might be beneficial.
**1349 - Poster Session**  
The krüppel-like factor5 (KLF5) regulates uterine endometrial cancer proliferation and migration  
J. Kojima, K. Kubota, T. Moritake, T. Nagashima and H. Nishi. *Hospital, Tokyo, Japan*

**Objective:** Endometrial cancer (EC) is one of the most common gynecologic malignant tumors. The morbidity of EC was about 13,000 women in 2012, and the prevalence of EC has been significantly increasing in Japan. Effective therapies for this deadly disease are limited because the elaborate molecular mechanism underlying EC progression remains largely unknown. The Krüppel-like factors (KLFs) have been identified as 17 family genes. Members of this family have contributed to various cellular processes, including cell proliferation, differentiation, invasion, migration, and angiogenesis. The KLF5, one of the KLFs, has been reported to have a critical role in tumorigenesis, whereas some studies have described its tumor-suppressive role. In this study, we elucidate the mechanism of KLF5 in EC.

**Method:** By quantitative RT-PCR and Western blot, we compared the expression level of KLF5 in EC with that in normal endometrial tissues. Normal endometrial samples were collected with informed consent from patients who had benign gynecological diseases. To analyze the function of KLF5, we utilized the EC cell line Ishikawa in the lentivirally infected shRNA-mediated knockdown strategy. Two different shRNAs targeting the human KLF5 gene were successfully infected into Ishikawa. The knockdown efficiency was confirmed by Western blot analysis.

**Results:** Transcription factor KLF5 expression was significantly higher in EC in both the transcriptional and translational level determined by quantitative RT-PCR and Western blot analyses. Knockdown of KLF5 significantly decreased both proliferation and migration in Ishikawa cells, indicating that KLF5 had an important role in EC.

**Conclusion:** We identified that KLF5 expression was high in EC. We also showed that KLF5 might play a crucial role in EC, indicating these findings shed light on the future therapeutic target for EC.

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**1350 - Poster Session**  
Celastrol inhibits the growth of ovarian cancer cells in vitro and In Vivo  
X. Yan\(^a\), N. Zhao\(^b\), L. Xu\(^a\), P. Ye\(^a\), X. Nan\(^a\), H. Zhou\(^a\) and Z. Shi\(^b\). *the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, \(^b\)Jinan University, Guangzhou, China*

**Celastrol inhibits the growth of ovarian cancer cells in vitro and In Vivo**

The potentiating effects of celastrol in ovarian cancer cells are explored through both in vitro and in vivo models. Celastrol, a natural product known for its anti-inflammatory and cytotoxic properties, was examined for its efficacy in inhibiting ovarian cancer growth. In vitro studies confirmed a significant reduction in cell proliferation and viability, suggesting potential therapeutic benefits.

In vivo experiments further supported these findings, demonstrating the drug's efficacy in reducing tumor burden. The combination of celastrol with conventional chemotherapy agents could offer a promising therapeutic strategy.

**Conclusion:** The findings support celastrol as a potential agent for the treatment of ovarian cancer, warranting further investigation in clinical settings.
**Objective:** Celastrol is a natural triterpene isolated from the Chinese plant Thunder God Vine with potent antitumor activity. Our aim is to identify the effect of celastrol on the growth of ovarian cancer cells in vitro and in vivo.

**Method:** The effects of treatment with celastrol on cell growth were determined by MTT assay. Apoptosis and cell cycle were measured by flow cytometry. ROS generation was measured by fluorescence microscope and flow cytometry with DHE staining. Changes of apoptotic and cell cycle-related proteins were analyzed by Western blotting. C57BL/6 mice were used to determine the antitumor effect of celastrol in vivo.

**Results:** We found that celastrol induced cell growth inhibition, cell cycle arrest in G2/M phase, and apoptosis with the increased intracellular reactive oxygen species (ROS) accumulation in ovarian cancer cells. Pretreatment with ROS scavenger N-acetyl-cysteine totally blocked the apoptosis induced by celastrol. In addition, celastrol inhibited the growth of ovarian cancer xenografts in nude mice.

**Conclusion:** These findings suggest celastrol is a potential therapeutic agent for treating ovarian cancer.

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**1351 - Poster Session  
Prognostic significances of markers of preoperative preoperative lymphocyte-monocyte ratio in ovarian clear cell carcinoma patients.**

* S.Y. Hwang, H.J. Yoon and K.H. Kim. *Pusan National University Hospital, Pusan, Korea, Republic of (South)*

**Objective:** The aim of the present study was to determine the prognostic significance of markers of preoperative systemic inflammatory response (SIR) in patients with ovarian clear cell carcinoma (OCCC).

**Method:** A total of 109 patients diagnosed with OCCC who underwent primary cytoreductive surgery and adjuvant platinum-based chemotherapy from 2009 to 2012 were enrolled in this retrospective study. SIR markers were calculated from complete blood cell counts determined before surgery. Receiver operating characteristic (ROC) curve analysis was used to determine optimal cutoff values for neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR). Prognostic significance with respect to OS and PFS was determined by Kaplan–Meier curve and multivariate Cox regression analysis.

**Results:** The optimized NLR, LMR, and PLR cutoff values as determined by ROC curve analysis for PFS and OS were 2.3, 4.2, and 123.6, respectively. When the cohort was divided using these optimized cutoffs, NLR and LMR were found to be significantly associated with clinicopathologic factors: NLR with FIGO stage, the presence of malignant ascites, and platinum response; and LMR with FIGO stage, lymph node metastasis, malignant ascites, and platinum response. Kaplan-Meier analysis revealed a high NLR (>2.3) was significantly associated with low 5-year PFS and OS rates and that a high LMR was significantly associated with high 5-year PFS and OS rates. Multivariate analysis identified FIGO stage, residual mass, and platinum response as independent prognostic factors of PFS, and FIGO stage, residual mass, platinum response, and LMR as independent prognostic factors of OS.

**Conclusion:** Markers of systemic inflammatory response provide useful prognostic information, and LMR ratio is the most reliable independent prognostic factor of OS in patients with ovarian clear cell carcinoma.

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**1352 - Poster Session  
CXCL1 mediates adiponectin-induced angiogenesis in ovarian cancer**

* Y.T. Oub, Y.J. Leea, H.W. Chob, J.K. Leec and J.H. Hongc. *Korea University College of Medicine, Seoul, Korea, Republic of (South), Guro Hospital College of Medicine Korea University, Seoul, Korea, Republic of (South), Guro Hospital, Korea University College of Medicine, Seoul, Korea, Republic of (South)*

**Objective:** Adiponectin is a cytokine secreted from adipose tissue that regulates energy homeostasis, inflammation, and cell proliferation. Obesity is associated with increased risk of various cancers, including ovarian cancer. Adipokines, including adiponectin, have been implicated as a factor linking obesity and carcinogenesis. The oncogenic role of adiponectin is not known with regard to various cancer types. We sought to determine the role of adiponectin in angiogenesis in ovarian cancer in vitro.
**Method:** We transfected SKOV3 cells with vascular endothelial growth factor (VEGF) small interfering RNA (siRNA) in order to identify the independent angiogenic role of adiponectin in ovarian cancer. The VEGF-knockdown SKOV3 cell lines were treated with adiponectin for 48 hours. The cytokines involved in adiponectin-mediated angiogenesis were explored using the human angiogenesis cytokine array and were verified with the enzyme-linked immunosorbent assay. The angiogenic effect of adiponectin was evaluated using the human umbilical vein endothelial cell (HUVEC) tube formation assay. We also investigated the effects of adiponectin treatment on the migration and invasion of SKOV3 cells.

**Results:** The number of tubes formed by HUVEC decreased significantly after knockdown of VEGF (via transfection of VEGF siRNA into SKOV3 cells). When these VEGF-knockdown SKOV3 cells were treated with adiponectin, there was an increase in the number of tubes in a tube formation assay. Following adiponectin treatment, the CXC chemokine ligand 1 (CXCL1) secretion increased in a cytokine array. This was confirmed by both enzyme-linked immunosorbent assay and Western blot. The increased secretion of CXCL1 by adiponectin occurred regardless of VEGF-knockdown. In addition, the induction of migration and invasion of SKOV3 cells were significantly stronger with adiponectin treatment than they were without.

**Conclusion:** Adiponectin treatment of ovarian cancer cells induces angiogenesis via CXCL1 independently of VEGF. These findings suggest that adiponectin may serve as a novel therapeutic target for ovarian cancer.

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**Global Strategies and Standards**

1356 - Poster Session
Withdrawn at author's request

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1357 - Poster Session
Patterns of utilization and outcomes of ovarian conservation for young women with minimum-risk endometrial cancer
R.S. Mandelbaum\(^a\), L. Chen\(^b\), D. Shoupe\(^c\), L.D. Roman\(^d\), J.D. Wright\(^b\) and K. Matsuo\(^a\). \(^a\)LAC+USC Medical Center, Los Angeles, CA, USA, \(^b\)Columbia University College of Physicians and Surgeons, New York, NY, USA, \(^c\)University of Southern California, Los Angeles, CA, USA

**Objective:** To profile patient characteristics associated with and outcomes of ovarian conservation at the time of hysterectomy in young women with minimum-risk endometrial cancer.

**Method:** A population-based retrospective analysis of the Nationwide Inpatient Sample between 2007 and 2015 was performed. Women aged <50 years with minimum-risk endometrial cancer were grouped based on whether they received oophorectomy versus ovarian conservation at the time of hysterectomy. A classification-tree model with recursive partitioning analysis was constructed to examine patterns of ovarian conservation. Propensity score matching was performed, and total charges, length of stay, and perioperative complications were compared.

**Results:** There were 8,191 (78.0%) women who underwent oophorectomy and 2,314 (22.0%) women who had ovarian conservation. In a classification-tree model, nine patterns of patient characteristics were identified, and ovarian conservation rates ranged from 11.7% (women aged 40–49 years who underwent abdominal hysterectomy at an urban teaching hospital) to 60.5% (nonobese women aged <40 years with median household income ≥$63,000) (absolute difference, 48.8%, 95% CI 39.9–57.7, \(P < 0.001\)). After propensity score matching, ovarian conservation was significantly associated with a decreased proportion of hospital stays >2 days (36.2% vs 43.5%, relative risk reduction, 16.7%, \(P < 0.001\)) and lower median total charges ($24,937 vs $27,204, net difference −$2,267, \(P < 0.001\)). Rates of surgical complications were not different between those who received ovarian conservation and those who underwent oophorectomy (8.2% vs 8.3%, \(P = 0.91\)).

**Conclusion:** There has been great variability in the utilization of ovarian conservation for young women with minimum-risk endometrial cancer based on patient, surgical, and hospital factors. Ovarian conservation in this population may also be
associated with modestly reduced treatment costs and shorter length of hospital stay.

1358 - Poster Session
Cervical cancer with intermediate risk factors: Is there a role for adjuvant radiotherapy? A systematic review and a meta-analysis.
L. Dain-Sagi\(^a\), S. Abo-folb, O. Lavie\(^c\), S. Sagib and Y. Segeva. \(^a\)Carmel Medical Center, Technion Israel Institute of Technology, Haifa, Israel, \(^b\)Technion Israel Institute of Technology, Haifa, Israel

**Objective:** The yield of adjuvant radiotherapy in cervical cancer patients with intermediate risk factors (large tumor size, deep stromal invasion, and lymphovascular invasion) is controversial. The objective of our meta-analysis was to shed light on this important issue.

**Method:** Several databases were searched, with no language or time restrictions. By independent screening of titles and abstracts, two investigators selected original research examining the effect of adjuvant radiation treatment on overall survival and progression-free survival (PFS) in cervical cancer patients with intermediate risk factors. The effect estimates were presented as odds ratios (OR) with 95% CI.

**Results:** Of 219 initial references, five articles were included, encompassing a total of 591 patients with intermediate risk factors. Statistical significance was noted in favor of radiation therapy in a subgroup of patients with two or more intermediate factors in terms of recurrence (OR = 0.46, 95% CI 0.28–0.74, \(P = 0.001\)) and overall survival (OR = 1.86, 95% CI 1.03–3.36, \(P = 0.04\)) (Figure 1). After adding patients with one risk factor, radiation exerted a nonsignificant effect on recurrence rate, overall survival, disease-free survival, and 5-year cancer-specific survival, while increasing the rate of gastrointestinal side effects (2.4% vs 0%, \(P = 0.0156\)). Overall quality of evidence was rated as very low using Grading of Recommendations Assessment, Development and Evaluation criteria.

**Conclusion:** Adjuvant radiation therapy decreases the risk for recurrence and increases the overall survival in patients with two intermediate risk factors. These benefits were not shown after adding patients with one risk factor.

![Figure 1](image)

1359 - Poster Session
Trends and characteristics of epithelial ovarian cancer in Japan: JSGO-JSOG joint study
H. Machida\(^a\), K. Matsuo\(^b\), W. Yamagami\(^c\), Y. Ebina\(^d\), Y. Kobayashi\(^e\), T. Tabata\(^f\), M. Kaneuchi\(^g\), S. Nagase\(^h\), T. Enomo\(^i\) and M. Mikami\(^j\). \(^a\)Tokai University School of Medicine, Kanagawa, Japan, \(^b\)Keck School of Medicine of USC, Los Angeles, CA, USA, \(^c\)Keio University, School of Medicine, Tokyo, Japan, \(^d\)Kobe University Graduate School of Medicine, Kobe, Japan, \(^e\)Kyorin University, Tokyo, Japan, \(^f\)Meie University School of Medicine, Tsu, Japan, \(^g\)Otaru General Hospital, Hokkaido, Japan, \(^h\)Yamagata University, Yamagata, Japan, \(^i\)Niigata University Graduate School of Medicine, Japan, \(^j\)Tokai University School of Medicine, Isehara, Japan

**Objective:** To examine temporal trends in histologic subtypes of epithelial ovarian cancer in Japan.

**Method:** This was a nationwide society-based retrospective study between 2002 and 2015 (Japan cohort, \(n = 48,640\)). The Surveillance, Epidemiology and End Results Program was used as the control (U.S. cohort, \(n = 49,936\)). Time-specific proportional changes in four major histology subtypes (serous, clear cell, endometrioid, and mucinous) were examined.
**Results:** Women in the Japan cohort were more likely to have stage I disease (44.1% vs 24.9%) but less likely to have stage IV disease (10.0% vs 23.1%) compared to those in the U.S. cohort ($P < 0.001$). Women in the Japan cohort were more likely to have nonserous histologies, particularly clear cell (26.9% vs 8.4%), compared to those in the U.S. cohort ($P < 0.001$). In the Japan cohort, the proportion of clear cell significantly increased from 23.4% to 29.1% between 2002 and 2010 ($P < 0.001$). Among stage I disease, the proportion of clear cell significantly increased in the Japan cohort (from 32.9% to 40.3%, $P < 0.001$), whereas mucinous significantly increased in the U.S. cohort (from 15.0% to 24.8%, $P = 0.01$) between 2002 and 2015. Among women aged <60 years, the most common histology type was clear cell in the Japan cohort (30.4%) and serous in the U.S. cohort (10.8%) in 2015. In the Japan cohort, peak of age was 75 years for serous, 57 years for clear cell, and 45 years for endometrioid ($P < 0.001$). Nadiral age of mucinous was 43 years, but mucinous became more common after age 73 years with bidirectional changes ($P < 0.001$). See Figure 1.

**Conclusion:** Our study demonstrated that women with epithelial ovarian cancer in Japan have distinct characteristics compared to U.S. women: clear cell histology has significantly increased in recent years, reaching nearly 30% of ovarian cancer.

![Figure 1](image-url)
Conclusion: Minimally invasive RH should be performed more cautiously in optimal surgical candidates to obtain en bloc resection without positive margin and tumor spillage, using PMI criteria and VC after CO₂ evacuation.

1401 - Poster Session
Recurrence patterns after complete surgical resection for advanced-stage ovarian cancer: A comparison of primary and interval debulking surgery
A.A. Gockleya,b, B.L. Manning-Geistc,d, A. Greerab, A. Melamedb,c, A. Bercowa,b,c, W.B. Growdonb,c, M.G. del Carmemb,e, N.S. Horowitzb, R.S. Berkowitzbd and M.J. Worley Jr.d. aBrigham and Women’s Hospital, Boston, MA, USA, bHarvard Medical School, Boston, MA, USA, cMassachusetts General Hospital, Boston, MA, USA, dBrigham and Women’s Hospital/Harvard Medical School, Boston, MA, USA, eMassachusetts General Hospital/Harvard University, Boston, MA, USA

Objective: To compare patterns of recurrence among women with advanced-stage epithelial ovarian cancer (EOC) who underwent either primary debulking surgery (PDS) or interval debulking surgery (IDS) and had a complete surgical resection (CSR).

Method: Patients with stage IIIC or IV EOC undergoing either PDS or IDS at two academic medical centers between January 1, 2010, and December 31, 2014, were evaluated. Patient and clinical characteristics were abstracted for all patients who underwent CSR. Sites of recurrence were abstracted and grouped into single-site (abdomen/pelvis), extra-abdominal, or multiple sites. Categorical variables were compared with the Fisher exact test, and continuous variables were compared with the rank sum test.

Results: There were 510 patients with advanced-stage EOC who underwent PDS or IDS resulting in a CSR. A total of 240 (47.1%) patients underwent PDS, and 270 (52.9%) underwent IDS. Patients who underwent IDS were older (P = 0.04) and more likely to have stage IV disease (P < 0.001). After a median follow-up of 64 months, 443 (86.9%) patients had recurred. The median progression-free survival (PFS) for PDS patients was 17 months (95% CI 15–19 months), and the median PFS for IDS patients was 9 months (95% CI 7–9 months) (P < 0.001). Among patients who recurred, patients undergoing IDS were more likely to recur with multiple affected sites (53.3% vs 39.7%, P < 0.001). In contrast, PDS patients were more likely to recur with a single affected site within the abdomen/pelvis (50.3 vs 25%, P < 0.001).

Conclusion: Compared to IDS, patients undergoing PDS experienced a longer PFS. At the time of recurrence, patients initially managed with PDS were more likely to have a single affected site within the abdomen/pelvis.

1402 - Poster Session
Independent radiologic review in ovarian cancer research
C. Polen-Dea, A. Loreena, C.C. Billingsleya, A.L. Jacksonb and T.J. Herzogc. aUniversity of Cincinnati Academic Health Center, Cincinnati, OH, USA, bUniversity of Cincinnati, UC Health Medical Arts Building, Cincinnati, OH, USA, cUniversity of Cincinnati, Cincinnati, OH, USA

Objectives: Independent radiologic review (IRR) has been increasingly utilized in ovarian cancer clinical trials to minimize potential bias when evaluating for progression. Although there is potential for bias in nonblinded trials given the inherent subjective nature of PFS evaluation, an IRR has the potential to introduce new biases and is associated with significant added study cost and logistical burden. The aim of our study is to evaluate the concordance in PFS and HR between investigator (INV) and (IRR) among key trials in ovarian cancer.

Methods: PubMed was systematically queried for randomized controlled trials involving ovarian cancer, utilizing the terms “ovarian cancer” plus “independent radiologic review,” “independent central review,” and “independent review committee.” All landmark randomized phase II–III, registration, and GOG ovarian cancer trials in addition to their supplemental data, if available, were reviewed. Studies were excluded if patients were not randomized, if they reported IRR data only, and if they did not utilize IRR in the study. Studies with a separate IRR analysis were included.

Results: Eight studies met study criteria out of 29 evaluated. Differences in PFS medians and HRs were analyzed between INV and IRR for each study, and associations were calculated utilizing logistic regression analysis. The PFS between INV and IRR was found to have a mean difference of −1.76 months (INV-IRR), median −0.4 (95% CI −3.44 to −0.08). The degree of association between INV and IRR HR was high by logistic regression analysis, with R² = 0.957 (correlation coefficient 0.97,
95% CI 0.91–0.99, P < 0.0001). This illustrates in the majority of cases the INV HR and IRR HR are highly concordant. The HR ratio was determined for each study (HR IRR/HR INV) (Table 1) with a mean HR ratio of 1.03 (95% CI 0.94–1.12, P = 0.82) and an estimated HR difference illustrating a 10% average absolute difference between the evaluations.

Conclusions: Concordance was noted between both INV and IRR reported PFS and HR data in ovarian cancer. Since IRR adds significant cost, logistical burden, and potential bias while not altering the primary endpoint conclusion in any of these trials, the need for IRR is questionable and these data support use of primary investigator-assessed PFS.

Table 1. Summary of ovarian cancer trials as well as progression free survivals and hazard ratios in INV versus IRR.

<table>
<thead>
<tr>
<th>Study</th>
<th>PFS - INV</th>
<th>PFS - IRR</th>
<th>PFS Diff (INV-IRR)</th>
<th>HR - INV</th>
<th>HR - IRR</th>
<th>HR Ratio</th>
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<td>OEC 218</td>
<td>CT + PL</td>
<td>12.9</td>
<td>11.3</td>
<td>1.1</td>
<td>0.89</td>
<td>0.99</td>
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<td>Burger</td>
<td>PEP + (cycles 2.8)</td>
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<td>0.89</td>
<td>0.99</td>
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<td>0.89</td>
<td>0.99</td>
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<td>AUREAGEL</td>
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<td>0.99</td>
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<tr>
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<td>0.99</td>
</tr>
<tr>
<td>OYA-301</td>
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<tr>
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<tr>
<td>Coleman</td>
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<tr>
<td>FRED</td>
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<td>NOVA</td>
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<td>0.89</td>
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<tr>
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<td>PL + IR</td>
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</table>

Objective: To examine the impact of volume of residual disease at the completion of interval debulking surgery (IDS) on timing and patterns of recurrence among women with advanced-stage epithelial ovarian cancer (EOC).

Method: Patients with stage IIIC/IV EOC who underwent IDS at two academic medical centers between January 1, 2010, and December 1, 2014, were reviewed. Demographics, volume, and anatomic site of residual disease and outcomes data were collected. Among patients without complete surgical resection (CSR) but with ≤1 cm of residual disease, the number of anatomic sites (single location, <1 cm SL, vs multiple locations, <1 cm ML) was utilized to describe volume of residual disease.

Results: A total of 270 patients with stage IIIC/IV EOC who underwent IDS. The median age was 65 years. Most patients were stage III (55.9%) with serous histology (92.6%). At the completion of IDS rates of CSR, <1 cm SL, <1 cm ML, and suboptimal were 64.1%, 12.6%, 17.4%, and 5.9%, respectively. Excluding patients who were suboptimally debulked, median PFS for CSR, <1 cm SL, and <1 cm ML was 10 months (95% CI 8–12), 9 months (95% CI 5–11), and 5 months (95% CI 4–7), respectively (P = 0.008). At recurrence, the presence of ascites was likely among patients with CSR (17.2%, P = 0.004), than with <1 cm SL.
(36.4%), and <1 cm ML (31.8%). Volume of residual disease at IDS did not affect location of recurrence, and most patients recurred at multiple abdominal/pelvic sites (CSR, 58.9%; <1 cm SL, 45.5%; <1 cm ML, 59.1%).

**Conclusion:** After IDS, patients with CSR and <1 cm SL have the longest PFS. At the time of recurrence, patients with CSR at IDS were less likely to present with ascites. However, volume of residual disease at IDS did not have an impact on distribution of disease at recurrence.

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**1404 - Poster Session**

Enhanced recovery after surgery protocol decreases postoperative opioid use in an area with high narcotics abuse rate

*K. Whitea, S. Azadib, M. Parsons*, A. Huckc and N. Bou Zgheibb. aMarshall University School of Medicine, Huntington, WV, USA, bMarshall University School of Medicine, Huntington, WV, USA, cMarshall University, Huntington, WV, USA

**Objective:** We evaluated the efficacy of the enhanced recovery after surgery (ERAS) protocol for the control of postoperative pain after minimally invasive gynecological surgery in an area with the highest per-capita narcotics overdose cases in the country. We sought to investigate the rate of narcotics use and the postoperative pain score in our patient population.

**Method:** We conducted a retrospective cohort study that included all patients who underwent minimally invasive hysterectomy for both benign and malignant indications over a 2-year period. Four different postoperative pain control modalities were identified. Group 1 received the ERAS protocol. Group 4 was the control group, which included those who received no local anesthetics and the use of postoperative oxycodone-acetaminophen. Group 3 included the use of a local anesthetic pump, and group 4 patients received as needed intravenous hydromorphone. Patients' medical records were evaluated for demographics, surgical characteristics, postoperative opioid type and dose, preoperative opioid exposure, pain scores, and length of stay. Opioids were converted to oral morphine dose equivalents.

**Results:** There were 930 patients included within the 4 groups. Median opioid usage was the lowest in the ERAS group and highest in the control group (22.5 mg vs 55.0 mg, \( P < 0.001 \)). Group 2 had a median opioid use of 51 mg, while group 3 median opioid use was 42.5 mg. After the first hour following surgery and when compared to the control, ERAS patients utilized 67% less opioids. In patients with malignant diagnosis the ERAS protocol was associated with 38% decrease in opioid use compared to the control group (22.5 mg vs 36 mg, \( P < 0.001 \)). Patients suffering from chronic pelvic pain received 26.3 mg of opioid on the ERAS protocol, versus 55 mg for the control group, a 52% less opioid use. When compared to the control group, median pain score in the ERAS group was 25% lower. The preoperative opioid exposure was not different between the groups.

**Conclusion:** A multimodal approach to pain control is an acceptable alternative to traditional methods of pain control, regardless of BMI, for those with benign or malignant disease and appears to decrease opioid use with no concomitant increase in pain scores in our patient population.

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**1405 - Poster Session**

Role of paraaortic nodal evaluation in women with uterine cancer

*A. Buskwyofie*, L. Chenb,c, J.Y. Houd, C.M. St. Claird, A.I. Tergasd, F. Khoury Colladod and J.D. Wrightb. aNew York-Presbyterian Hospital, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA, bColumbia University College of Physicians and Surgeons, New York, NY, USA, cNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, dNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA

**Objective:** The utility of paraaortic lymph node examination in patients with uterine cancer remains uncertain. We analyzed the patterns of performance of paraaortic lymph node dissection (PaLND) and its association with survival in women with endometrial cancer.

**Method:** The National Cancer Data Base was used to identify patients diagnosed with endometrioid endometrial cancer from 2010 to 2015. PaLND was defined as removal of any paraaortic lymph nodes. We examined trends over time in performance of PaLND as well as clinical and demographic characteristics associated with PaLND. Cox proportional hazard models were used to determine the association with PaLND and overall survival after propensity score matching.

**Results:** A total of 114,685 women were identified, of whom 76,610 (66.8%) underwent pelvic lymph node dissection (PLND) and 36,341 (31.7%) underwent PaLND. Use of PaLND declined from 36% in 2010 to 28% in 2015 (\( P < 0.001 \)). Similarly, of the
women who underwent PLND, simultaneous PaLND decreased from 52% to 41% over the same years ($P < 0.001$). Positive paraaortic LNs were identified in 25% of women with a positive pelvic LN and in 1% of women with negative pelvic LNs. Older patients, those treated more recently, those with comorbid conditions, those treated at academic centers, and those with well-differentiated tumors were less likely to undergo PaLND ($P < 0.05$ for all). After propensity score matching, there was no association between PaLND and survival ($HR = 1.03, 95\% CI 0.98–1.08$).

**Conclusion:** The proportion of patients undergoing paraaortic lymph node examination has steadily decreased over time. Performance of PaLND is not independently associated with survival.

**1406 - Poster Session**

**Characteristics and management of women with CHEK2 truncating versus missense mutations after hereditary breast and ovarian cancer gene testing**

N.T. Nguyen, S. Durrant, C. Kobelka and B. Powell

Kaiser Permanente Oakland Medical Center, Oakland, CA, USA, Kaiser Permanente Northern California, San Francisco, CA, USA, The Permanente Medical Group, San Francisco, CA, USA, Kaiser Permanente Northern California Gynecologic Oncology Program, San Francisco, CA, USA, Kaiser Permanente San Francisco Medical Center, San Francisco, CA, USA

**Objective:** To identify cancer history and surveillance management in CHEK2 truncating versus missense mutations after hereditary breast and ovarian cancer (HBOC) testing. The literature implies variations of cancer risk by mutation type.

**Method:** This was a retrospective cohort study at a large integrated health system from 2014 to 2016. Women were at least 18 years old, met National Comprehensive Cancer Network (NCCN) criteria for HBOC, and had OvaNext 24 multigene panel testing (Ambry, Aliso Viejo, CA). We excluded concurrent non-CHEK2 gene mutations. The primary objective was difference in risk and personal or family history of cancer based on truncating or missense CHEK2 mutations. Secondary outcomes include cancer surveillance offered and cancer prevention interventions completed by CHEK2 mutation type. $\chi^2$ test and Fisher exact test were used for analysis.

**Results:** We identified 1.8% ($n = 72/3,926$) with CHEK2 meeting study criteria, 59.7% truncating and 40.3% missense mutations; 58.3% had multigene testing for personal and family history of cancer; and 80.6% ($n = 58$) had personal history of cancer, 82.9% breast, 6.1% ovarian, and 1.2% endometrial. There was no difference in history of any cancer ($P = 0.7$) or type of cancer with ovarian cancer in 6.4% of truncating and 5.7% of missense mutations. There were 105 first-degree relatives with cancer, 9% breast, 7.4% prostate, 5.7% ovarian, and 5.7% colon. Only difference in family history was higher, prostate cancer in truncating group (13.1% vs 2.1%, $P = 0.05$). NCCN surveillance guidelines for breast and colon cancer were offered to 84.7% ($n = 61$) and 52.8% ($n = 38$), but 53.3% and 44.4% completed the surveillance, respectively. Surveillances offered or completed did not differ with mutation groups; 59.7% ($n = 43$) were offered non-guideline-compliant cancer surveillance for ovarian, thyroid, and skin cancers; 30.6% ($n = 22$) were offered salpingo-oophorectomy, 3 (average age 51 years, 1 relative with ovarian cancer) proceeded with surgery, and 5 transvaginal ultrasounds were done for ovarian cancer surveillance.

**Conclusions:** There was no difference in personal or family history of cancer or cancer surveillance between CHEK2 mutations. Despite no difference in cancer history, 60% were offered non-guideline-compliant procedures for CHEK2 mutation, leading to unnecessary interventions or treatments.

**1407 - Poster Session**

**What is the opportunity cost of postmolar surveillance for women of advanced maternal age seeking pregnancy? A Monte Carlo microsimulation model.**

R. Harrison, S.B. Cantor, C.C.L. Sun, M. Villanueva, K.I. Stewart, T.L. Woodard, A. Shafer, K.H. Lu and L.A. Meyer. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Objective:** Age is associated with both gestational trophoblastic disease (GTD) and natural decline in fertility. Guidelines recommend 6 months surveillance after beta-hCG normalization. However, the gestational trophoblastic neoplasia (GTN) risk after normalization is very low. Our goal is to examine the opportunity cost of postmolar surveillance in terms of fertility outcomes for women of advanced maternal age (AMA).

**Method:** A Monte Carlo microsimulation of 2 surveillance strategies was modeled with TreeAge: the current 6-month strategy of beta-hCG surveillance versus an alternate strategy of 1 additional test 1 month after normalization (Figure 1). Model inputs
for GTN risk, loss of follow-up, rate of attempting pregnancy, fecundity, and pregnancy outcome were derived from the literature. Four simulated cohorts of 10,000 women aged 35–39 years and 40–45 years with a partial (PM) or complete molar pregnancy (CM) were simulated in 1,000 parallel trials. A 6-month time horizon was set. A tornado sensitivity analysis was used to evaluate model inputs. The primary outcome was pregnancy rate; secondary outcomes were live births and GTN cases occurring in and out of surveillance.

Results: Among 10,000 women age 35–39 years with a CM, the mean pregnancies occurring in the alternate strategy was higher than the current strategy (pregnancy, 2,040.0 vs 1,440.8; live birth, 1,427.7 vs 1,007.8). The mean number of GTN cases occurring outside of surveillance was 1.7 per 1,000 women with CM in the alternate strategy (Table 1). For women age 35–39 years with a PM, the alternate strategy also led to more pregnancies; the GTN cases occurring outside of surveillance was 0.22 per 1,000 women with PM. For women age 40–45 years, the alternate strategy yielded fewer additional pregnancies (1,198.5 vs 1,174.4); the mean GTN cases occurring outside of surveillance was 2.3 per 1,000 and 0.23 per 1,000 women with a CM and PM, respectively. A tornado sensitivity analysis of the model inputs showed that the rate of attempting pregnancy/month, chance of unintended pregnancy, and fecundity accounted for most of the uncertainty in the model (50.3%, 28.6%, and 19.4%, respectively).

Conclusion: Our analysis demonstrates that in women with partial moles, shorter surveillance is safe and improves live birth rates. Among women with complete molar pregnancies, these findings may allow for individualized decision making regarding the value of surveillance in the context of GTN risk and desire to attempt pregnancy.

Fig. 1. Model for comparing current postmolar surveillance strategy [top] and alternate shortened strategy [bottom]. ¹case of GTN diagnosed during surveillance, ²case of GTN diagnosed outside of surveillance

Table 1. Pregnancy, live birth, and cases of GTN by cohort.
1408 - Poster Session
Publication trends in Gynecologic Oncology: A 45-year history
A. Kuan-Celarier, R. Peneva, K.E. Kerdolff, A.M. Jernigan and J. Miller. Louisiana State University Health Science Center, New Orleans, LA, USA

Objective: Production and publication of quality research is critical to advancements in gynecologic cancer prevention and care. Gynecologic Oncology has been the leading journal in the field since its first issue in 1972. This study sought to evaluate trends in categories of articles published in Gynecologic Oncology over time.

Method: PubMed was queried for articles published in Gynecologic Oncology from 1972 to 2017. The percentages of randomized controlled trials (RCTs), cohort studies, case control studies, and case reports were calculated, and trends were analyzed by 11–12 year quartiles.

Results: Between November 1972 and December 2017, 13,130 articles were published in Gynecologic Oncology. Overall, 340 (2.6%) were RCTs; 3,308 (25.2%) were cohort studies; 2,252 (17.1%) were case control studies; and 2,088 (15.9%) were case reports. RCT, cohort, case control studies, and case reports represented 2.0%, 8.2%, 2.8%, and 26.1% of studies published from 1972 to 1983; 2.5%, 21.1%, 10.0%, and 26.2% from 1984 to 1995; 19%, 22.0%, 15.5%, and 20.7% from 1996 to 2006, and 3.4%, 33.5%, 25.3%, and 3.6% from 2007 to 2017, respectively. There was an increase in the percentages of RCTs, cohort studies, and case control studies over time, and a decrease in percentage of case reports published. The greatest increase was seen in cohort studies, from 8.0% in 1972–1983 to 33.5% in 2007–2017, followed by case control studies (2.8% to 25.3%), and RCTs (2.0% to 3.4%). Case reports decreased from 25.8% to 3.6%. The difference between these trends was statistically significant (P < 0.00001).

Conclusion: In the Gynecologic Oncology journal, trends demonstrate a decrease in publication of case reports in favor of higher level evidence. In particular, cohort studies and case control studies are more represented than they were 4 decades ago. Randomized controlled trials, while more common in recent years, still only represent 3.4% of articles published in this journal.

1409 - Poster Session
Reducing short interval advanced imaging in gynecologic oncology patients presenting to the emergency department
Objective: To evaluate the indications and appropriateness of short-interval advanced imaging in gynecologic oncology patients presenting to the emergency department for acute care.

Method: Review of all established gynecologic oncology patients admitted through the emergency department was performed from April 1, 2017, to June 30, 2018. Details regarding advanced imaging, length of stay (LOS) in the emergency department, and patient oncologic history were abstracted. Advanced imaging was defined as a computerized tomography (CT) or magnetic resonance imaging (MRI). The appropriateness of imaging was reviewed by two abstractors.

Results: During the study period, there were 135 unique ED encounters in gynecologic oncology patients leading to admission. The mean age was 59.9 years. Most patients (92%) were full code. Ovarian cancer was the most common cancer diagnosis (45.2%), and most patients had recurrent disease (72%). Of all patients, 48.2% had chemotherapy within 30 days of presentation to the emergency department; 15.6% had surgery with 30 days of presentation. There were 99 (73.3%) patients with a CT or MRI performed in the emergency department; 44.4% were deemed beneficial upon review. The most common reasons for imaging included concern for bowel obstruction (31.1%), sepsis (23.7%), and urologic obstruction (13.3%). CT or MRI was repeated within 3 weeks of the same imaging modality in 31.3% of patients; 74.2% of these tests were deemed unnecessary. The most common admitting diagnoses were dehydration, bowel obstruction, and sepsis. Mean length of stay (LOS) in the emergency department was 8.5 hours. Based upon these results, guidelines to reduce short-interval imaging (within 3 weeks of a prior study) was initiated on August 1, 2018.

Conclusion: While advanced imaging may provide important clinical information for some gynecologic oncology patients presenting to the emergency department for acute care, most repeat imaging was deemed unnecessary. Following guideline implementation, we anticipate a significant reduction in advanced imaging and decreased emergency department LOS.

Towards eliminating cervical cancer in East Africa: Feasibility of visual inspection with acetic acid (VIA) screening and immediate cryotherapy in rural and urban Tanzania

Objective: We sought to report the logistics and feasibility of a visual inspection with acetic acid (VIA) screening program in northern Tanzania, based on evidence that VIA screening and government subsidies for such programs reduce disease-specific mortality.

Method: A University of California Irvine Institutional Review Board-approved risk factor study and associated cervical cancer screen-and-treat was held from July 2 to 6, 2018, at an urban and rural site in Ilemela District, Tanzania. Advertising included banners, fliers, church announcements, and a loudspeaker-equipped van. Participants completed an intake survey, an educational video, optional HIV testing, and VIA screening with cryotherapy per World Health Organization (WHO) guidelines. Translators were fluent in English, Swahili, and Sukuma. The estimated program cost was $2,040. Risk factors for VIA+ or cancer-suspicious lesions were examined by χ², ANOVA, and univariate and multivariate logistic regression. Site-stratified analyses were also performed. Significance was P < 0.05.

Results: A total of 828 women were screened. The prevalence of VIA+ and cancer-suspicious lesions was 24.9% (206/828) and 1.8% (15/828), respectively (Figure 1). The rural site had a significantly higher prevalence of VIA+ and cancer-suspicious lesions (29.5%, 95/322) than the urban site (21.9%, 111/506) (P = 0.0047). Cryotherapy was performed on 147 VIA+ women without complications. In multivariate analysis, factors associated with VIA+ and cancer-suspicious lesions included rural site (OR = 1.71, 95% CI 1.20–2.44, P = 0.0033), having 2–4 children (OR = 2.79, 95% CI 1.47–5.30, P = 0.0018), or having >5 children (OR = 3.97, 95% CI 1.94–8.11, P < 0.001). Among urban women, visiting a health care provider in the last year (OR = 0.51, 95% CI 0.27–0.98, P = 0.0422) and having current circumcised sex partners (OR = 0.23, 95% CI 0.09–0.61, P = 0.003) were protective. Urban women had more extensive lesions than rural women (3.14 vs 2.37 quadrants, P < 0.001). Intravaginal tobacco leaf placement to enhance fertility was noted among 3 rural women, 2 of whom were VIA+. Following this model, partner clinics in Tanzania have since held 3 screenings.
Conclusion: VIA screening is feasible in Tanzania. Sustainability is limited by trained providers and instrumentation (e.g., speculums, cryotherapy units, CO₂ tanks). The potential risk for cervical changes induced by vaginal tobacco may warrant further investigation.

Fig. 1.
Objective: Elderly age is one of the poor prognostic factors in epithelial ovarian cancer (EOC), but the optimal cutoff is not known. The present study sought to identify the ideal age cutoff that represents a negative prognostic factor in EOC, considering the geriatric assessment.

Method: HRs with \( P \) values were calculated using all possible age cutoffs with stage, histology, grade, optimality, and comorbid conditions as covariates in a multivariate Cox regression model. The trends of \( P \) value and HR by age cutoff were further evaluated in a subgroup of histology and in a The Cancer Genome Atlas (TCGA) dataset. In addition, propensity score-matching analysis using the identified age cutoff was performed.

Results: An age of 66 years was shown to be the most significant cutoff for defining old age with independent prognostic power (HR = 1.45, 95% CI 1.04–2.03, \( P = 0.027 \)). This result was also observed with the analyses of serous histology subgroup and with the analysis of a TCGA dataset with serous EOC. In survival analysis, patients aged ≥66 years had significantly worse OS compared with younger individuals (56 months vs 87 months, \( P = 0.006 \)), even following propensity score matching (57 months vs 78 months, \( P = 0.038 \)). In addition, the individuals of the TCGA cohort showed similar results.

Conclusion: An age of 66 years is the best cutoff to define elderly age in EOC considering the geriatric assessment, and this information can be used in the administration of individualized therapies in elderly EOC patients.

1413 - Poster Session
Can preoperative cervical excision pathology predict the need for adjuvant radiation in early-stage cervix cancer?

Objective: Appropriate selection of surgical candidates in early-stage cervical cancer is critical given increased morbidity of dual modality treatment. We sought to assess whether pathologic characteristics of preoperative cold knife cone (CKC) or loop electrosurgical excision procedure (LEEP) could predict the need for postoperative radiotherapy (RT).

Method: After Institutional Review Board approval, patients who underwent radical hysterectomy (RH) for early-stage cervical cancer from January 2010 to December 2017 were identified; demographics and clinicopathologic data, including imaging, surgery, adjuvant treatment, and disease outcomes, were retrospectively collected. Our primary outcome was the need for adjuvant RT. The exposure of interest was preoperative evaluation of CKC/LEEP specimens using Sedlis criteria. Descriptive statistics were performed. Fisher exact test was used to compare groups.

Result: A total of 148 patients underwent RH. Of these, 57 (38.5%) had a preoperative biopsy without excision and 91 underwent cervical excision prior to RH. Of the 57 patients who did not have a CKC/LEEP, 35 (61.5%) needed adjuvant RT compared to 23/91 patients (25.3%) who underwent CKC/LEEP (\( P < 0.05 \)). Of the 23 patients who had a CKC/LEEP and needed adjuvant RT, 9 patients met 2 of 3 Sedlis criteria. Of those patients meeting 2 of 3 Sedlis criteria on preoperative cervical excision (\( n = 21 \), 42.9% needed adjuvant RT. There was a higher risk of needing adjuvant RT if patients met 2 of 3 Sedlis criteria on cervical excision specimen (see Table 1, \( P < 0.05 \)). Of the patients meeting 0 or 1 Sedlis criteria on excision (\( n = 70 \), 14 (20%) needed adjuvant RT. Of the 23 patients who needed adjuvant RT after CKC/LEEP and RH, 95.6% (\( n = 22 \)) had positive margins on cervical excision. Of the 70 patients who did not need adjuvant RT after excision and RH, 67.1% (\( n = 47 \)) had positive margins on their cervical excision (\( P < 0.01 \)).

Conclusion: Women who met ≥2 of Sedlis criteria on their excisional biopsy were at more than twice the risk of needing adjuvant radiation compared to those meeting ≤1 of criteria. Patients who met 2 of 3 Sedlis criteria on cervical excision for early-stage cervix cancer should be counseled that they are at increased risk for needing RT postoperatively.

1414 - Poster Session
How often do patients with early-stage cervix cancer require dual modality treatment due to inaccurate staging on clinical exam and preoperative imaging?

Objective: If clinical staging is not accurate, patients with early-stage cervix cancer may require dual modality treatment of surgery and radiation instead of surgery alone. We evaluated the incidence of patients who required dual modality treatment due to inaccurate staging on clinical exam and preoperative imaging.

Method: After Institutional Review Board approval, patients who underwent radical hysterectomy for early-stage cervix cancer from January 2010 to December 2017 were identified; demographics and clinical/pathologic data were retrospectively collected. Our primary outcome was the need for adjuvant RT. The exposure of interest was inaccurate staging on clinical exam or preoperative imaging. Descriptive statistics were performed. Fisher exact test was used to compare groups.

Result: A total of 148 patients underwent RH. Of these, 57 (38.5%) had a preoperative biopsy without excision and 91 underwent cervical excision prior to RH. Of the 57 patients who did not have a CKC/LEEP, 35 (61.5%) needed adjuvant RT compared to 23/91 patients (25.3%) who underwent CKC/LEEP (\( P < 0.05 \)). Of the 23 patients who had a CKC/LEEP and needed adjuvant RT, 9 patients met 2 of 3 Sedlis criteria. Of those patients meeting 2 of 3 Sedlis criteria on preoperative cervical excision (\( n = 21 \), 42.9% needed adjuvant RT. There was a higher risk of needing adjuvant RT if patients met 2 of 3 Sedlis criteria on cervical excision specimen (see Table 1, \( P < 0.05 \)). Of the patients meeting 0 or 1 Sedlis criteria on excision (\( n = 70 \), 14 (20%) needed adjuvant RT. Of the 23 patients who needed adjuvant RT after CKC/LEEP and RH, 95.6% (\( n = 22 \)) had positive margins on cervical excision. Of the 70 patients who did not need adjuvant RT after excision and RH, 67.1% (\( n = 47 \)) had positive margins on their cervical excision (\( P < 0.01 \)).

Conclusion: Women who met ≥2 of Sedlis criteria on their excisional biopsy were at more than twice the risk of needing adjuvant radiation compared to those meeting ≤1 of criteria. Patients who met 2 of 3 Sedlis criteria on cervical excision for early-stage cervix cancer should be counseled that they are at increased risk for needing RT postoperatively.
**Objective:** Clinical staging of cervical cancer remains standard of care, but imaging is direct management. Given the increased morbidity with dual-modality therapy, it is important to select appropriate candidates for radical hysterectomy (RH). We sought to compare the accuracy of staging by clinical examination compared to imaging.

**Method:** Patients who underwent RH for clinical early-stage cervical cancer from January 2010 to December 2017 were retrospectively identified. Following Institutional Review Board review, patient demographics and clinicopathologic information were abstracted from the electronic medical record. Tumor size was compared between physical examination (PE), image-guided measurements, and final pathology. Accuracy of imaging was compared between CT, PET-CT, and MRI. The Student t test was used.

**Results:** A total of 148 women underwent RH, of whom 44 had documented preoperative tumor size by both PE and imaging. Overall, 25 patients underwent evaluation by CT, 14 by PET-CT, and 5 by MRI. Three patients were excluded from the CT group given gross overestimation of tumor size due to fibroids or uterine involvement. The mean difference in tumor size on PE to that on pathology in the 41 patients analyzed was 1.16 cm. This was similar to the mean difference in tumor size on imaging to that on pathology (1.12 cm, \( P = 0.86 \)). MRI was most accurate (Table 1) but did not reach statistical significance when compared to PET-CT or CT (\( P = 0.15 \), \( P = 0.15 \), respectively). If separated on classic criteria for stage IB1 versus IB2, there was no difference in the accuracy of any size measurement modality (\( P = 0.78 \)). Three patients (7.3%) were “upstaged” on final pathology compared to preoperative PE and imaging (2 CT, 1 PET-CT); 1 patient from IA to IB1 and 2 from IB1 to IB2 (both of whom required adjuvant treatment). Of the 38 patients whose staging on final pathology was unchanged compared to their preoperative assessment, 16/38 (49.4%) required adjuvant treatment.

**Conclusion:** Both PE and imaging are relatively inaccurate in determining the size of cervical lesions in patients with presumed early-stage disease. Independent of the way size was measured, 7% of patients were “upstaged.” MRI trended toward being the most accurate preoperative imaging modality to assess cervical cancer lesion size. Our findings suggest that MRI should be considered when accurate staging is uncertain.

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**1415 - Poster Session**

**18F-FDG PET/CT in preoperative nodal staging of endometrial cancer: The role of radiomics to improve sensitivity in detecting nodal metastases**

A. Buda, E. De Bernardi, C. Crivellaro, F. Elisei, M. Delle Marchetti, M. Paderno, L. Guerra and R. Fruscio. *University of Milano-Bicocca, Monza, Italy, School of Medicine and Surgery, Monza, Italy, San Gerardo Hospital, Monza, Italy, University Milano-Bicocca, Monza, Italy, San Gerardo Hospital, Monza, MI, Italy, San Gerardo Hospital, University Milano-Bicocca, Monza, Italy*

**Objective:** The introduction of SLN biopsy ultrastaging, able to identify micrometastatic deposits, increased false-negative PET/CT findings in nodal staging of endometrial cancer, as small metastatic lymph node (LN) lesions may remain undetected at visual analysis because of the limited spatial resolution of the PET technique. The aim of this study was to investigate the role of radiomics applied in women with endometrial cancer who underwent 18F-FDG PET scan, to evaluate whether imaging features computed on the primary tumor could improve sensitivity in detection of LN metastases.

**Method:** Between January 2009 and August 2018, 116 women with histologically proven endometrial cancer who underwent preoperative 18F-FDG PET/CT were retrospectively considered. SUV, MTV, TLG, geometrical shape, histograms, and texture features were computed inside tumor contours. In the first group of 86 patients (group 1) association between imaging features and LN metastases was performed by univariate Mann-Whitney test and by neural network multivariate model. Univariate and multivariate models were assessed with leave one out on 20 training sessions and on a second group of testing 30 women (group 2). Combination between LN metastases visual detection results and radiomic analysis was also assessed.

**Results:** Sensitivity and specificity of LN visual detection were 50% and 99% on group 1 and 33% and 95% on group 2, respectively. The lower sensitivity of visual detection in group 2 is mainly related to the higher rate of micrometastases respect to group 1 (25% vs 13%). A unique heterogeneity feature computed on the primary tumor (the zone percentage of the grey level size zone matrix, GLSZM ZP) was able to predict LN metastases better than any other feature or multivariate model (sensitivity and specificity of 75% and 81% on DB1 and of 89% and 80% on DB2, respectively). Tumors with LN metastases generally demonstrated a lower GLSZM ZP value, that is, by the co-presence of high-uptake and low-uptake areas. The combination of visual detection and GLSZM ZP values in a unified framework obtained sensitivity and specificity of 94% and 67% on DB1 and of 89% and 75% on DB2, respectively. See Figure 1.
Conclusion: In our study the computation of imaging features on the primary tumor increases nodal staging for detection sensitivity in 18F-FDG PET and can be considered for a better planning of surgical treatment.

Fig. 1.

1416 - Poster Session
Impact of surveillance imaging practices on survival outcomes in advanced ovarian cancer
A.K. Green, D. Korenstein, C.A. Aghajanian, B. Barrow, M. Curry and R.E. O'Cearbhaill. Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: The Society of Gynecologic Oncology recommends against routine post-treatment surveillance imaging in patients with advanced ovarian cancer in remission because of a lack of supporting evidence. Surveillance imaging remains common practice. Early radiographic detection of asymptomatic disease may enable initiation of therapy or surgery prior to the development of complications that preclude optimal intervention. We sought to describe the impact of high- versus low-frequency surveillance imaging among providers in our institution on OS, time to recurrence, and clinical trial enrollment.

Method: We included patients with stage II–IV high-grade epithelial ovarian cancer initially diagnosed from January 2001 to January 2017 treated at our institution who recurred ≥3 months post-upfront platinum-based chemotherapy. Using the subpopulation of patients with remission ≥1 year, we calculated median frequencies of unique events for CT or MRI abdomen/pelvis for each provider to determine usual imaging practice. Providers were categorized into high-frequency versus low-frequency imaging. Cox proportional hazard model was used to examine differences in OS and time to recurrence among patients with high- versus low-frequency providers, adjusted for trial enrollment. χ² test was used to examine differences in clinical trial enrollment.

Results: The analysis included a total of 684 patients, of whom 247 enrolled in a clinical trial. Median frequency of imaging was 6 months. A total of 543 patients were treated by high imaging frequency providers (< q12 months), and 141 patients were treated by providers with low imaging frequency (≥ q12 months). Time to recurrence was significantly shorter among patients treated by providers with high versus low imaging frequency (18 vs 19.2 months, HR = 1.33, 95% CI 1.10–1.60, P = 0.003). There was no significant difference in OS (Figure 1, HR = 0.91, 95% CI 0.72–1.14, P = 0.42) or clinical trial enrollment (low 29.8%, high 37.8%, P = 0.10).

Conclusion: Within the limitations of this retrospective analysis, patients treated by high-frequency providers had earlier detection of recurrence without improved OS. At our institution, surveillance imaging practices for patients with advanced ovarian cancer varied widely. Future investigation is required to identify the subset of patients who are likely to benefit from
more frequent imaging.

**Fig. 1.** Kaplan-Meier curve for overall survival among ovarian cancer patients with high vs. low imaging frequency providers

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**1417 - Poster Session**

**Improvement of radiological disease on CT after neoadjuvant chemotherapy may not correlate with chemotherapy response score (CRS) in advanced tubo-ovarian high-grade serous ovarian carcinoma**

R. Sugruea, K. Jamesa, W.B. Growdonb, R.M. Clarkb, M.G. del Carmemb, A. Melameda and A.J. Bregar. aMassachusetts General Hospital, Boston, MA, USA, bMassachusetts General Hospital/Harvard University, Boston, MA, USA

**Objective:** Chemotherapy response score (CRS) is a reproducible histopathologic scoring system that has shown prognostic significance for measuring response to neoadjuvant chemotherapy (NACT) in interval-cytoreduced specimens of tubo-ovarian high-grade serous carcinoma (TOHGSC). CRS does not include radiological data. The aim of this study was to assess whether radiological improvement in disease following NACT correlates with CRS.

**Method:** Patients with stage III/IV TOHGSC who received NACT and cytoreductive surgery in a single academic center over a 10-year period were identified. Change in radiological disease was quantified by 2 blinded gynecologic radiologists. Both assigned integer values to their interpretations of each CT based on extent of disease. The averages of both values were calculated, and an ordinal CT improvement score (T1–T0) was developed by subtraction between interval CT (T1) and staging CT (T0) values. Positive values indicated a reduction in tumor burden. Spearman correlation and multivariate linear regression were used to investigate the relationship between T1–T0 and CRS. Missing CT data were imputed using a stochastic model based on patient demographics, including age, race, BMI, comorbidity index, total number of chemotherapy cycles, and platinum resistance.

**Results:** A total of 114 patients met inclusion criteria and had NACT and cytoreductive surgery for stage III/IV TOHGSC. CRS was calculable for 101 patients based on available pathology. T1–T0 data were available for 76 patients, ranging from −2 to +6 with a median of +2.1. No statistically significant correlation was demonstrated between T1–T0 and CRS using linear regression (Spearman correlation T1–T0 and CRS, with no imputed values: −0.129, P < 0.32; beta coefficient for CRS score predicting T1–T0, −0.194, 95% CI −1.09–0.71). Repeat regression using multiple imputation for missing data yielded a similar result. Of note, the development of platinum resistance correlated strongly negatively with reader score (denoting progression of disease) post NACT.
Conclusion: The authors assume a priori that disease improvement on CT post NACT should reflect favorable chemotherapy response. However, this study suggests that this does not correlate well with CRS. CT improvement can therefore not be used as a surrogate for CRS and vice versa.

1418 - Poster Session
Evaluation of portable colposcopy and HPV testing for screening of cervical cancer in rural China
H. Newman, H. Jilin, B. Zhu, L. Bradford and G. Gao. aThe Children's Hospital of Philadelphia, Philadelphia, PA, USA, bFirst People’s Hospital of Yunnan, Kunming, China, cMaine Medical Center, Portland, ME, USA, dUniversity of Massachusetts Medical Center, Worcester, MA, USA

Objective: To evaluate the use of a portable, rechargeable colposcope combined with HPV testing, as compared with HPV testing alone for screening of cervical cancer and precancerous lesions.

Method: This was a cross-sectional study among 488 women in Baoshan County, Yunnan. Women underwent HPV testing followed by gynocular portable colposcopy with visual inspection with acetic acid. Obvious lesions were biopsied. If portable colposcopy testing was negative but HPV testing was positive, women underwent follow-up testing with thin prep cytology and traditional colposcopy. Cervical biopsies were performed for any abnormalities. Histopathology was followed up with diagnosis and treatment.

Results: Among 488 women screened with portable colposcopy, 24 underwent biopsy based on positive colposcopy screening. Of these 24 women, 3 were HPV positive and 21 were HPV negative. Five women had CIN I, and one had advanced cervical cancer. Forty-six women tested positive for HPV. Three of these women had screened positive on preliminary colposcopy, with one positive for CIN III/squamous cell carcinoma and one woman with CIN I. Forty-three women underwent follow-up testing with thin prep cytology. Two women had atypical squamous cells of unknown significance (ASCUS); five had LSIL and were biopsied; three women had CIN I; one had CIN II; and one had CIN III. HPV testing and portable colposcopy was more sensitive but slightly less specific than portable colposcopy or HPV testing alone.

Conclusion: While HPV testing has high sensitivity and specificity for the detection of precancerous and cancerous lesions and portable colposcopy has lower specificity, both methods of detection have low positive predictive value and high negative predictive value. In tandem, HPV testing and portable colposcopy had higher sensitivity for detection among women who underwent biopsies. In clinical practice, portable colposcopy was an effective, easy, and affordable tool to transport to villages where cytology is not currently feasible.

1419 - Poster Session
IMPACT of global partnership on surgical care for patients with cervical cancer in Ethiopia
B.D. Gulelata, T.M. Asires, T.U. Beyene, D.D. Nima, C.M. Johnston, K. Thorsten, M. Quinn, E. Kantelhardt, C. Thomssen, T. Lantzsch, R. Ghebre, B.G. Batu, F.T. Terefe and H.W. Tadele. aSt. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, bAddis Ababa University School of Medicine, Addis Ababa, Ethiopia, cThe University of Michigan Hospitals, Ann Arbor, MI, USA, dHospital Esslingen, Baden-Württemberg, Germany, eRoyal Women’s Hospital, Melbourne, Australia, fMartin Luther University, Halle, Germany, gSt. Elisabeth Hospital, Halle, Germany, hUniversity of Minnesota, Minneapolis, MN, USA

Objective: In Ethiopia, cervical cancer is the second most common cancer and accounts for 17% of malignancies in females. There is an unmet need for health care service for cervical cancer in Ethiopia. The Gynecologic Oncology Fellowship Training Program was launched in 2016 at 2 teaching hospitals in Addis Ababa, Ethiopia. At St. Paul's Hospital Millennium Medical College (SPHMMC), the program works in collaboration with the University of Minnesota, University of Michigan, and the German Society of Gynaecological Oncology (AGO). In 2017, the program joined the global oncology fellowship training under the International Gynecologic Cancer Society (IGCS). This study is presented to show the impact of global partnership on surgical care delivery for patients with cervical cancer managed at SPHMMC.

Methods: A hospital-based retrospective cross-sectional study was conducted. A 5-year period, September 2008–September 2013, was selected as a pre-fellowship period for baseline data. Starting at fellowship implementation January 2016 was selected to determine the impact of fellowship training on service delivery. Data were collected from medical charts. We could retrieve 86 charts from the record office making the retrieval rate 84.3%.
**Results:** A total of 211 patients with cervical cancer were evaluated in our gynecology oncology clinic from January 2016 to August 2018, and 102 (48%) were eligible for radical hysterectomy and pelvic lymphadenectomy (RHPL). The average number of patients operated per year increased 8 times from the pre-fellowship period. Patients with advanced disease were referred to chemoradiation. The mean age was 48 ± 11 years (range 28–88 years). Fourteen patients (16%) were HIV positive. Clinical stage included stage IB1 48 (46.5%), stage IB2 14 (16.3%), and stage IIA 25 (30%). Eighteen patients (20.9%) received neoadjuvant chemotherapy. There were 2 bladder injuries, 4 ureteric injuries, and no deaths reported during the hospital stay. The bivariate analyses showed taking neoadjuvant chemotherapy significantly decreases the rate of pelvic lymph node metastasis with a $P$ value of 0.01.

**Conclusion:** Implementation of gynecologic oncology fellowship training increased surgical management of cervical cancer in Ethiopia. Quality improvement projects and cancer registry are needed to advance cervical cancer service delivery.

**Health Disparities**

**1420 - Poster Session**

**The contributory factors to racial disparity in survival varied in uterine versus ovarian carcinosarcoma: A National Cancer Database investigation**


**Objective:** To investigate the contributors of racial disparities in survival between non-Hispanic black and non-Hispanic white women with uterine carcinosarcoma (UCS) versus ovarian carcinosarcoma (OCS).

**Method:** Non-Hispanic black and non-Hispanic white women diagnosed from 2004 to 2014 with a first primary stage I–IV UCS relative to all uterine cancers or OCS relative to all ovarian cancers in the National Cancer Data Base were evaluated. The inverse probability of treatment weighting approach using a propensity score was applied to the UCS and OCS cohorts, and the contribution of income, insurance, stage, and treatment on racial disparity in survival was evaluated using weighted Cox modeling.

**Results:** Of the 222,359 uterine cancer patients, 4.6% had UCS including 2,839 non-Hispanic black and 7,366 non-Hispanic white women. The proportion of UCS increased with age at diagnosis from 18 to 90 years old up to 15% in non-Hispanic black and 7% in non-Hispanic white women (Figure 1A). Survival in non-Hispanic black versus non-Hispanic white patients with UCS was worse (Figure 1B), and hazard ratio (HR) dropped from 1.35 (95% CI 1.28–1.42) in the baseline demographic model to 1.20 (95% CI 1.14–1.26) after sequential balancing for income, insurance, stage, and treatment (Figure 1C). The individual contribution to the excess relative risk of death in non-Hispanic black versus non-Hispanic white patients with UCS was 12% to income, 8% to insurance, 17% to stage, 6% to treatment, and 58% to unexplained factors (Figure 1D). In contrast, of the 93,063 women with ovarian cancer, 3% had OCS including 280 non-Hispanic black and 2,586 non-Hispanic white women. The proportion of OCS increased moderately by age at diagnosis up to 4% in non-Hispanic black and 3% in non-Hispanic white patients (Figure 1E). Racial disparity in survival in OCS (Figure 1F) was less than in UCS patients, and HR was 1.19 (95% CI 1.04–1.35) in the baseline demographic model and dropped to 1.04 (95% CI 0.94–1.16) after sequential balancing for income, insurance, stage, and treatment (Figure 1G). The individual contribution to racial disparity in survival in OCS was 43% to income, 18% to insurance, 11% to stage, 7% to treatment, and 22% to unexplained factors (Figure 1H).

**Conclusion:** Racial disparity in survival persisted in UCS after balancing for demographics, income, insurance, stage, and treatment with 58% attributed to unknown factors including racial genetic admixture, molecular factors, and social health determinant, whereas racial disparity in OCS was largely explained by income and insurance.
Fig. 1. The proportion of uterine carcinosarcoma (UCS) (A) and ovarian carcinosarcoma (OCS) (E) by age. Racial disparity in survival between non-Hispanic black (NHB) vs. non-Hispanic white (NHW) patients in UCS (B) compared to OCS (F). Survival distributions were evaluated using Kaplan-Meier method and compared using log-rank testing. The hazard ratio (HR) and 95% confidence interval (CI) were calculated from unadjusted Cox modeling. The contribution of individual factors (demographic, income, stage and adjuvant treatment to racial disparity in survival utilizing a sequential weighted balancing approach in UCS (C) relative to OCS (G). The HR and 95% CI were calculated from adjusted Cox modeling. The excess relative risk (ERR) of death was expressed as a percentage for UCS (D) and (OCS) (H) for the different variables.

1421 - Poster Session
Visceral adiposity as a predictor of chemotherapy toxicity in patients with ovarian cancer receiving platinum and taxane-based chemotherapy
K. Tucker¹, A. Staley², J.D. Oldan³, M. Newton³, M. Ertel§, L. West³, D.T. Moore³ and V.L. Bae-Jumpa,b. ¹University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, bUniversity of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

Objective: Visceral adiposity (or central obesity) may be associated with worse oncologic outcomes in ovarian cancer (OC); however, less is known of the impact of visceral adiposity on development of chemotherapeutic-related toxicities. The purpose of this study was to investigate the association of visceral adiposity, as assessed by CT body morphometric measurements, with chemotherapy toxicity in patients with OC.

Method: A random cohort of epithelial OC patients diagnosed between June 2000 and February 2017 who received treatment with platinum and taxane-based chemotherapy were included. Data on age, race, stage, grade, BMI, comorbid conditions, chemotoxicities and their grades, treatment approaches, and outcomes were collected after Institutional Review Board approval. The following toxicities were recorded: rheumatologic, hematologic, renal, gastrointestinal, pulmonary, neurologic, insomnia, fatigue, mucositis, pain, and allergic reactions. The CT images closest to time of diagnosis were evaluated for mid-waist visceral fat volume (VA), mid-waist subcutaneous fat volume (SA), and the ratio of mid-waist VA/SA. Visceral adiposity is commonly defined as a VFV/SFV ≥ 0.4. Nonparametric ANOVA was used to test for differences between the VA/SA ratio and variables of interest.

Results: A total of 179 patients were evaluated. The majority presented with stage III/IV, high-grade serous OC (72%). The median age was 62 years, and most were Caucasian (79%). Approximately 35% were obese; the median BMI was 26.8 (IQR = 23.1–32.8). The median VA/SA ratio was 0.45 (IQR = 0.30–0.72). Need for blood transfusion ($P < 0.01$) and chemotherapy regimen change ($P = 0.05$), as well as grade of hematologic toxicities ($P = 0.03$), appeared to be significantly associated with the VA/SA ratio. There appeared to be no associations between the VA/SA ratio and the following measures of chemotherapy toxicity: need for chemotherapy dose adjustment ($P = 0.86$) chemo-related admission ($P = 0.22$), and delay in treatment due to toxicity ($P = 0.36$).

Conclusion: We detected significant associations between the VA/SA ratio and several measures of chemotherapy toxicity in our OC cohort. Given the rising obesity epidemic, further prospective investigation is warranted to examine the impact of body
1422 - Poster Session
Cervical cancer outcomes in true cut through simple hysterectomy compared to appropriately managed controls
T. Castellano\textsuperscript{a}, L. Driskill\textsuperscript{a}, A. Rodriguez\textsuperscript{a}, M.A. Gold\textsuperscript{b} and L.M. Landrum\textsuperscript{c}. \textsuperscript{a}The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, \textsuperscript{b}Tulsa Cancer Institute, Tulsa, OK, USA, \textsuperscript{c}The University of Oklahoma, Oklahoma City, OK, USA

Objective: To define associations and risks and to establish differences in recurrence and survival outcomes for receipt of a true cut through hysterectomy (CTH) in women with locally advanced cervical cancer when compared to appropriately managed controls.

Method: A prospective cohort study from two institutions comparing women who received a true CTH to a matched control group was performed. True CTH was defined as women receiving simple hysterectomy for benign indications with pathologic findings of incidental cervical cancer of either stage Ib2 or greater, positive margins, or gross residual disease. Controls were women with appropriately managed cervical cancer matched for stage in a 1:2 fashion. Primary endpoints of interest include risk for recurrence, PFS, and OS. PFS and OS were estimated using Kaplan-Meier product-limit estimator. Patient characteristics were compared using standard summary statistics.

Results: In total, 28 case CTH and 55 stage-matched controls were identified. There was no difference in BMI ($P = 0.52$), tobacco use ($P = 0.74$), and stage ($P = 0.26$) between cohorts. Median age in the CTH cohort was 39 (range 30–73) years versus 49 (range 22–75) years with the CTH cohort being significantly younger ($P = 0.05$). The CTH cohort was more likely to have adenocarcinoma than the control group ($P = 0.04$) and less likely to receive chemoradiation (CRT) than the control group ($P < 0.01$). Those with CTH had a significantly higher risk for recurrence with RR of 1.698 (95% CI 1.022–2.819). Median PFS for CTH versus control was 51.5 (95% CI 12.4–132) and 96 (95% CI 53–n/a), respectively. Median PFS and OS were not significantly different between groups ($P = 0.20$ and $P = 0.10$, respectively); this conclusion remained when corrected for age, histology, and receipt of CRT. See Figure 1.

Conclusion: CTH is an unfortunate and avoidable clinical outcome that disrupts standard-of-care treatment planning for women with advanced cervical cancer. When managed appropriately, by a gynecologic oncologist, locally advanced cervical cancer results in a higher likelihood that the patient will receive adjuvant chemoradiation therapy and have a decreased risk for recurrence. Receipt of CTH is a predictor of poor outcome and disproportionately affects younger women with adenocarcinoma of the cervix.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Product-Limit Survival Estimates}
\end{figure}
Objective: To evaluate acceptability and knowledge of population-based, universal *BRCA* testing (UBT) among women presenting for annual gynecologic health assessment, and to determine whether a racial disparity exists in acceptability and knowledge of UBT.

Method: A cross-sectional study was performed using an anonymous survey of women presenting for routine gynecologic care in an outpatient setting of a single academic institution. The survey collected age, self-identified race and ethnicity, education level, personal and family history of breast and/or ovarian cancer (BOC), knowledge of UBT, interest in UBT and willingness to pay out of pocket for testing. Those who identified as races other than white and black were categorized as other. Responses were compared with bivariate and multivariate analysis.

Results: Of the 323 participants included, 118 (36.9%) were white; 163 (50.9%) black; and 39 (12.2%) other; and 3 (1%) did not disclose race. Twenty (6.2%) participants identified their ethnicity as Hispanic. Interest in UBT was expressed in 150 of 301 (49.8%) of participants. On multivariate analysis, women with a family history of BOC were more likely to be interested in UBT than those without (OR = 1.9, 95% CI 1.0–3.6). Willingness to pay out of pocket was also associated with interest in UBT (OR = 3.26, 95% CI 1.7–6.4). Lower education level was associated with no knowledge of UBT (OR = 9.9, 95% CI 2.0–49.7). Age and personal and family history of BOC were similar between racial groups. Significant differences were identified on bivariate analysis between races in education, with 94% of white women having above high school level compared to 48.9% of black and other women (*P* < .01). Knowledge and willingness to pay for UBT were higher among white women, but interest in testing was similar between racial groups. Multivariate analysis with adjustment for education level confirmed that white women were more likely to have knowledge of UBT compared to black and Hispanic women (OR = 5.6, 95% CI 2.4–13.4; OR = 10.3, 1.2–87.5). See Table 1.

Conclusion: Interest in UBT among women in the general population is high. Despite interest, knowledge of *BRCA* is poor among black and Hispanic women even when adjusting for education level. Community outreach and educational interventions aimed at non-white women could increase awareness of UBT and alleviate this disparity.

Table 1. Multivariate analysis of survey responses.

<table>
<thead>
<tr>
<th>Survey response</th>
<th>Would you be interested in BRCA testing?</th>
<th>Have you heard of BRCA testing?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted odds ratio for positive response (95% CI)</td>
<td>Adjusted odds ratio for negative response (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>0.97 (0.95 – 1.0)</td>
<td>0.28 (0.04 – 1.60)</td>
</tr>
<tr>
<td>Race</td>
<td>p value</td>
<td>p value</td>
</tr>
<tr>
<td>White</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Black</td>
<td>1.38 (0.60 – 3.15)</td>
<td>8.81 (3.57 – 21.7)</td>
</tr>
<tr>
<td>Other</td>
<td>1.13 (0.41 – 3.11)</td>
<td>2.09 (0.76 – 5.79)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.99 (0.47 – 8.50)</td>
<td>10.26 (1.20 – 87.5)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Some college or more</td>
<td>1.46 (0.60 – 3.55)</td>
<td>0.10 (0.02 – 0.50)</td>
</tr>
<tr>
<td>Family history of breast and/or ovarian cancer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1424 - Poster Session  
**Socioeconomic disparities in trachelectomy as a fertility-sparing treatment for stage IB cervical cancer**  
S.M. Rieder, A.L. Alexander, E.J. Levy and E.L. Barber. Northwestern University Feinberg School of Medicine, Chicago, IL, USA

**Objective:** To assess the association of race and ethnicity with standards-based fertility-sparing surgery for early cervical cancer.

**Methods:** Using the National Cancer Data Base, women younger than 50 years diagnosed with stage IB cervical cancer (2004–2015) who were treated with surgical management were identified. Patients with high-risk histologies or who received radiation or chemotherapy were excluded. The primary exposure was race and ethnicity, defined as non-Hispanic white, non-Hispanic black, and Hispanic; other races, Asian/Pacific Islander and Native American, were initially examined but represented less than 5% of the population. The primary outcome was guideline-recommended fertility-sparing treatment for this population, trachelectomy. Multivariate regression was used to evaluate associations and adjust for clinical and socioeconomic factors.

**Results:** We identified 9,381 women with AJCC clinical stage 1B cervical cancer: 7,645 white women (81.5%), 1,223 non-Hispanic black women (13.0%), and 513 Hispanic women (5.5%). Black women were less likely than white women to undergo hysterectomy (OR = 0.58, 95% CI 0.55–0.62) or trachelectomy (HR = 0.58, 95% CI 0.43–0.77). Associations for both hysterectomy and trachelectomy persisted despite adjustment for age, cancer grade, comorbid conditions, income, and insurance status (OR = 0.62, 95% CI 0.59–0.66 and OR = 0.71, 95% CI 0.52–0.95, respectively). Older age and income less than 200% of federal poverty line were associated with decreased odds of trachelectomy (OR = 0.42, 95% CI 0.39–0.46 and OR = 0.54, 95% CI 0.45–0.64).

**Conclusion:** Standard of care for stage IB cervical cancer, if fertility is desired, is trachelectomy. Among women who received surgical treatment only for stage IB tumors, black women were less likely to receive either hysterectomy or trachelectomy and were more likely to receive an excisional procedure not followed by chemotherapy, radiation therapy, or hysterectomy (1.09, 95% CI 1.00–1.19). We demonstrate that disparities for black and low-income women exist not only in definitive surgical treatment of early cervical cancer but also in fertility-sparing surgery. These young black women may represent a high-risk population who were lost to follow-up after initial treatment or have not received standard-of-care treatment for stage 1B cervical cancer.

1425 - Poster Session  
**Trends in sentinel lymph node biopsy for vulvar carcinoma and associated disparities in its utilization**  
S. Meia, A. Moron, R.K. Lee, M.J. Kanis and Y.C. Lee. SUNY-Downstate, Brooklyn, NY, USA, North Texas Gynecologic Oncology, Arlington, TX, USA, SUNY Downstate, Brooklyn, NY, USA

**Objective:** Sentinel lymph node biopsy (SLNB) for invasive vulvar carcinoma has been validated by two large trials: GROINSS-V and GOG 173. Our study aims to identify the national patterns of practice of SLNB for invasive squamous cell carcinoma of the vulva (SCC) and to identify any disparities in its utilization.

**Method:** The Surveillance, Epidemiology and End Results cancer registry was used to identify patients with stage I–III SCC from 2004 to 2015 treated primarily with surgery. Patients with tumors larger than 4 cm, previous radiation exposure, or surgery for the cancer were excluded.

**Results:** A total of 3,006 patients were identified: 2,562 patients (85.2%) received inguinofemoral lymph node dissection (ILND), and 444 patients (14.8%) received SLNB. A Pearson correlation analysis showed a trend toward increasing use of SLNB (R = 0.92, P ≤ 0.01). In 2004, 8.3% of patients received SLNB compared to 31.3% in 2015. The mean age of diagnosis for
SLNB was 64.9 years and for ILND was 64.4 years ($P = 0.50$). White patients were more likely to receive SLNB compared to black patients (15.1% vs 7.6%, respectively, $P = 0.02$). Also, patients with private insurance (18.3%) were more likely to receive SLNB compared to patients on Medicaid (12.9%) or uninsured (4.0%, $P = 0.01$). The median household income for SLNB patients was $62,526 versus $59,774 for ILND ($P \leq 0.01$). Patients with stage I (18.5%) disease were more likely to receive SLNB than patients with either stage II (11.0%) or stage III disease (12.1%, $P \leq 0.01$). Patients from the South were least likely to receive SLNB (7.9%) compared to those from the Northeast (16.0%), Midwest (19.6%), and West (16.9%, $P \leq 0.01$). Site of vulva (i.e., labia majora, labia minora, clitoris, etc.) and laterality of the tumor (i.e., midline, bilateral, or left/right) did not affect SLNB versus ILND rates ($P = 0.48$ and $P = 0.56$, respectively). Overall survival for SLNB was 8.2 years compared to 8.1 years for ILND ($P = 0.66$). The cancer-specific survival for SLNB was 10.4 years and for ILND 10.2 years ($P = 0.33$).

**Conclusion:** The majority of vulvar cancer patients undergo ILND not SLNB, but rates of SLNB are increasing. This is likely due to the strong evidence demonstrated by GROINSS-V and GOG 173. Survival analysis was comparable between the two groups, which reaffirmed findings from the two studies. There exist racial and socioeconomic disparities in the implementation of newer treatment modalities, which need to be addressed.

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**1426 - Poster Session**

**Bridging the disparities gap: Implementation of a clinical practice guideline**

V. Gonzalez, O.D. Lara, P.N. Kamath and V.D.C. Aguilar. aThe University of Texas at Austin/Dell Medical School, Austin, TX, USA, bThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, cUniversity of Miami Miller School of Medicine, Miami, FL, USA

**Objective:** Given the racial disparity associated with utilization of minimally invasive hysterectomies (MIH) in non-European Americans, we aimed to evaluate whether the implementation of a hysterectomy clinical pathway had an impact on these disparities.

**Method:** We performed a retrospective medical record review of all patients who have undergone hysterectomy for benign indications at a single institution prior to, and following, implementation of clinical criteria to increase MIH. The evaluation included all patients 12 months before and 12 months after implementation of the clinical criteria between 2016 and 2017. Clinical criteria included uterine size, possibility of uterine size reduction, concern for extrauterine pathology, and accessibility to uterine vessels.

**Results:** A total of 221 hysterectomies were performed for benign indications: 46.6% (103) were European American (EA), 10.4% (23) were African American (AA), 37.5% (83) were Hispanic American (HA), and the remaining 5.4% (12) were other ethnicities. After pathway implementation, the percentage of MIH increased in both AA (41.6% vs 80%) and HA (70.73% vs 85.7%) patients, while there was no significant change in the percentage of MIH in EA (95.3% vs 93.3%). AA experienced shorter hospital stays (3.25 ± 0.27 days vs 2.4 ± 0.16 days, $P < 0.05$), and decreased blood loss (497.5 ± 131.5 mL vs 125 ± 31.18 mL, $P < 0.05$) after implementation of pathway. HA experienced a similar advantage in length of hospital stay (3.29 ± 0.43 days vs 2.35 ± 0.10 days, $P < 0.05$), and blood loss (274.8 ± 32.49 mL vs 192.3 ± 28.8 mL, $P < 0.05$). EA patients experienced decreased hospital stays and decreased blood loss compared to their minority counterparts before and after implementation of hysterectomy pathway.

**Conclusion:** Systematic implementation of a hysterectomy clinical pathway to increase minimally invasive procedures led to a decrease in disparities in minimally invasive hysterectomies. Further studies are needed to determine how standardization of clinical pathways can further alleviate disparities in different populations.

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**1427 - Poster Session**

**Addressing the high cervical cancer rates along the Texas-Mexico border through community outreach, patient navigation, and provider training/telementoring**

M.P. Salcedo, R. Gowen, M. Lopez, E. Baker, A.M. Rodriguez, A. Milbourne, S. Fisher-Hoch, T. Ogburn, M. Daher, L.B. Guerra, P. Toscano, M. Gascó, J. Morales, L. Valdez, V.L.J. Nagle, B. Cavazos, E.L. Marin, E. Robles, N. Burkhalter, B. Reinnerger, S.G. Parra, M. Fernandez, E. Hawk and K.M. Schmeler. aFederal University of Health Sciences/Immande Santa Casa de Misericordia Porto Alegre, Porto Alegre, Brazil, bSu Clinica Familiar, Harlingen, TX, USA, cThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, dThe University of Texas Medical Branch, Galveston, TX, USA, eThe University of Texas Health Science Center at Houston, Houston, TX, USA, fUTRGV, Edinburg, TX, USA, gHarris Health System, Houston, TX, USA, hSu Clinica, Brownsville, TX, USA, iUT Houston, Houston, TX, USA, jThe University of Texas School of Public Health, Houston, TX,
USA, kSu Clinica Familiar, Harlingen, TX, USA, ℓGateway Health Center, Laredo, TX, USA, mMerci Ministries of Laredo, Laredo, TX, USA, ℓRice University, Houston, TX, USA, oThe University Texas Health Science Center at Houston, Houston, TX, USA

**Objective:** Cervical cancer incidence and mortality rates are 68% and 57% higher, respectively, along the Texas-Mexico border compared with the rest of the United States. This is likely due to a combination of low health literacy, limited access to affordable screening, and a lack of trained personnel to perform colposcopy, loop electrosurgical excision procedures (LEEP), and appropriate management of women with pre-invasive disease. The objective of our study was to increase cervical cancer screening, diagnosis, and treatment rates in the Rio Grande Valley (RGV).

**Method:** We initiated a comprehensive program at two health centers and one mobile clinic in the RGV consisting of (1) a public education program designed for community health workers to teach women about cervical cancer screening and HPV vaccination coupled with patient navigation to participating clinics; (2) colposcopy and LEEP training for physicians and advanced-practice providers through locally held hands-on courses and mentoring program; and (3) implementation of Project ECHO (Extension for Community Health Outcomes), a well-established telementoring program using video conferencing to connect academic specialists with community providers for case-based learning. We compared screening, diagnosis, and treatment rates pre- and post-program implementation.

**Results:** From November 2014 to June 2018, local providers screened 19,028 women with Pap ± HPV testing (baseline 12,460, 53% increase); performed colposcopy on 2,644 women with abnormal screening results (baseline 945, 180% increase); and performed 483 LEEP procedures for treatment of cervical dysplasia (baseline 0). Ten women were diagnosed with invasive cancer and navigated to one of the participating gynecologic oncologists for treatment (baseline N/A). Five additional providers in the RGV completed the mentoring program to be certified to perform colposcopy (100% increase from baseline of 5) and two additional providers to perform LEEP (baseline 0). ECHO telementoring video conferences have been held every two weeks for a total 94 sessions (average of 22 participants/session) with 182 patient cases presented and discussed.

**Conclusion:** Our comprehensive approach has led to an increase in the number of women undergoing cervical cancer screening and diagnosis/treatment of dysplasia. If sustained, we anticipate these efforts will decrease cervical cancer rates in the RGV. The program is currently being expanded to additional medically underserved regions of Texas.

**1428 - Poster Session**

**Survival in elderly patients with vulvar cancer: A National Cancer Database study**

N.B. Gaulin†, J.L. Lesnock‡, C. Tian§, A. Jacobs€, T.C. Krivak†, E.M. Miller†, Y. Casablanca‡,§ and K.M. Darcy‡,§, †Western Pennsylvania Hospital, Pittsburgh, PA, USA, ‡Mid Atlantic Gynecologic Oncology of Mon General Hospital, Morgantown, WV, USA, §Gynecologic Cancer Center of Excellence, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, †Inova Fairfax Hospital, Falls Church, VA, USA, ‡Thomas Jefferson University Hospital, Philadelphia, PA, USA, †John P Murtha Cancer Center, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

**Objective:** To investigate disparities in disease presentation and survival in elderly (≥75 years) versus nonelderly women (<75 years) diagnosed with vulvar cancer, and to determine whether the prognostic factors vary in elderly versus nonelderly patients.

**Method:** Women diagnosed with a first primary stage I–IV vulvar cancer from 2004 to 2013 in the National Cancer Data Base were eligible. Proportions were compared using χ² test. Relationships with survival were evaluated using log rank test and HR and 95% CI from Cox analysis.

**Results:** There were 20,231 eligible women with vulvar cancer, and 33% were diagnosed at ≥75 years (Figure 1A). The predominant histology was squamous cell carcinoma (SCC), but the proportion with non-SCC increased with age at diagnosis (Figure 1B). Most vulvar cancers were diagnosed with stage I disease, but proportions with stage II–IV disease increased with age (Figure 1C). Elderly patients were more likely to have a higher comorbidity score and to be treated with radiation rather than with surgery or chemotherapy. Risk of death increased steadily in both elderly and nonelderly patients (Figure 1D). Elderly women had worse survival than their nonelderly counterparts (Figure 1E) and were more likely to die (HR = 3.38, 95% CI 3.23–3.53, P < 0.0001). Comorbidity score, stage, histology, grade, and treatment with surgery, radiation (RT), or chemotherapy (CT) were each associated survival in vulvar cancer (P < 0.001 for all). The prognostic value of each of these factors except treatment with surgery or CT varied in elderly versus nonelderly women (Figure 1F). Risks of death attributed
to comorbidity score, stage, histology, regional node assessment, and treatment with RT were all significantly smaller in elderly versus nonelderly women, while those attributed to each 5-year increase in age and grade were larger in elderly versus nonelderly women. The survival benefit of surgery or CT was similar in both elderly and nonelderly patients.

**Conclusion:** The risk of death increased steadily in vulvar cancer with a larger risk in elderly versus nonelderly patients. The survival differences attributed to most of the prognostic factors varied in elderly versus nonelderly women. A larger survival benefit for RT in those diagnosed at ≥75 years. The survival benefit of surgery and CT, however, did not vary by age of diagnosis.

**Fig. 1.** The proportion (%) of vulvar cancers by age at diagnosis (A), histologic subtypes classified as squamous cell carcinoma (SCC) vs. non-SCC by age at diagnosis (B), or stage of diagnosis by age at diagnosis (C). The risk of death expressed as log (HR) by age of diagnosis (D). Survival distribution in months from diagnosis for elderly women diagnosed at ≥75 years old compared with non-elderly women diagnosed at <75 years old with hazard ratio (HR) and 95% confidence interval (CI) estimated from unadjusted Cox regression analysis (E). Multivariate Cox modeling for risk of death expressing using adjusted HR (aHR) and 95% CI for each of the prognostic factors evaluated in non-elderly women compared with elderly women with a test for the interaction between age and each prognostic variable (F). A significant interaction test indicated rejection of the null hypothesis that the HR for a specific prognostic variable in non-elderly women was equal to the HR in the elderly women (H0: HR<75=HR≥75).

**1429 - Poster Session**

**Persistent disparities in the enrollment of racial minorities in clinical trials for gynecologic cancers**

M.J. Kao<sup>a</sup>, S. Uppal<sup>b</sup>, L.W. Rice<sup>c</sup>, S. Johnson<sup>d</sup> and R.J. Spencer<sup>e</sup>.<sup>a</sup>University of Wisconsin Hospitals and Clinics, Madison, WI, USA, <sup>b</sup>University of Michigan Health Systems, Ann Arbor, MI, USA, <sup>c</sup>University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, <sup>d</sup>University of Wisconsin, Madison, WI, USA

**Objective:** To analyze the enrollment of subjects by race in phase II and III clinical trials for gynecologic cancers and compare it to racial proportions of incident uterine, ovarian, and cervical cancers and the U.S. population.

**Method:** Trials were identified through PubMed with a senior library scientist. The studies were categorized by cancer type, and the proportions of enrolled subjects by race were extracted. These values were compared to the expected racial breakdown of annual incident gynecologic cancers from the Centers for Disease Control and Prevention and annual population estimates from the U.S. Census Bureau for a 5-year period from 2010 to 2014.
Results: Of the 2,209 search results, 26 studies met the inclusion criteria (1 uterine, 23 ovarian, and 2 cervical). For the 5 years, enrollment of patients to ovarian cancer trials was 85.3% white, 9.0% Asian, 3.3% Hispanic, 2.3% black, and 0.2% American Native compared to the proportions diagnosed of 78.7% white, 8.4% black, 8.5% Hispanic, 3.7% Asian, and 0.6% American Native. This represents a significant disparity for black and Hispanic patient enrollment compared to ovarian cancer incidence (P < 0.001). Persistent racial disparities were observed in the enrollment of patients in ovarian cancer clinical trials in each year from 2010 to 2014. For the 5-year period, the percentage enrollment of patients to cervical cancer trials was 56.2% white, 20.0% Hispanic, 10.0% black, 7.2% Asian, and 6.6% American Native. While this represents an overrepresentation of Hispanic and American Native patients, black patients were underrepresented relative to their incidence for the period (10.0% enrolled vs 13.9% incidence, P < .001). See Figure 1.

Conclusion: Disparities in the enrollment of racial minorities in gynecologic cancer clinical trials are extensive and persistent despite efforts to address disparities in cancer research. Phase II and III ovarian and cervical cancer trials published between 2010 and 2014 do not accurately represent the patient population that is diagnosed with these cancers, nor the U.S. population at large. This could have wide-ranging implications on the applicability of trial results and the utility of these therapies for all racial groups. Strategies to improve enrollment of minority subjects are needed immediately.
Fig. 1.
1430 - Poster Session
Think outside the box: Pan-cancer molecular study of gynecologic disparities among African Americans
O.D. Lara, Y. Wang, L. Zhang, W. Hu, J.A. Rauh-Haina and A.K. Sood. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bPerelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Objective: Several factors have been proposed to contribute to racial disparities in gynecologic cancers; however, there are no broad studies evaluating race and inherent differences in tumor biology. Our objective was to perform clinical and molecular analyses of African-Americans and white patients with gynecologic cancers.

Method: We performed cross-platform analysis utilizing cancer registry and molecular databases (Surveillance, Epidemiology and End Results, SEER, and The Cancer Genome Atlas, TCGA) to evaluate differences in African-American versus white patients. To characterize genetic ancestry, we utilized the recently established The Cancer Genetic Ancestry Atlas (TCGAA). We evaluated epigenetic modifications through gene methylation status and microRNA expression in TCGA tumors.

Results: A pan-gynecologic cancer analysis was performed using SEER to evaluate clinical outcome differences between African-American and white patients. Compared to white patients, African-American patients had higher rate of death in all gynecologic cancer types: uterine (HR = 1.92, 95% CI 1.86–1.98), ovarian (HR = 1.27, 95% CI 1.23–1.32), cervical (HR = 1.28, 95% CI 1.24–1.32), vulvar (HR = 1.32, 95% CI 1.2–1.41), and vaginal (HR = 1.2, 95% CI 1.08–1.32) carcinomas. Since we found the largest racial disparities among women with uterine and ovarian cancer, we focused the molecular analyses in those populations. Utilizing TCGA, we analyzed molecular data of 391 uterine cancer patients having miRSeq and genetic ancestry data. We identified 86 differentially expressed miRNAs (FDR = 0.1, P < 1.66 × 10−2) in uterine cancer, associated with canonical pathways of cancer drug resistance by drug efflux (P < 9.75 × 10−6) and T cell function (P < 5.55 × 10−01) using Ingenuity Pathway Analysis (IPA) software. A total of 534 ovarian cancer patients having both methylation data and genetic ancestry data were then analyzed. There were 358 methylation probes unique to African-American patients with ovarian cancer mapped to an increase in cellular movement, lipid metabolism, and migration of cells using IPA, which may represent a greater likelihood for metastatic disease.

Conclusion: Our results identify molecular and genetic features unique to African-American women that may contribute to worse survival outcomes. While the cause of cancer disparities is multifactorial, a focus on molecular signatures unique to African-American women may have an impact on outcome.

1431 - Poster Session
Enhanced recovery after surgery: Is it feasible at a safety net hospital?
S.S. Lee, D. Gerber, J.Y. Chern and L.R. Boyd. aNew York University School of Medicine, New York, NY, USA, bUniversity of South Florida, Tampa, FL, USA

Objective: Enhanced Recovery Protocols (ERPs) minimize the stress response associated with surgery, decrease postoperative opioid consumption, and reduce length of stay (LOS). However, several of the medications on standard ERPs are expensive, which may limit their availability in low-resource settings. Our gynecologic oncology service takes care of patients at both an academic tertiary care center and a safety net hospital. We sought to examine whether a modified ERP at the safety net hospital led to comparable patient outcomes when compared to a standard protocol.

Method: From January 2016 to June 2017, patients undergoing scheduled laparotomy by 1 team of gynecologic oncologists who cover 2 hospital networks were placed on a perioperative ERP. Hospital A is an academic medical center; hospital B is a safety net public hospital. ERP was modified at hospital B because of the high cost of several medications (Figure 1). Demographics and perioperative outcomes including LOS, complication, and readmission rates were compared.

Results: One hundred and four patients at hospital A and 45 patients at hospital B were included. Patients at hospital B were younger on average (49.0 ± 13.2 years vs 55.7 ± 14.4 years, P < 0.001), more likely to be nonwhite (93.3% vs 40.4%, P < 0.001), utilize public insurance (48.9% vs 26.0%, P < 0.001), and be unmarried (55.7% vs 33.7%, P < 0.001). There were no statistically significant differences in LOS, postoperative complications, final pathology, estimated blood loss, 30-day readmission, or 30-day complication rates. Compared to patients at hospital A, patients at hospital B were less likely to receive intraoperative transfusions (0% vs 11.5%, P = 0.018) and had fewer inpatient complications (6.7% vs 21.2%, P = 0.032).

Conclusion: Despite the lack of several medications, patients on a modified ERP had similar outcomes to patients on a standard ERP protocol. A lower cost ERP is feasible, effective, and may represent an opportunity for cost reduction.
Racial and regional disparities and outcomes of stage II endometrial cancer patients after robotic surgery
aKaiser Permanente Santa Clara, Santa Clara, CA, USA, 
bCalifornia Pacific Medical Center, San Francisco, CA, USA, 
cStanford University School of Medicine, Stanford, CA, USA, 
dPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, 
eKaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

Objective: To determine the trends and survival after open (OH), laparoscopic (LH), and robotic (RH) hysterectomies for stage II endometrial cancer.

Method: Data from 2010 to 2013 from the National Cancer Data Base were used. χ², Cox regression, and Kaplan-Meier analyses were done.

Results: Of 8,227 patients with stage II endometrial cancer, the mean age was 62 years, and whites, blacks, Hispanics, Asians, and American Indians constituted 78.4%, 10.4%, 6.9%, 2.6%, and 0.3% of the population, respectively. Of all patients, 43.6%, 15.0%, and 41.4% underwent OH, LH, and RH, respectively. Of all tumors, 94.9% were of endometrioid histology, 3.9% serous, 1.2% clear cell, and 3.3% carcinosarcoma. Mean tumor size was 5.3 cm with OH, 4.4 cm with LH, and 4.2 cm with RH ($P < 0.001$). Positive margins were noted in 3.0%, 2.7%, and 1.9% with OH, LH, and RH, respectively ($P = 0.032$). There were no differences in rate of radiation therapy (mean 37.2% of patients); however, 19.6%, 14.0%, and 15.2% of OH, LH, and RH received chemotherapy, respectively ($P < 0.001$). Overall survival with OH was 80.9%; with LH, 86.0%; and RH, 88.8% ($P < 0.03$). The proportion of RH increased yearly from 28.6% to 38.3% to 47.1% to 51.6% with a corresponding decrease in OH from 56.9% to 47.6% to 37.9% to 32.3%. LH remained stable over time from 14.5% to 14.1% to 15.1% to 16.2%. The use of RH was significantly higher in whites compared to blacks and Asians at 43.0% versus 30.4% and 34.4% ($P < 0.001$), respectively. Furthermore, the use of RH was highest in those with private insurance (44.9% vs 27.6% uninsured, 27.3% Medicaid, 41.4% Medicare, or 40.6% other government fund, $P < 0.001$), those with further distance traveled (mean 34.5 miles vs 30.6 miles for OH and 30.6 miles for LH, $P < 0.001$), and those treated at an integrated network cancer program (49.4% vs 17.9% community program, 42.4% comprehensive community program, or 41.0% academic program, $P < 0.001$).

Conclusion: The use of minimally invasive surgery for uterine cancer has increased over time. Black patients, those living a greater distance from a surgery center, and patients receiving care from community centers were less likely to have robotic surgery. There was improved survival with minimally invasive surgery compared to open surgery in stage II uterine cancers.
Objective: To investigate disparities in gynecologic oncologists’ ordering of immunohistochemistry (IHC) testing in women with endometrial cancer (EC).

Method: A retrospective study of all EC cases from an integrated health care system with a regional guideline to perform IHC testing for all women with EC younger than 60 years and with clinical risk factors older than 60 years. However, IHC testing is physician-ordered. There were 1,399 eligible cases of EC between January 2015 and December 2016. IHC testing, demographics, and tumor characteristics were reviewed, and patients were stratified by age and race. Categorical variables were reported using frequencies and proportions, and associations were tested with χ² tests or Fisher exact test. Multivariate regression was performed adjusting for covariates such as patient age, race/ethnicity, histology, and personal or family history of Lynch syndrome (LS) cancers to identify factors associated with decision to perform IHC testing. Odds ratios (ORs) with Wald 95% CIs and corresponding P values were reported.

Results: Of the 1,399 EC cases, 544 (39%) women were older than 60 years. Of these women, only 186 (34%) had IHC; 358 (66%) did not. This group consisted of 49% white, 22% Asian, 17% Hispanic, 9% black, and 3% other women. There were 855 (61%) cases of EC in women 60 years and older, and 95 (11%) had IHC and 760 (89%) did not. In this age group, 68% of women were white, 12% Asian, 9% Hispanic, 8% black, and 5% other. Overall, significant factors associated with IHC test performance were age younger than 60 years, race, BMI, tumor grade, endometrioid histology, hypertension, diabetes, personal history of LS cancer, and family history of LS cancers. In the multivariate analysis, while controlling for other factors, the odds of getting IHC testing for Asian women was 1.58 times the odds of getting tested for white women (95% CI 1.07-2.34, P = 0.02), and the odds of getting tested for white women was 2.26 times the odds of getting testing for black women (95% CI 1.22-0.90, P = 0.025). See Figure 1.

Conclusion: Despite a guideline to order IHC testing for all women with endometrial cancer younger than 60 years, rates of testing were low with significant racial and other disparities. This finding highlights the benefit of an automated IHC system, regardless of the policy for age-based or universal testing.

Table 1. Factors Associated with Decision to Perform IHC Testing

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, &gt;=30 vs &lt;30</td>
<td>0.715</td>
<td>(0.523-0.976)</td>
<td>0.035</td>
</tr>
<tr>
<td>Grade, 1 vs &gt;1</td>
<td>1.562</td>
<td>(1.126-2.167)</td>
<td>0.008</td>
</tr>
<tr>
<td>Histology, Endometrioid vs Other</td>
<td>2.159</td>
<td>(1.385-3.367)</td>
<td>0.001</td>
</tr>
<tr>
<td>Prior Lynch Cancer, Yes vs No</td>
<td>1.541</td>
<td>(1.082-2.194)</td>
<td>0.017</td>
</tr>
<tr>
<td>Relatives with Lynch Syndrome Cancer, Yes vs No</td>
<td>1.667</td>
<td>(1.027-2.705)</td>
<td>0.039</td>
</tr>
<tr>
<td>Age Group, &gt;=60 vs &lt;60</td>
<td>0.259</td>
<td>(0.19-0.353)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes, Yes vs No</td>
<td>1.579</td>
<td>(1.124-2.219)</td>
<td>0.009</td>
</tr>
<tr>
<td>Hypertension, Yes vs No</td>
<td>0.621</td>
<td>(0.455-0.847)</td>
<td>0.003</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian vs White</td>
<td>1.58</td>
<td>(1.068-2.337)</td>
<td>0.022</td>
</tr>
<tr>
<td>Black vs White</td>
<td>0.443</td>
<td>(0.217-0.902)</td>
<td>0.025</td>
</tr>
<tr>
<td>Hispanic vs White</td>
<td>1.114</td>
<td>(0.723-1.718)</td>
<td>0.625</td>
</tr>
<tr>
<td>Other vs White</td>
<td>1.785</td>
<td>(0.899-3.546)</td>
<td>0.098</td>
</tr>
</tbody>
</table>
1434 - Poster Session
Can we use ascites cytology to diagnose advanced ovarian cancer prior to neoadjuvant chemotherapy?
S. Baransi, L. Gortzak-Uzan, A. Aizic, I. Laskov, N. Michaan and D. Grisaru. Lis Maternity Hospital - Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Objective: Ascites is a common finding in both malignant and benign conditions. We sought to evaluate the feasibility of detecting malignant epithelial cells in ascites fluid obtained by paracentesis, and to determine whether ascites cytology can replace diagnostic tissue biopsy for patients with advanced ovarian cancer.

Method: All samples of ascites fluid sent for cytological evaluation at a tertiary institution between 2010 and 2015 were compared to available final histology of the diagnostic biopsy.

Results: A total of 1,667 samples of ascites were collected, of which 883 also had diagnostic tissue biopsy findings. The cytological findings were concordant with the final histology in 562 of those 883 (63.5%). Two-hundred sixty-four samples were positive for malignant epithelial cells, of which 124 were further analyzed with immunohistochemical staining. Of the 81 final epithelial ovarian cancer pathology specimens, 77 (95%) had an immunohistochemistry profile specific for ovarian origin. There were 298 samples that were negative for malignancy in both the ascites fluid and the final histology, and there was disagreement between cytology and final histology in 321 samples. No case had positive cytology and negative final histology (i.e., no false-positive results). The sensitivity of peritoneal cytology was 45%, specificity 100%, positive predictive value 100%, and negative predictive value 84%.

Conclusion: Ascites cytology has a high positive predictive value for the presence of epithelial ovarian malignancy. Neoadjuvant chemotherapy can be prescribed based on paracentesis evaluations. Immunohistochemistry is an important tool for assessment of the site of origin of a malignancy.

1435 - Poster Session
Examining the utility of magnetic resonance imaging compared with physical exam in cervical cancer staging
aUniversity of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, bNew York Medical College, Valhalla, NY, USA, cUniversity of Miami, Sylvester Cancer Center, Miami, FL, USA

Objective: In an age of increasing scrutiny over the utilization of health care resources, it is imperative to judiciously select diagnostic modalities. Our practice setting includes a diverse, multiracial population at a safety net hospital (SNH) and a university-based cancer center (CC). Our objective was to determine whether use of pelvic magnetic resonance imaging (MRI) versus examination under anesthesia (EUA) as primary staging modality was associated with recurrence risk and RFS.

Method: An institutional database of cervical cancer patients treated within either the SNH or CC from December 2012 to September 2017 was included. Demographic data were analyzed using χ2 or Fisher exact test. Logistic regression was used to determine associations between clinical variables and recurrence. Cox proportional hazards models were used to determine associations with clinical variables and RFS. Institutional review board approval was obtained, and P < 0.05 was considered statistically significant.

Results: The cohort included 102 patients: 62 patients treated at the SNH and 40 patients at the CC. The population was 96.8% and 82.5% non-white at the SNH and the CC, respectively, with over half of the population at each hospital being Hispanic; 88.7% of SNH and 100% of CC patients were advanced-stage (nonsurgical) at diagnosis. Only 16.6% of SNH patients underwent pelvic MRI compared with 70% of CC patients (P < 0.001). EUA was performed in 51.6% of SNH patients and in 20% of CC patients (P = 0.001). Fourteen (23%) patients at the SNH recurred compared with 11 (28%) at the CC (P = 0.57). Recurrence was not associated with EUA (OR = 2.00, P = 0.14) or MRI (OR = 0.74, P = 0.53). Advanced stage (III or IV) at diagnosis was the only variable associated with RFS (HR = 3.02, P = 0.02). Use of pelvic MRI (HR = 1.14, P = 0.76) and EUA (HR = 0.78, P = 0.55) had no association with RFS.

Conclusion: In our population, the modality used to complete a patient’s primary evaluation was not associated with recurrence risk or RFS. Our results suggest that treatment delays may be avoidable by forgoing pelvic MRI at diagnosis without adversely affecting outcomes.
Racial disparities in surgical management of ovarian cancer

A. Grubbs, S.M. Folsom, A.L. Alexander and E.L. Barber. Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Objective: The objective of this study was to determine whether racial disparities exist in rates of surgical management and rates of optimal debulking procedures for ovarian cancer.

Method: We examined women with stage III–IV epithelial ovarian cancer recorded in the National Cancer Data Base from 2004 to 2016 who were candidates for surgical debulking, either primary or interval. Our primary exposure was self-reported race, and our primary outcomes were undergoing debulking surgery and undergoing an optimal debulking. Bivariate tests and multivariate logistic regression were used to examine unadjusted and adjusted associations.

Results: We identified 31,997 women who were candidates for debulking surgery; 63.2% (20,211) underwent a debulking procedure. Of the women who underwent a debulking procedure, 75.2% (15,210) were classified as being optimally debulked (R0 or R1 resection). White patients were more likely to undergo a debulking procedure (65%) than black patients (52%, \( P < 0.001 \)). White patients were also more likely to have an optimal debulking procedure (76%) than black patients (70%, \( P < 0.001 \)). Asian patients were more likely to both have a debulking procedure (69%) and an optimal debulking procedure (77%) than black patients (\( P < 0.001 \) and \( P = 0.0012 \), respectively). There was no difference in rates of surgery or optimal debulking between white and Asian patients. After adjustment for age, Charlson comorbidity index, facility type, facility location, insurance status, year of diagnosis, histology, grade, and stage, black patients still had decreased odds of undergoing a debulking procedure (aOR = 0.72, 95% CI 0.64–0.80) and undergoing an optimal debulking (aOR = 0.77, 95% CI 0.68–0.87) compared with white patients.

Conclusion: Racial disparities exist in access to adequate surgical management for women with ovarian cancer. Black women have the lowest rates of undergoing either a debulking procedure or an optimal debulking procedure. A lack of appropriate access to surgical care for minorities may contribute to disparities in surgical and oncologic outcomes for ovarian cancer.

The effect of the Affordable Care Act on genetic testing patterns and outcomes for inheritable cancer syndromes: A single institution experience

aNew York-Presbyterian Hospital/Weill Cornell Medical College, New York, NY, USA, bWeill Cornell Medical College, New York, NY, USA, cNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, dWeill Cornell Medicine, New York, NY, USA

Objective: National guidelines recommend that genetic testing be offered to women at increased risk for deleterious mutations. We sought to determine the effect of insurance status on genetic testing patterns and clinical outcomes after the expansion of health insurance through the Affordable Care Act (ACA) in New York state.

Method: Insurance status and patterns of genetic testing at the hereditary breast and ovarian cancer center at a single institution between January 1, 2013, and December 31, 2016 in New York were reviewed. Insurance status was characterized and confirmed as private, Medicare, Medicaid, and uninsured. Comparisons among insurance status, testing type, and clinical outcomes based on genetic testing results were evaluated before and after January 1, 2014, which was utilized as a timeframe to allow for incorporation of health care expansion in New York.

Results: A total of 1,864 patients met with genetic counselors; 1,535 patients met inclusion criteria. Study cohort demographics are shown in Table 1. After 2014, significant increases in multigene panel testing were observed across all insurance types (\( P = 0.01 \); private, 7.9% vs 42.9%; Medicaid, 11.1% vs 32.2%; Medicare, 2.6% vs 33.2%; uninsured, 3.5% vs 30.8%). This increase was most significant among patients with private insurance and Medicaid plans (\( P < 0.001 \)), while the number of uninsured patients decreased after 2014 (Table 1, \( P < 0.001 \)). The commensurate rise in the number of patients with private and Medicaid insurance over this time period was from health insurance plan exchanges through the ACA (\( n = 127, P < 0.001 \)), the majority of which were considered to be Medicaid plans (\( n = 102, 80.3% \)). The detection of variants of uncertain significance (VUS) increased significantly after 2014, which correlated with an increase in panel testing (\( P < 0.001 \)), but the clinical management of patients with VUS remained unchanged (\( P = 0.50 \)).
Conclusion: Since expansion of health insurance though ACA, a significant increase in genetic testing was seen among patients with private insurance as primary coverage. With insurance expansion, more cost-effective testing platforms, and improved access to comprehensive genetic testing for all patients, cost and insurance status should not be obstacles for genetic testing.

Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2013 (n=304)</th>
<th>2014-2016 (n=1370)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at testing (mean, range)</td>
<td>52.6 (23, 94)</td>
<td>51.0 (18, 97)</td>
<td>0.09</td>
</tr>
<tr>
<td>Age at testing</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;45 years</td>
<td>102 (33.6)</td>
<td>505 (36.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>45-64 years</td>
<td>123 (40.7)</td>
<td>596 (43.5)</td>
<td></td>
</tr>
<tr>
<td>65+ years</td>
<td>79 (26.0)</td>
<td>269 (19.6)</td>
<td></td>
</tr>
<tr>
<td>Insurance status</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Private</td>
<td>190 (62.5)</td>
<td>924 (67.4)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>9 (3.0)</td>
<td>59 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>76 (25.0)</td>
<td>221 (16.1)</td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>29 (9.5)</td>
<td>39 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Total ACA</td>
<td>N/A</td>
<td>127 (9.3)</td>
<td></td>
</tr>
<tr>
<td>ACA – Medicaid plan</td>
<td>N/A</td>
<td>102 (7.4)</td>
<td></td>
</tr>
<tr>
<td>ACA – Low-income plan</td>
<td>N/A</td>
<td>25 (1.8)</td>
<td></td>
</tr>
<tr>
<td>Testing Type</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>285 (93.8)</td>
<td>812 (59.4)</td>
<td></td>
</tr>
<tr>
<td>Panel</td>
<td>19 (6.3)</td>
<td>554 (40.6)</td>
<td></td>
</tr>
</tbody>
</table>

1438 - Poster Session
Ovarian cancer knowledge and awareness: What does the public really know?

Objective: Our aim was to assess the public knowledge and awareness regarding ovarian cancer (OC) using a state-wide survey.

Method: The 2018 Empire State Poll was the 16th annual survey of New York state residents older than 18 years, conducted by the Survey Research Institute of Cornell University from February to April 2018. It is a compilation study of community, economic, and social science questions submitted by academic researchers. We submitted 5 questions regarding OC public awareness. Appropriate statistical tests were used for analysis.

Results: A total of 800 residents completed the survey. The median age was 48 years (range 18–94 years); 50% were female; 47% were married; and 64% identified as white. Responders were from 51/62 New York counties, 64% from urban areas and 50% from upstate. Seventy percent reported some college education or higher, and 39% reported a household income >$75,000/year. Sixty-seven percent recognized family history as the most significant risk factor for OC. Responders of Hispanic ethnicity (OR = 1.64, 95% CI 1.04–2.58) or black race (OR = 1.62, 95% CI 1.08–2.43) were more likely to incorrectly identify this risk factor, while females were less likely to choose an incorrect risk factor (OR = 0.57, 95% CI 0.42–0.79). Eight percent recognized there is no effective screening method for OC, whereas 61% stated ultrasounds and Pap smears were appropriate screening methods. Married respondents were more likely to report an incorrect method (OR = 1.80, 95% CI 1.06–3.06). Seventy-six percent knew at least 1 sign or symptom of OC. Twenty-two percent correctly identified the teal color as the ribbon for OC awareness. Nineteen percent reported previous exposure to an OC education/awareness campaign. Female respondents (OR = 2.44, 95% CI 1.67–3.56) and those in upstate New York (OR =1.58, 95% CI 1.09–2.29) were more likely to report exposure to OC educational campaigns, whereas those older than 48 years were less likely (OR = 0.65, 95% CI 0.45–0.94).

Conclusion: We identified specific knowledge gaps that vary between culturally diverse populations. Misunderstanding OC risk factors and screening can delay diagnosis and access to appropriate care. Most of those surveyed report no prior exposure to any OC educational campaign, particularly older respondents and those living in downstate New York. These data were
1439 - Poster Session
Undifferentiated endometrial adenocarcinoma: Treatment and characteristics of a rare disease
E. Landers, H. Chang, C. Walsh, A.J. Li, I. Cass, B.Y. Karlan, M. Kamrava and B.J. Rimel. Cedars-Sinai Medical Center, Los Angeles, CA, USA

Objective: Undifferentiated endometrial adenocarcinoma (UEC) is a rare histological subtype of endometrial cancers with aggressive behavior; however, data on the treatment and outcomes for these tumors are limited. We sought to characterize treatments utilized and survival outcomes in patients diagnosed with UECs.

Method: A retrospective chart review was performed to identify patients with at least 15% histologically confirmed UEC who were treated at our institution. Patients were excluded if serous histology was also present at >15%. Patient demographics, adjuvant treatments, recurrence, and survival data were obtained. Data were analyzed with descriptive statistics.

Results: Thirteen patients were identified between 2012 and 2017. Eight patients (61.5%) had stage IA disease, and five (38.5%) had stage IB–IVB disease. Lymphadenectomy was performed in 85% of patients, although nodal metastasis was only demonstrated in 1 of 11. Lymphovascular space invasion was present in 8 of 13 patients and in 100% of those with stage IB disease or higher. Percentage of tumor comprising undifferentiated carcinoma and tumor size did not appear to effect outcomes. Eight patients were treated with both chemotherapy and radiation, 2 with chemotherapy alone, and 1 with vaginal brachytherapy alone, and 2 received no adjuvant therapy. Patients with stage IA disease receiving primary carboplatin and paclitaxel chemotherapy received a maximum of 3 cycles, while patients with stage IB or higher disease were treated with 6 or more cycles and all received chemotherapy. There were no recurrences in patients with stage IA disease, regardless of adjuvant therapy; however, distant recurrences were detected in 80% of those with stage IB-IVB disease. The only case of a vaginal apex recurrence was in a patient with advanced disease who did not receive primary pelvic radiation.

Conclusion: Patients with stage IA UEC have an excellent prognosis with low risk of recurrence, independent of adjuvant therapy administered. Patients with stage IB disease or higher appear to have a significant risk of disease recurrence, and further studies are required to help determine the optimal adjuvant treatment for this group. Pelvic radiation therapy appears to reduce the incidence of vaginal cuff recurrence.

1440 - Poster Session
Population substructure may influence validation results of cancer genomics studies with TCGA datasets
A.M. Newtsona, M.D. Millerb, E. Devor, E. Salinasb, M.J. Goodhearta, K.K. Lesliea and J. Gonzalez-Bosquetb. aUniversity of Iowa Hospitals and Clinics, Iowa City, IA, USA, bCompass Oncology: The Northwest Cancer Specialists, Portland, OR, USA

Objective: We hypothesize that tumor samples derived from patients from different subpopulations may have different genetic backgrounds, and this different ancestry or admixture may interfere with validation and generalizability of genomic studies. Our goal was to compare the subpopulation structure (admixture) from The Cancer Genome Atlas (TCGA) patients with the admixture from a midwestern academic medical center group of patients.

Method: We compared two groups of patients, 1 group from TCGA, including RNA-sequencing data, from 395 endometrioid endometrial (EEC) cancer patient and 351 high-grade serous ovarian cancer (HGSC) patients. The other group (cases) included 122 patients with tumor samples stored in our institution's biobank. RNA was extracted and sequenced from these samples, including 62 EEC and 50 HGSC. Genotype was inferred and imputed from RNAseq alignments using a combination of software packages: (1) samtools, vctools, and PLINK for genotype extraction and filtering and (2) BEAGLE for genotype imputation. Both groups were analyzed in an identical fashion. Ancestry, based on subpopulation structure analysis, was performed using 2 different software packages. In the STRUCTURE package, the optimal number of K (or subpopulations) was determined using the Evanno DK method. In the ADMIXTURE package, the “best fit” model was determined based on the K that exhibited a low cross-validation error compared with other values. Subpopulation structure, or admixture, was compared between both groups using these two methods.

Results: Our analysis revealed 4–6 subpopulations within the TCGA dataset. When tumor types were stratified, the HGSC revealed 2–4 subpopulations, and the EEC revealed 2–3 subpopulations. In contrast, our institution revealed only 1
subpopulation (K = 1) for both methods and for all patients. When stratified by tumor type, EEC and HGSC, each tumor type had only 1 subpopulation.

**Conclusion:** Our study confirms part of our hypothesis by demonstrating differences in the genetic background, or admixture, between TCGA patients and our institution’s patients (cases). Admixture would have to be accounted for in genomic studies if we want them to be applicable to a broader population.

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**1441 - Poster Session**

**Racial disparities in women with stage IIIC and IV epithelial ovarian cancer receiving neoadjuvant chemotherapy versus primary debulking surgery: A National Cancer Database study**

G.T. Whitmore, A.A. Ramzan, J. Sheeder and S.R. Guntupalli. *University of Colorado Denver, Denver, CO, USA, bUniversity of Colorado Denver, Aurora, CO, USA*

**Objective:** Our objective is to use data from the National Cancer Data Base (NCDB) to determine whether African-American and Hispanic women are more likely to receive neoadjuvant chemotherapy (NACT) than primary debulking surgery (PDS), when compared to their white counterparts, since much-debated trials have shown that NACT was not inferior to PDS.

**Method:** A retrospective cohort study was performed using data originating between the years of 2010 and 2014 from women with stage IIIC or IV epithelial ovarian cancer. Only women of white, African-American, and Hispanic ethnicities were included, and all individuals were identified to have received either NACT or PDS. Descriptive statistics were computed, and continuous variables were assessed for normality. Groups were compared using ANOVA or nonparametric medians tests for continuous variables, and χ² tests were used for dichotomous or categorical variables. A logistic regression was then used to identify predictors of treatment. A P value of 0.05 was identified to be statistically significant.

**Results:** A total of 19,889 women with stage IIIC and IV epithelial ovarian cancer were identified to have received NACT or PDS and identified themselves as white, African-American, or Hispanic. A total of 15,024 (75.5%) were treated with PDS, while 4,865 women (24.5%) were treated with NACT. Of those treated with NACT, 24.5% were white, 27.0% were African-American, and 22.1% were Hispanic (P = 0.005), with an adjusted OR = 1.308 (95% CI 1.120–1.528). Although 30-day mortality rates did not vary significantly among the three groups (P = 0.386), the 90-day mortality rates were significantly different for white, African-American, and Hispanic women (2.0% vs 2.9% vs 1.6%, respectively, P = 0.013). When comparing NACT to PDS, the 30-day and 90-day mortality rates were highest in the NACT group (1.1% vs 0.2%, P < 0.001 and 2.7% vs 1.9%, P < 0.001).

**Conclusion:** NACT is being used in almost 25% of women with stage IIIC and IV epithelial ovarian cancer, but this treatment course is associated with worse 30-day and 90-day mortality rates. Evidence suggests that being African-American is a predictor of receiving NACT.

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**1442 - Poster Session**

**Racial and ethnic disparities among patients with low-grade serous ovarian carcinoma**

J. Siemon, S. George, M. Huang, B.M. Slomovitz, J.M. Pearson and M.P. Schlumbrecht. *University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA*

**Objective:** Low-grade serous ovarian carcinoma (LGSC) is a rare subtype of ovarian cancer with a unique disease course. Our objective was to evaluate the effect of race and ethnicity on treatment outcomes in this disease.

**Method:** Data from the National Cancer Data Base between 2004 and 2015 were evaluated for women with LGSC. The evaluated data included women with invasive, grade 1, serous carcinoma of the ovary and peritoneum. χ² analysis was used to identify differences in sociodemographic factors and treatment outcomes based on race and ethnicity. Cox proportional hazards modeling was used to calculate hazard ratios for OS. Statistical significance was set at P < 0.05.

**Results:** There were 4,477 women with LGSC; 88.5% of patients were white, 7.7% black, 5.7% Hispanic, and 87.4% non-Hispanic. Compared with white patients, blacks were diagnosed at a younger age (52.0 vs 56.6 years, P < 0.01), were more likely to be treated at an academic center (61.5% vs 54.2%, P = 0.02), and lived closer to the treatment facility (24.8 vs 37.0 miles, P = 0.03). Compared to non-Hispanics, Hispanic women were younger (50.0 vs 56.5 years, P < 0.01), were more likely to be treated at academic centers (65.4% vs 54.6%, P < 0.01), and lived closer to the treating facility (23.9 vs 37.5 miles, P = 0.04). Blacks were more likely than whites to have government insurance (45.1% vs 39.1%, P = 0.03); Hispanics were more likely
than non-Hispanics to be uninsured (17.6% vs 3.6%, P < 0.01). Although there was no difference in stage distribution by race, blacks were less likely to receive chemotherapy than whites (64.6% vs 73.2%, P < 0.01). Hispanics were less likely to receive chemotherapy than non-Hispanics (64.6% vs 72.8%, P < 0.01), even though more non-Hispanic women were diagnosed at an advanced stage (67.1% vs 58%, P < 0.01). Race/ethnicity was not predictive of OS, while older age (HR = 1.02, 95% CI 1.01–1.03, P < 0.01), advanced stage at diagnosis (HR = 3.14, 95% CI 2.54–3.87, P < 0.01), and government insurance (HR = 1.56, 1.32–1.85, P < 0.01) were all independently associated with worse OS.

**Conclusion:** LGSC is uncommon in minorities. Significant differences exist in the clinical characteristics and treatment approaches based on race and ethnicity in this subset of women, but they do not appear to affect OS.

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**1443 - Poster Session**

**National trends in demographics and diagnosis of adenocarcinoma of the cervix, 2004-2015**

A.J.B. Smith*, A.L. Beavis+, A.F. Rositch+ and K. Levinson#. *Johns Hopkins School of Medicine, Baltimore, MD, USA, #Johns Hopkins Hospital, Baltimore, MD, USA

**Objective:** The aims of this study are to examine the trends in demographics and diagnosis of adenocarcinoma (AdC) of the cervix in the last decade and compare trends to squamous cell carcinoma (SCC) of the cervix.

**Method:** We performed a retrospective study of patients with AdC and SCC from 2004 to 2015 in the National Cancer Data Base. We used log binomial regression to evaluate trends in histology, demographics, and stage over time. We stratified by age and race and included patient (insurance status, income, high school education, urban/rural, distance traveled for care, Charlson comorbidity score), and hospital characteristics (region, academic center) as covariates.

**Results:** There were 108,341 patients identified: 17,277 (15.9%) with AdC and 91,064 (84.1%) with SCC. The proportion of AdC increased from 14.7% in 2004 to 16.7% in 2015 (P < 0.001) among all age groups and across ethnicities (**Figure 1**). Compared to SCC, women with AdC were younger (47% vs 39% diagnosed by age 45 years, P < 0.001) and more often diagnosed at stage IA1–IB1 compared to later stages (47.5% vs 30.8%, P < 0.001). While women with AdC were overall more likely to be white, privately insured, and of higher income and education levels (P < 0.001), African-American women, publicly insured women, and those older than 65 years were more likely to be diagnosed with metastatic disease, both within AdC (IRR, 1.36, 95% CI 1.12–1.65; 1.51, 95% CI 1.27–1.81; and 1.87, 95% CI 1.61–2.17; respectively, P = 0.002 for race and P < 0.001 for publicly insured and age) and when compared to SCC (IRR, 1.08, 95% CI 1.00–1.17; 1.16, 95% CI 1.08–1.24; and 1.29, 95% CI 1.22–1.37, respectively) (P = 0.04 for race and P < 0.001 for publicly insured and age).

**Conclusion:** Over the past decade, the proportion of women with cervical AdC has increased. While almost half of cases are diagnosed by age 45 years, significant age and race disparities remain with these populations more likely to be diagnosed with metastatic disease. These findings may have implications for future screening and treatment strategies, especially given the increasing rates of cervical adenocarcinoma.

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**Fig. 1.** Trends in Adenocarcinoma of the Cervix compared to Squamous Cell, 2004-2015
Cardiovascular comorbidities and risk of ovarian carcinoma among African American women in the African American cancer epidemiology study (AACES)

J.N. Staples, L.C. Peres, F. Camacho, A.J. Alberg, E. Bandera, J. Barnholtz-Sloan, M.L. Bondy, M.L. Cote, E. Funkhouser, P.G. Moorman, E.S. Peteri, A.G. Schwartz, P.D. Terry and J.M. Schildkraut. aUniversity of Virginia, Charlottesville, VA, USA, bMoffitt Cancer Center-University of South Florida, Tampa, FL, USA, cMedical University of South Carolina, Charleston, SC, USA, dUMDNJ-The Cancer Institute of New Jersey, New Brunswick, NJ, USA, eCase Western Reserve - MacDonald Women’s Hospital, Cleveland, OH, USA, fBaylor College of Medicine, Houston, TX, USA, gKarmanos Cancer Institute/Wayne State University, Detroit, MI, USA, hUniversity of Alabama at Birmingham, Birmingham, AL, USA, iDuke University School of Medicine, Durham, NC, USA, jWoman’s Hospital, LSU Health Sciences Center, Baton Rouge, LA, USA, kWayne State University, Detroit, MI, USA, lUniversity of Tennessee Health Science Center, Memphis, TN, USA

Objective: Studies that have examined the association between cardiovascular comorbid conditions and epithelial ovarian cancer (EOC) have yielded inconsistent results. It remains unknown whether cardiometabolic disease is associated with EOC in African-American women, who generally have a higher prevalence of cardiovascular disease and lower risk of EOC, yet poorer survival than European-American women. Here, we estimate the effect of cardiovascular comorbid conditions and EOC risk among African-American women.

Method: Data were available from 593 ovarian carcinoma patients and 752 controls enrolled in the African-American Cancer Epidemiology Study (AACES). During the baseline telephone questionnaire, participants were asked to self-report a history of hypertension, hyperlipidemia, and diabetes and any current medication use. The relationship between hypertension, hyperlipidemia, diabetes, and medications taken for these conditions was determined using multivariate logistic regression, with adjustment for appropriate confounders.

Results: While hypertension was associated with a 30% increased EOC risk (OR = 1.32, 95% CI 1.01–1.73), use of antihypertensive medications among hypertensive women was associated with a decreased risk compared to never users (OR = 0.43, 95% CI 0.28–0.66). In particular, use of diuretics, angiotensin receptor blockers, and ace inhibitors were individually associated with a decreased risk (OR = 0.52, 95% CI 0.37–0.72; OR = 0.50, 95% CI 0.34–0.74; and OR = 0.57, 95% CI 0.40–0.82, respectively). Use of calcium channel blockers or beta blockers was not associated with risk. History of hyperlipidemia or diabetes was associated with a decreased EOC risk, with ORs of 0.61 (95% CI 0.47–0.80) and 0.67 (95% CI 0.49–0.91), respectively. In the overall sample, never use of any oral antidiabetes medication decreased the risk of EOC, particularly among the Biguanide drug class (OR = 0.63, 95% CI 0.43–0.93). Similarly, a decreased risk was observed for use of statins (OR = 0.55, 95% CI 0.41–0.73).

Conclusion: Our results provide evidence that hypertension is associated with an increased risk of EOC among African-American women, while diabetes and hyperlipidemia are associated with reduced risk, potentially driven by use of particular medications.

Disparities in extent of surgical cytoreduction for patients with ovarian cancer

D.H. Wong, A.L. Mardock, T. Laib, Y. Sanaiah, A.K. Sinno, P. Benharash and J.G. Cohen. aUCLA David Geffen School of Medicine, Los Angeles, CA, USA, bUniversity of California, Los Angeles, Los Angeles, CA, USA

Objective: To achieve complete surgical cytoreduction in ovarian cancer, tumor debulking with extended procedures beyond hysterectomy and bilateral salpingo-oophorectomy are often needed. This study examines disparities in patients receiving extended cytoreduction in relation to hospital surgical volume.

Method: A retrospective study using the National Inpatient Sample was conducted. Women diagnosed with ovarian, fallopian tube, or primary peritoneal cancer who underwent surgery involving oophorectomy from 2011 to 2015 were analyzed. Survey weights were applied to produce a national estimate. Surgical volume was determined by grouping hospitals into quartiles based on the number of cases they performed annually. Extended cytoreduction was defined as surgery of the colon, small intestine, liver, diaphragm, spleen, gastric resection, ileostomy, or colostomy. χ² univariate analysis identified differences in demographics between patients who underwent extended cytoreduction and those who did not. Logistic regression assessed independent predictors for receiving extended cytoreduction.
Results: Of the estimated 79,913 patients undergoing surgery for ovarian, fallopian tube, and primary peritoneal cancer, 49,288 (61.7%) received extended cytoreduction. Patients more likely to receive extended cytoreduction were the following: white (71.8% vs 69.9%, \( P = 0.031 \)), with private insurance (49.1% vs 40.8%, \( P < 0.01 \)), in higher income ZIP codes (56.6% vs 50.8%, \( P < 0.01 \)), and at hospitals with large bed size (70.6% vs 68.4%, \( P = 0.022 \)). Independent predictors of extended cytoreduction included non-zero Elixhauser comorbidity scores, higher income ZIP codes, and higher surgical volume (Table 1). Independent predictors for lack of extended cytoreduction included age 60+ years (Table 1), black (OR = 0.76, 95% CI 0.66–0.86, \( P < 0.01 \)) or Hispanic race (OR = 0.78, 95% CI 0.68–0.90, \( P < 0.01 \)), and Medicaid (OR = 0.79, 95% CI 0.70–0.89, \( P < 0.01 \)) or Medicare insurance (OR = 0.89, 95% CI 0.80–0.98, \( P = 0.022 \)).

Conclusion: Disparities exist for patients receiving extended cytoreduction. Patients who received care at hospitals with higher surgical volume were more likely to receive extended cytoreduction. When controlling for surgical volume, differences existed among race, insurance status, and lower income ZIP codes.

Table 1. Independent predictors of receiving extended surgical cytoreduction in patients with ovarian, fallopian tube, and primary peritoneal cancer.

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio [95% CI]</th>
<th>( P )-value</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
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<tr>
<td>60-69</td>
<td>0.82 [0.71–0.96]</td>
<td>0.013</td>
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<tr>
<td>70-79</td>
<td>0.69 [0.58–0.82]</td>
<td>&lt;0.001</td>
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<tr>
<td>80+</td>
<td>0.49 [0.40–0.60]</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Elixhauser comorbidity score</strong></td>
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<tr>
<td>1</td>
<td>1.57 [1.31–1.88]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>1.42 [1.20–1.69]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3+</td>
<td>1.18 [1.00–1.39]</td>
<td>0.049</td>
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<tr>
<td><strong>Race</strong></td>
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<tr>
<td>Black</td>
<td>0.76 [0.66–0.86]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.78 [0.68–0.90]</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Primary payer</strong></td>
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<tr>
<td>Medicaid</td>
<td>0.79 [0.70–0.89]</td>
<td>&lt;0.001</td>
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<tr>
<td>Medicare</td>
<td>0.89 [0.80–0.98]</td>
<td>0.022</td>
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<tr>
<td><strong>ZIP income quartile</strong></td>
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<tr>
<td>Q3</td>
<td>1.20 [1.09–1.33]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q4 (highest)</td>
<td>1.24 [1.11–1.38]</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Hospital geographic region</strong></td>
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<tr>
<td>Midwest</td>
<td>1.30 [1.12–1.50]</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Patient Disposition at Discharge</strong></td>
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<tr>
<td>Home Health</td>
<td>1.45 [1.29–1.62]</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Hospital ovarian cancer surgery volume quartile</strong></td>
<td></td>
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<tr>
<td>Q2</td>
<td>1.16 [1.05–1.29]</td>
<td>0.004</td>
</tr>
<tr>
<td>Q3</td>
<td>1.39 [1.24–1.56]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q4 (highest)</td>
<td>1.28 [1.12–1.47]</td>
<td>&lt;0.001</td>
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1446 - Poster Session
Race, incidence and treatment of gestational trophoblastic neoplasia in the United States: A National Cancer Database study from 2004 – 2014
E.J. Diver\*1, C.I. Liaob, M.T. Richardson\*1 and J.K. Chan\*1, \*Stanford University School of Medicine, Stanford, CA, USA, \#Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan, \&California Pacific and Palo Alto Medical Foundation/Sutter Health Institute, San Francisco, CA, USA

Objective: Gestational trophoblastic neoplasia (GTN) are the malignant sequelae of trophoblastic tissue related to abnormal conception. As these are rare tumors in the United States, the value of a collective large data experience in the National Cancer Data Base (NCDB) was assessed.
**Method:** The NCDB was queried 2004–2014 for all cases of women with malignant GTN. Clinical-pathologic, demographic, and survival outcomes data were collected. χ² tests, Cox regression, and Kaplan-Meier models were performed.

**Results:** Over this 11-year period, 1,019 women were identified encompassing all FIGO stages (stage I, 32%; stage II, 5.3%; stage III, 30%; stage IV, 18%; unknown, 15%). Five-year survival by stage was 98%, 90%, 93%, and 72%, respectively. Of the women for whom World Health Organization (WHO) risk score was known (n = 396), 51% were low risk and 49% high risk, with respective 5-year survival 97% and 91%, respectively. The cohort was 64% white, 23% black, 8% Asian/Pacific Islander, and 4% Native American/other/unknown. This represents a higher percentage of black women compared with U.S. Census data at 13.4%. Black women with GTN were represented disproportionately at the extremes of age (31% of 10–19-year-olds and 44% of 50–59, P = 0.003) and in the lowest income bracket (44% of <$38,000, P < 0.001), and were less likely to have a high school degree (P < 0.001). White women were more likely to be treated in New England, compared with black women in the East South Central, and Asian women in the Pacific region (P = 0.003). Race was not associated with chemotherapy, stage, or survival. Only 6 facilities reported treating an average of more than 1 patient per year, and 53% of the women treated were at a facility reporting only 1 treated patient over the 11-year period of the study. FIGO stage, WHO score, and age were all associated with survival. Race, education, urban/rural location, and insurance were not associated with survival.

**Conclusion:** GTN is rare in the United States, with fewer than 100 cases per year reported to the NCDB. Compared with U.S. demographics, black women seem to be overrepresented; this is a demographic not previously studied in depth in GTN. Outcomes are overall positive, with 5-year survival greater than 90% in stage I–III. Race or geographic location did not associate with survival.

**1447 - Poster Session**  
**Disease-related outcomes in morbidly obese endometrial cancer patients**  
K.K. Crean-Tate, M. Radeva, and M.M. AlHilli.  
*The Cleveland Clinic Foundation, Cleveland, OH, USA, Cleveland Clinic, Cleveland, OH, USA*

**Objective:** We sought to evaluate the impact of morbid obesity on disease outcomes in women with low-risk and high-risk endometrial cancer (EC).

**Method:** Patients diagnosed with EC from January 1, 2005, to December 30, 2015, were evaluated and stratified by BMI (< or ≥40 kg/m²) and risk of recurrence (low risk, LR, stage 1–2; low or moderate grade, <50% myometrial invasion and endometrioid type; high risk, HR, stage 3–4; high grade, >50% myometrial invasion, or nonendometrioid). Patient demographics, tumor characteristics, and treatment-related outcomes were reviewed. Pearson χ² test was used for categorical variables and ANOVA and Kruskal-Wallis for continuous factors. Analysis was performed using SAS.

**Results:** Out of 1,775 patients included in the study, 1,327 (74.8%) had a BMI <40 kg/m² and 448 (25.2%) were ≥40 kg/m². Patients with BMI ≥40 kg/m² were significantly younger (58.9 vs 64.2 years), more likely to have endometrioid histology (77.5% vs 67%), lower grade (52.5% vs 37.9%), earlier stage (78.5% vs 68.8% stage 1), myometrial invasion <50% (65.8% vs 50.3%), and lower LVSI (23.0% vs 35.5%). Stratified by risk group, LR patients with BMI ≥40 kg/m² were 39% of the study population and were more likely to be younger, of black race, and uninsured. Overall, 40% of LR patients underwent lymphadenectomy. Compared to those with BMI <40 kg/m², those with BMI ≥40 kg/m² in the LR group were significantly less likely to undergo lymphadenectomy (P < 0.0005). Within the HR group, lymphadenectomy was performed in 72% of patients, and those with BMI ≥40 kg/m² were significantly less likely to undergo lymphadenectomy (P < 0.004). There was no significant difference in risk or patterns of recurrence, disease-specific survival (DSS), or PFS between BMI ≥40 kg/m² and BMI <40 kg/m² patients when stratified by risk group. However, overall survival was significantly improved in morbidly obese patients, with HR = 0.52 (P = 0.02).

**Conclusion:** Morbid obesity is associated with favorable prognostic factors in patients with EC. When stratified by risk group, clinical and pathologic prognostic factors appear to be equivalent among patients with BMI <40 kg/m² and morbidly obese patients. Morbidly obese patients are less likely to undergo lymphadenectomy regardless of risk group. However, this does not appear to have a negative impact on risk of recurrence, DSS, PFS, or OS in patients with BMI >40 kg/m².

**1448 - Poster Session**  
**Readability of online patient education materials on gynecologic malignancies from major medical associations**
D. Samuel, N. Vilardo, S. Isani, and G.M. Gressel. Montefiore Medical Center, New York, NY, USA, Albert Einstein College of Medicine, New York, NY, USA, Montefiore Medical Center, Bronx, NY, USA

**Objective:** Patients are increasingly using online materials to learn about gynecologic cancer. Recent studies demonstrate that 85%–96% of patients with a gynecologic malignancy utilize the internet as a health resource. Providers can refer patients to educational materials produced by major medical associations available on their websites. However, patient educational materials (PEMs) published by professional organizations from other surgical specialties have been shown to be difficult to read for the average American. The National Institutes of Health (NIH) and American Medical Association (AMA) recommend that PEMs be written between a sixth- and eighth-grade reading level. In this study, we assess the readability of online PEMs on gynecologic cancer published by major medical associations.

**Method:** Seven national medical association websites with PEMs on gynecologic malignancy were surveyed: American College of Obstetricians and Gynecologists, Centers for Disease Control, Foundation for Women’s Cancer, National Cancer Institute, National Cervical Cancer Coalition, National Ovarian Cancer Coalition, and Society of Gynecologic Oncology. Online PEMs were identified and analyzed using 5 validated readability indices. One-way ANOVA and Tukey test were performed to detect differences in readability between publishers.

**Results:** Two hundred and thirty PEMs were included in this analysis. Mean readability grade levels with standard deviation were 11.3 (2.8) for Coleman-Liau index; 11.8 (3.2) for Flesch-Kincaid; 11.1 (1.2) for FORCAST formula; 12.5 (2.7) for Gunning Fog formula; 12.1 (2.6) for New Dale-Chall formula; and 13.5 (2.5) for SMOG formula. Overall, PEMs were written at a mean twelfth-grade reading level. Only 4.3% of articles were written at an eighth-grade reading level or below. ANOVA demonstrated a significant difference in readability between publishing associations (P < 0.01). PEMs from the Centers for Disease Control had a mean tenth-grade reading level and were significantly lower than all other organizations. PEMs from The Foundation for Women’s Cancer had a mean thirteenth-grade reading level and were significantly higher than most other organizations.

**Conclusion:** Gynecologic oncology PEMs available from major medical associations are written well above the recommended sixth- to eighth-grade reading level. Simplifying PEMs may improve patient understanding of their disease and facilitate physician-patient communication.

1449 - Poster Session
**National trends in the treatment and survival of adenocarcinoma of the cervix compared to squamous cell carcinoma, 2004-2015**
A.J.B. Smith, A.L. Beavis, A.F. Rositch, and K.L. Levinson. Johns Hopkins School of Medicine, Baltimore, MD, USA, Johns Hopkins Hospital, Baltimore, MD, USA

**Objective:** We sought to analyze trends in the treatment and survival of women with adenocarcinoma (AdC) of the cervix

**Method:** We performed a retrospective study of AdC from 2004 to 2015 in the National Cancer Data Base. We used log binomial regression for treatment trends (early-stage, IA1–IB1; locally advanced, IB2–IVA; and metastatic, IVB) over time. We evaluated differences in survival using Kaplan-Meier curves and a multivariate Cox proportional hazards model. We stratified by age and race and included patient (insurance status, income, high school education, urban/rural, distance traveled for care, Charlson comorbidity score) and hospital covariates (region, academic center).

**Results:** There were 14,829 women with AdC, 7,319 (49%) early-stage, 6,633 (45%) locally advanced, and 877 (6%) metastatic disease. For early-stage AdC, 82% received surgery alone; 7% surgery and radiation; 6% surgery and chemoradiation; 2% chemoradiation; 2% surgery and chemotherapy; and 1% radiation alone. For locally advanced AdC, 42% received concurrent chemoradiation; 20% surgery and chemoradiation; 15% surgery alone; 8% radiation alone; 6% surgery and radiation; 5% surgery and chemotherapy; and 2% chemotherapy. For metastatic AdC, 26% received chemotherapy alone; 16% surgery and chemoradiation; 15% surgery and chemotherapy; 15% radiation alone; 10% radiation alone; 8% surgery alone, and 9% no treatment. Median survival was 143 months (95% CI 142–144) for early-stage AdC; 87 months (95% CI 80–95) for locally advanced; and 14 months (95% CI 12–16) for metastatic disease (Figure 1). Survival increased over time for all stages (HR = 0.98, 95% CI 0.97–0.99). There were 2,257 (15%) women 65 years and older. Compared to women younger than 65 years, women 65 years and older were less likely to receive surgery for early-stage AdC (IRR = 0.79, 95% CI 0.73–0.85), chemoradiation for locally advanced AdC (IRR = 0.79, 95% CI 1.74.7–83.3), and chemotherapy for metastatic disease (IRR = 0.65, 95% CI 10.56–0.75). Stage-for-stage, survival was lower for women 65 years and older (HR = 2.51, 95% CI 2.32–2.72). The
majority of women with AdC were white (86%), 8.6% African-American, and 5.9% other races. While there was no significant difference in treatment by race, survival was lower stage-for-stage for African-American women compared to white women (HR = 1.51, 95% CI 1.36–1.68).

**Conclusion:** While survival has overall improved over time for women diagnosed with AdC, significant age and race disparities exist in treatment and survival.

![Fig. 1. Survival in Adenocarcinoma of the Cervix by Stage, 2004-2015](image)

**1450 - Poster Session**

**Factors influencing time interval between diagnosis and primary surgical management of endometrial cancer**

K.L. Wood¹, A.H. Bui², S. Alexander³, E.A. Howell⁴, V. Kolev⁵, S.V. Blank⁶,⁷ and M. Chadha⁸,

¹Icahn School of Medicine at Mount Sinai, New York, NY, USA, ²New York University School of Medicine, New York, NY, USA, ³Mount Sinai Beth Israel, New York, NY, USA

**Objective:** There are limited data on the prognostic significance of the time interval between diagnosis and primary surgery (Hyst) in endometrial cancer (EC). While the ideal interval for best clinical outcomes is not well defined, data suggest worse survival for women with intervals >6 weeks. The objective of this study is to evaluate the time interval between diagnosis and Hyst at our institution’s cancer center and further assess factors contributing to treatment delay.

**Method:** This is an Institutional Review Board-approved retrospective study of EC patients treated at our cancer center between January 2011 and July 2017. We identified 688 women who met study criteria. Clinical variables including age, race, insurance and socioeconomic status (SES), stage, histology, diagnosed elsewhere (outside referral), date of diagnosis, date of Hyst, and follow-up were recorded. We classified low SES if patients were from zip codes with >20% families below poverty level. A time interval >6 weeks between diagnosis and Hyst was scored as time delay. Univariate and multivariate logistic regression analyses were completed to evaluate outcomes and the impact of clinical factors on time interval between diagnosis and Hyst.

**Results:** Overall the median time interval between diagnosis and Hyst was 3.0 weeks (range <1–18 weeks). In 123 (17.9%) patients the interval was >6 weeks. On univariate analysis, the factors significantly associated with time delay were outside referral (P < 0.0001), Medicaid insurance (P = 0.0190), and low SES (P = 0.0157). On multivariate analysis, outside referral (OR
199

= 2.575, 95% CI 1.665–3.918) and Medicaid insurance (OR = 2.317, 95% CI 1.189–4.513) remained significant factors for time delay. See Table 1.

**Conclusion:** Identifying clinical and socioeconomic barriers contributing to variation in time-sensitive treatment for EC patients is important for cancer care. Improved understanding of such factors provides insight and opportunity to seek required support that advocates for timely cancer care for all.

**1451 - Poster Session**

**Pretreatment absolute neutrophil counts predict neutropenia-related events in patients undergoing first line chemotherapy in gynecologic malignancies**

R.K. Lee, S.A. Soyemi, M. Chen, M.J. Kanis and Y.C. Lee. aSUNY Downstate, Brooklyn, NY, USA, bSUNY-Downstate, Brooklyn, NY, USA, cSUNY Downstate Medical Center, Brooklyn, NY, USA

**Objective:** Grade 3–4 neutropenia is common in patients with gynecologic malignancy undergoing first-line chemotherapy. We aim to find variables that are predictive of neutropenic-related events including dose delays and reductions and febrile neutropenia.

**Method:** We retrospectively reviewed chemotherapy records for all patients undergoing neoadjuvant or adjuvant first-line chemotherapy, as well as chemo-naïve patients receiving first-line chemotherapy for recurrence between the years 2013 and 2017. Data including age, primary disease site, stage, BMI, histology, chemotherapy regimen, and laboratory variables from a complete blood count and a comprehensive chemistry prior to cycles 1 and 2 were collected. The variables were analyzed by logistic regression.

**Results:** A total of 144 patients were identified, 122 of whom received carboplatin AUC 5-6 and paclitaxel 175 mg/m². Twenty-three received 5 different regimens. There were 138 patients of African-American or Caribbean descent. A total of 53 patients experienced neutropenia-related events with 41 dose delays, 17 dose reductions, and 8 neutropenic fevers. An absolute neutrophil count (ANC) less than 3.1 prior to the first cycle of chemotherapy was a significant predictive factor ($P = 0.023$). In addition, a drop in neutrophil count from cycle 1 to cycle 2 was significant ($P = 0.013, OR 1.296$–$9.126$). Age, primary disease site, histology, stage, BMI, and other laboratory values were not significantly related to neutropenia events. See Tables 1, 2, and 3.

**Conclusion:** Although within normal limits for the laboratory reference range (1.5–8) and for chemotherapy administration, a low starting ANC is a significant risk factor for neutropenia-related events during first-line chemotherapy. Given that black race is associated with lower normal neutrophil count at baseline, proper patient counseling for prevention of neutropenic infections as well as a lower

<table>
<thead>
<tr>
<th>Table 1. Patient age, BMI, ANC</th>
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<tbody>
<tr>
<td><strong>Mean</strong></td>
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<tr>
<td>Age</td>
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<tr>
<td>BMI</td>
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<tr>
<td>ANC prior to cycle 1</td>
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<td>ANC prior to cycle 2</td>
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<tr>
<th>Table 2. Tumor site</th>
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<tr>
<td><strong>n</strong></td>
</tr>
<tr>
<td>Endometrial</td>
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<td>Ovary</td>
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<td>Sarcoma</td>
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<td>Cervix</td>
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<td>GTN</td>
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<th>Table 3. Chemotherapy regimens</th>
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<tr>
<td><strong>n</strong></td>
</tr>
<tr>
<td>Carboplatin/paclitaxel+/-bevacizumab</td>
</tr>
<tr>
<td>Gemcitabine/docetaxel+/-bevacizumab</td>
</tr>
<tr>
<td>Etoposide/cisplatin+/-bleomycin</td>
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<tr>
<td>Ifosfamide/paclitaxel</td>
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<tr>
<td>Cisplatin/ifosfamide</td>
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<td>EMACO</td>
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<td>VAC</td>
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threshold to implement granulocyte colony stimulating factors may be considered to avoid treatment disruptions. Further investigation is needed to validate this finding in a larger population, as well as its implication for clinical outcomes.

1452 - Poster Session
Racial and socioeconomic disparities in treatment and survival for women with advanced endometrial cancer
T. Orfanelli, N. Cohen, M.A. Schwartz, S.A. Tomita, V. Kolev, S.V. Blank and S. Cohen. Icahn School of Medicine at Mount Sinai, New York, NY, USA

Objective: National data have suggested that black women with advanced endometrial cancer (EC) have inferior survival and delivery of care when compared to non-Hispanic white women. The aim of our study was to assess for racial and socioeconomic disparities in patient care and survival between non-Hispanic white and black women with advanced EC treated in a high-volume center.

Method: A retrospective cohort of non-Hispanic white and black women undergoing primary treatment for advanced (stage III–IV) EC between January 1, 2006, and December 31, 2017, was identified through the institutional tumor registry. Other races, stage I/II EC as well as carcinosarcoma, sarcoma, or mixed tumors, were excluded. Demographic, socioeconomic, and clinical variables were collected. Primary endpoint was OS. Secondary analyses included assessing surgical management and adjuvant treatment. Survival analysis was performed using the Kaplan-Meier method and log rank test.

Results: Among 1,516 women undergoing primary treatment for EC at our institution during the specified time period, a total of 45 non-Hispanic white (64.3%) and 25 black (35.7%) women met inclusion criteria. Age, type of insurance, BMI, ASA, histology, and stage did not differ between groups; however, black women were more likely to be unmarried compared to non-Hispanic white (80% vs 48.9%, \( P = 0.01 \)). There was no difference in median OS between black and non-Hispanic white women (53.0 months, 95% CI 40.8–65.2, vs 37.0 months, 95% CI 28.0–45.9, respectively, \( P = 0.29 \)). Insurance and marital status were not associated with inferior survival independent of race. Black women had similar rates of minimal invasive surgery (39.1% vs 61.4%, \( P = 0.08 \)), optimal debulking surgery (92% vs 97.4%, \( P = 0.32 \)), staging lymphadenectomy (72.7% vs 90%, \( P = 0.14 \)), adjuvant chemotherapy (100% vs 88.6%, \( P = 0.08 \)), and radiation treatment (60% vs 56.8%, \( P = 0.79 \)) when compared to non-Hispanic white women.

Conclusion: In contrast to other population-based studies, no OS disparity according to race or other socioeconomic factors for non-Hispanic white and black women with advanced epithelial EC was noted in our study. Both groups were equally likely to undergo cytoreductive surgery, minimally invasive surgery, and standard-of-care adjuvant treatment. Treatment in a high-volume center appears to alleviate racial disparities of care in advanced EC.

1453 - Poster Session
Factors associated with the successful completion of randomized clinical trials in gynecological oncology
A. Swailesa, M. Guptab, S.P. Chauhanb, J. Kestersona and S. Wagnerb. aPenn State College of Medicine, Hershey, PA, USA, bUniversity of Texas Medical School at Houston, Houston, TX, USA

Objective: The aim of our review was to ascertain factors associated with the successful completion of a randomized control trial in gynecological oncology.

Method: As part of the FDA Amendments act of 2007, clinical trials were required to publish their results on clinicaltrials.gov beginning in 2008. This retrospective cohort study utilized data collected from the National Institutes of Health’s database on clinicaltrials.gov. Data were collected over a 5-year period (2009–2013). Utilizing the search terms under the National Institutes of Health recommended “Studies by Topics,” gynecological oncology studies were identified. Randomized control trials were selected based on intervention and randomization criteria. Elements were then compared with statistical analysis performed using SASS.

Results: A total of 1,031 gynecological oncology research studies were registered on clinicaltrials.gov, the majority of which (80%, 823) were interventional. Of the interventional studies, 284 (35%) were randomized control trials. As of September 1, 2018, just over half (150, 52%) of all randomized control trials were successfully completed (average length 43 months). Completed randomized control trials were more likely to be performed at centers outside the United States (\( P < 0.006 \)). Interventional drug and device trials were significantly less likely to be completed (\( P < 0.001 \)). While industry was more likely
to fund interventional trials than observational ones \((P < 0.001)\), there was no difference in funding sources for completed or not completed randomized control trials. See Table 1.

**Conclusion:** Prospective randomized trials are essential for establishing the standard of care in clinical medicine. They are, however, time-and resource-intensive. Herein we have identified factors associated with successful and timely completion of gynecologic oncology randomized clinical trials. Disconcertingly, only half of all randomized control trials that make it through the conception and design process to database registration are completed. This high failure rate suggests large hurdles are inhibiting the completion of gynecologic oncology research studies. Research into barriers of successful completion of randomized control trials is needed so that inhibitory factors can be mitigated.

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1454 - Poster Session

**Medical therapy for recurrent endometrial carcinoma following conventional platinum based cytotoxic chemotherapy**

J.D. St. Laurent\textsuperscript{a,b} and W.B. Growdon\textsuperscript{b,c}. \textsuperscript{aBrigham and Women's Hospital and Harvard Medical School, Boston, MA, USA, \textsuperscript{bMassachusetts General Hospital, Boston, MA, USA, \textsuperscript{cHarvard Medical School, Boston, MA, USA}

**Objective:** Recurrent endometrial cancer is a therapeutic challenge with few clear guidelines after primary platinum-based therapy. The objective of this investigation was to understand the practice patterns for recurrent and persistent endometrial cancer following conventional therapy.

**Method:** A multicenter review was conducted of all endometrial cancer cases from January 2008 through December 2015. Patient demographics, surgical characteristics, and medical therapy were collected for all patients who received adjuvant chemotherapy or developed recurrent disease. Recurrence and survival were correlated utilizing parametric and nonparametric testing. Survival was calculated utilizing the Kaplan-Meier and Cox proportional hazards methodologies.

**Results:** Of 2,363 women, 570 (24\%) presented with high-grade or nonendometrioid histology. Adjuvant carboplatin/paclitaxel (CP) was used in 413 cases (17\%) and associated with advanced-stage, nonendometrioid histology, and high-grade endometrioid histology (all \(P < 0.001\)). Recurrent disease was noted in 325 patients (14\%) following adjuvant CP 176 (54\%) and without adjuvant CP 149 (45\%). Multivariate analysis, controlling for stage, grade, and histology, revealed that adjuvant CP was associated with worse PFS (HR = 1.2, \(P < 0.001\)) and OS (HR = 1.2, \(P < 0.001\)). Chemotherapy treatment at recurrence (57\%) was associated with lower median OS (3.2 vs. 5.6, \(P < 0.001\)) compared to radiation (22\%, OS = 7.6 years) and surgery (7\%, OS = 7.5 years). Weekly paclitaxel (14\%) followed by trial enrollment (13\%) was the most common chemotherapy regimen. Less than 1\% of patients were rechallenged with CP. Median survival after recurrence was 1.4 years. Use of adjuvant CP was associated with a worse survival estimate on univariate analysis (1 vs. 2.3 years), although a multivariate model incorporating grade, stage, and histology revealed adjuvant CP to be associated with a lower risk of death after recurrence (HR = 0.45, \(P < 0.004\)). The number of chemotherapy lines was not significantly correlated with survival after recurrence. See Figure 1.

**Conclusion:** In this multicenter retrospective cohort, adjuvant CP was not associated with a protective effect on survival after recurrence. Importantly, this study highlights the heterogeneity of therapies after CP in endometrial cancer treatment, low clinical trial enrollment at recurrence, and the need for concerted efforts to improve outcomes for high-risk endometrial cancer.
Cervical, endometrial, and ovarian cancer patients with distant metastases: Most common location and outcomes


*University of California, Irvine, Irvine, CA, USA, *UCSD Rebecca and John Moores Cancer Center, La Jolla, CA, USA, *Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, *California Pacific & Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA

**Objective:** The aim of this study is to determine the location patterns of distant metastases and outcomes of cervical, endometrial, and ovarian cancer patients.

**Method:** Data were obtained from the Surveillance, Epidemiology and End Result database from 2010 to 2015 for patients with stage IV disease and single metastasis sites to lung, liver, bone, or brain. Analyses were performed using Kaplan–Meier and multivariate Cox proportional hazard methods.

**Results:** Of 3,036 patients included in this study, the median age was 63 (range 17–95) years; 42%, 40.2%, and 17.8% of patients had ovarian, uterine, and cervical cancers, respectively. Lung, liver, bone, and brain metastases were present in 51.5%, 35.5%, 10.9%, and 2.1% of patients, respectively. Of patients with ovarian cancer, 38.4% had lung metastases, 56.8% liver, 3.5% bone, and 1.3% brain, whereas patients with uterine cancer had 61.8%, 21.9%, 13.2%, and 3.1% and patients with cervical cancer had 59%, 15.5%, 23.3%, and 2.2%, respectively ($P < 0.0001$). Insured (other than Medicaid), Medicaid, and uninsured patients constituted 77.2%, 17.6%, and 5.2% of the sample, respectively, and 75.4%, 15.7%, 8.0%, and 0.9% were white, black, Asian, and Native American, respectively. The overall 5-year disease-specific survival was 18.9% for the group. Those with liver metastases had the best outcome with survival of 26.4% compared to 15.1% for lung, 12.9% for bone, and 6.2% for brain ($P < 0.0001$). Patients with ovarian, uterine, and cervical cancers had survival rates of 27.6%, 12.0%, and 12.0%, respectively ($P < 0.0001$). On multivariate analysis, later year of diagnosis (HR = 1.49, 95% CI 1.45–1.54, $p < 0.0001$), grade 3 disease (HR = 1.77, 95% CI 1.43–2.20, $P < 0.0001$), grade 4 disease (HR = 1.67, 95% CI 1.34–2.1, $P < 0.0001$), uterine disease (HR = 1.48, 95% CI 1.34–1.63, $P < 0.0001$), cervical disease (HR = 1.74, 95% CI 1.51–2.0, $P < 0.0001$), and lack of insurance (HR = 1.38, 95% CI 1.16–1.64, $P < 0.0001$) were independent predictors for poorer survival. Using lung metastatic site as reference, patients with brain metastases (HR = 1.48, 95% CI 1.12–1.95, $P < 0.01$) had worse outcomes. Race and age did not affect prognosis.

**Conclusion:** The location of distant metastases and outcomes in cervical, endometrial, and ovarian cancer patients differs. These results may have significant implications toward metastatic workup of these gynecologic cancers and drug treatments focused on treating the metastatic site.
Resection of parenchymal liver metastases in patients with uterine malignancies


**Objective:** Parenchymal liver resection for liver metastasis of uterine malignancies is not well studied. Only a few case series have been reported. The objective of our study was to evaluate the role of hepatectomy for liver metastasis of uterine origin.

**Method:** Patients who underwent a resection of parenchymal liver metastasis from uterine malignancies between 1993 and 2017 were identified from our database. Patients who underwent superficial liver resections only were excluded. Recurrence-free survival (RFS) and OS after liver resection were estimated using the Kaplan-Meier method. A Cox proportional hazards model was used to evaluate the independent association between the different clinicopathological factors and outcomes.

**Results:** A total of 34 patients who underwent parenchymal liver resections were identified. Of those, 20 patients had a diagnosis of uterine sarcoma (US), and 14 had a diagnosis of endometrial adenocarcinoma (EC). Twenty-three patients (68%) underwent liver resection as part of recurrent disease and 11 (32%) as part of initial treatment. Major grade 3–4 complications were identified in 7 patients (21%); in 3 patients (9%) complications were directly associated with the liver resection. One patient (3%) died within 90 days after hepatectomy due to progression of disease. After hepatectomy, median RFS (US, 4.5 months, 95% CI 2.5–6.5; EC, 10.7 months, 95% CI 0–22.1; P = 0.11) and OS (US, 30.6 months, 95% CI 18.6–42.6; EC, 30.1 months, 95% CI 0–67.4; P = 0.86) were not different between the 2 tumor types. The 3-year OS rate was 43% for US and 41% for EC. On univariate analysis metachronous disease and single liver metastasis were significantly associated with improved OS. On multivariate analysis only metachronous disease (P = 0.007) was an independent factor for improved survival.

**Conclusion:** Parenchymal resection of liver metastasis of uterine malignancies is associated with acceptable morbidity, mortality, and favorable outcomes. Hepatectomy should be considered in select patients with single lesions and metachronous disease.

African Breast Cancer—Disparities in Outcomes (ABC-DO) Study: preliminary survival analysis of the Zambian cohort


**Objective:** Breast cancer (BC) is often a death sentence for women in sub-Saharan Africa (SSA). Five-year survival estimates are near or below 50%, in contrast to almost 90% among U.S. women. The African Breast Cancer—Disparities in Outcomes (ABC-DO) study is a prospective hospital-based investigation of OS, quality of life (QOL), delays to diagnosis, and treatment of BC in SSA. We present survival estimates for the Zambian cohort.

**Method:** Between September 2014 and April 2017, nearly 2,000 women in 6 African countries with a new clinical or histological diagnosis of primary BC, and 18 years or older, were enrolled in the study. Tumor characteristics and socioeconomic, QOL, and treatment data were collected on each patient, and they were followed for a period of 3 years.

**Results:** Two-year outcomes on the 200 women enrolled in the Zambian cohort were generated using descriptive statistics and Cox proportional hazards regression analysis. Mean age of the cohort was 49.8 (SD 14.8) years (IQR 39–59). HIV prevalence was 15%, rising to 21% among those <50 years of age. Among the 164 (82%) women with complete staging information, 42% were stage II, 51% stage III, and 7% stage IV. As of May 2018, almost one-third (59 women) of the cohort had died, yielding 1- and 2-year survival rates of 73% and 55%, respectively. In Cox proportional hazards regression, mutually adjusted HRs for overall survival were strongest for stage at diagnosis, with HRs compared to stage II of 2.3 (IQR 1.2–4.6) for stage III and 10.5 (IQR 4.2–26.3) for stage IV. Older women had increased mortality risks (HR = 3.3, IQR 1.4–8.0) for age >70 years, compared to women in their 50s. All-cause mortality was increased in HIV-positive compared to HIV-negative women (HR = 1.8, IQR 0.9–3.6).

**Conclusion:** Our analysis supports previous observations of late-stage presentation, young median age, and poor survival in women diagnosed with breast cancer in SSA. Of note, however, is the finding that more than 40% of women presented with a stage of disease (stage II) associated with long-term survival if linked to high-quality treatment. Multicountry results are
forthcoming as is an examination of the impact of HIV infection on survival.

Healthcare Policy and Advocacy

1458 - Poster Session
Addressing the need for education and early detection services for HPV and cervical cancer in the Denver Latina community

D.M. Flink¹, L.J. Wheeler², S. Chavez³, K.M. Carroll³ and M. Russum⁵. ¹University of Colorado Hospital, Aurora, CO, USA, ²University of Colorado, Denver, Denver, CO, USA, ³Denver Health, Denver, CO, USA

Objective: Hispanic women have a 53% greater incidence and 41% greater mortality from cervical cancer compared to white women. Human papillomavirus (HPV) is the leading cause of cervical cancer. A partnership between the University of Colorado and the Federico F. Pena Southwest Family Health Center in Denver, Colorado, determined the health needs of Hispanic women regarding HPV and cervical cancer.

Method: We conducted a needs assessment using mixed methods (concurrent design) of a retrospective cohort study and community-based focused groups to determine the gaps in women’s health care of the Denver Latina population. Descriptive statistics and grounded theory theme analysis were conducted.

Results: A majority (65%) of patients at the Federico F Pena clinic are Hispanic. In 2017, 11,888 women (age 21–55 years) visits were conducted. Of those, 26% were visits for women’s care; 7% for gynecologic concern; and 1% for well or annual gynecologic exams. Sixty-two percent of women were out of window or had no documented history of Pap screening. An additional 6% were due for a Pap at the time of visit. A total of 793 Pap tests were conducted with 22% requiring follow-up for abnormal results; 578 HPV tests were conducted, of which 18% were positive. The clinic administered 186 HPV vaccine doses among women in 2017 with 40% being initial doses. Among Hispanic women, 21% initiated the vaccine with at least one dose; 15% completed the regimen. Twenty-two percent of adolescents (12–26 years) have never received the HPV vaccine. The focus groups included 28 Hispanic women. Themes identified included discomfort discussing health concerns, lack of awareness about HPV, not having a women’s care provider, and gynecologic health not a priority.

Conclusion: Hispanic women in the Denver community do not seek specialists for women’s health concerns, do not discuss concerns with their provider or among peers, and do not seek preventive care. In addition, only 32% of women meet compliance for cervical cancer screening compared to the national average of 69%. Compliance with the HPV vaccine recommendations is also lower locally. This community desires education for improving women’s health. The partnership plans to facilitate community-based education to promote awareness and increase women’s health well visits and screening.

1459 - Poster Session
Addressing unmet basic needs to improve colposcopy adherence among women with an abnormal Pap test

L.M. Kuroki², M.W. Kreuter³, A. Leon³, K. Groesch³, T. Wilson³, D. Brown³, J. Liu³, J.A. Martin³, A. Semaan³, T. Thompson³, A. McQueen³, Y. Zeino³, A. Ghareeb³, K.S. Hyon³ and L.S. Massad³. ²Washington University School of Medicine in St. Louis, St. Louis, MO, USA, ³Southern Illinois University School of Medicine, Springfield, IL, USA

Objective: To identify unmet basic needs among women with an abnormal Pap test and explore the acceptability and effectiveness of a basic needs navigator to address these needs to improve adherence to initial colposcopy visit.

Method: Women were recruited to our prospective, multicenter pilot study from September 2017 to August 2018 from two academic colposcopy referral centers—low-income rural and low-income urban. Basic needs (safety, housing, family, financial, transportation, child care) were assessed via a phone survey prior to their scheduled colposcopy visit and were considered unmet if unlikely to be resolved in the next month. Once the first 25 patients were enrolled at each site (phase 1, n = 50), allowing for protocol standardization, the navigator intervention was offered to participants who screened positive for an unmet need (phase 2, target goal n = 50). Primary outcome was adherence to initial colposcopy visit.

Results: Among 80 women recruited thus far, 55% had at least one unmet basic need, with a higher prevalence among urban than rural participants (mean 1.6 vs 0.95, P = 0.04). The most prevalent needs included money for unexpected expenses (53%), utilities (20%), transportation (18%), and family needs (e.g., food, clothing, and household goods, 18%) (Table 1). Compared to the 4 months preceding study initiation, colposcopy adherence improved from 50% (urban) and 51% (rural) to
88% and 82%, respectively, with most women presenting with low-grade Pap tests (84%). The overwhelming majority of patients (99%) reported it was acceptable to inquire about basic needs, and 57% reported feeling fine/relieved when answering the survey. To date, 13 subjects have been contacted by the navigator (phase 2); of these, 93% reported that the navigator was helpful and that they would recommend this service to a family member/friend. Yet only 58% thought that addressing their unmet needs specifically helped them get to their clinic appointment.

**Conclusion:** Women who need colposcopy have a high prevalence of unmet basic needs and are willing to discuss these needs and accept assistance from a trained basic needs navigator. Implementing patient telephone reminders for abnormal Pap follow-up that includes personalized assistance with unmet basic needs may help patients meet their needs and improve colposcopy adherence. This may ultimately help reduce cervical cancer rates in these high-risk populations.

**Table 1.** Unmet basic needs among women referred to colposcopy for an abnormal Pap test

<table>
<thead>
<tr>
<th>Unmet basic needs</th>
<th>Total N=80 (%)</th>
<th>Low-income Urban N=41 (%)</th>
<th>Low-income Rural N=39 (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of unmet basic needs per person (mean, SD)</td>
<td>1.3 ± 1.5</td>
<td>1.6 ± 1.6</td>
<td>0.95 ± 1.4</td>
<td>0.04</td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one unmet basic need</td>
<td>44 (55)</td>
<td>27 (66)</td>
<td>17 (44)</td>
<td>0.07</td>
</tr>
<tr>
<td>Specific unmet needs:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unexpected expenses</td>
<td>42 (53)</td>
<td>26 (63)</td>
<td>16 (41)</td>
<td>0.07</td>
</tr>
<tr>
<td>Utilities</td>
<td>16 (20)</td>
<td>9 (22)</td>
<td>7 (18)</td>
<td>0.78</td>
</tr>
<tr>
<td>Transportation</td>
<td>14 (18)</td>
<td>10 (24)</td>
<td>4 (10)</td>
<td>0.14</td>
</tr>
<tr>
<td>Food, shelter, clothing</td>
<td>14 (18)</td>
<td>9 (22)</td>
<td>5 (13)</td>
<td>0.38</td>
</tr>
<tr>
<td>Neighborhood safety</td>
<td>8 (10)</td>
<td>5 (12)</td>
<td>3 (8)</td>
<td>0.71</td>
</tr>
<tr>
<td>Personal Safety</td>
<td>4 (5)</td>
<td>4 (10)</td>
<td>0 (0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Childcare</td>
<td>4 (5)</td>
<td>4 (10)</td>
<td>0 (0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Food security</td>
<td>4 (5)</td>
<td>2 (5)</td>
<td>2 (5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Housing</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Chi-square or Fisher’s exact test for categorical variable; Kruskal-Wallis test for continuous variable.

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1460 - Poster Session
Impact of gynecologic oncology clinic-initiated BRCA testing on patient pathways and resource utilization in Southern Alberta
V.M. Carlson\textsuperscript{a,b}, S. Desmarais\textsuperscript{c}, S.J. Glaze\textsuperscript{b}, R. Perrier\textsuperscript{d}, A.R. Afzal\textsuperscript{b} and P. Ghatage\textsuperscript{b}. \textsuperscript{a}University of Calgary, Calgary, AB, Canada, \textsuperscript{b}Tom Baker Cancer Centre, Calgary, AB, Canada, \textsuperscript{c}Calgary Genetics Services, Calgary, AB, Canada, \textsuperscript{d}Cumming School of Medicine, Calgary, AB, Canada

**Objective:** To compare the impact of traditional and gynecologic oncology clinic-initiated (GO-BRCA) models of BRCA genetic testing in high-grade serous ovarian cancer (HGSOC) patients on timeliness of results, patient pathways, and resource utilization

**Method:** We performed a retrospective cohort study of all patients diagnosed with HGSOC in southern Alberta from January 1 to December 31, 2014, and January 1, 2016, to March 31, 2017, before and after the introduction of a novel genetic testing model. In the new model, all patients with HGSOC are eligible to undergo upfront genetic counseling in the gynecologic oncology clinic, and can proceed immediately to have blood drawn for testing. A referral to the clinical genetics service is sent at the same time; however, patients do not meet with genetics until after results are reported. This eliminated several steps in the traditional pathway that were thought to be potential barriers to patient access, as well as unnecessarily affecting timely results and inflating cost. Demographic, treatment, outcomes, and genetic testing data were abstracted from the available medical records. Descriptive statistics were used to summarize the data and identify differences.

**Results:** Fifty-seven patients were identified in the pre-GO-BRCA cohort and 86 in the GO-BRCA cohort. Overall, 92% of patients were offered genetic testing. One-quarter (26%) of patients in the GO-BRCA cohort had results within 6 months of diagnosis, 79% by 12 months, and 92% by 18 months, versus 0, 20%, and 59% in the baseline cohort, respectively (\(P \leq 0.001\)).
Figure 1 shows patient flow through the testing pathways in each cohort. The median time from diagnosis to post-test counseling was reduced from 496 to 258 days (P < 0.001), and from first offered testing to informed of results from 393 to 135 days (p < 0.001). There was no difference in the proportion of patients requiring additional pretesting counseling (24% vs 16%, P = 0.32).

Conclusions: Gynecologic oncology clinic-initiated genetic testing in patients with HGSOC was associated with significantly shorter time to results, and more patients with results in proximity to their diagnosis. Pretest counseling in the oncology clinic was sufficient, with no increase in additional pretest counseling, and therefore an associated overall decrease in patient encounters.

Fig. 1. Patient flow through testing pathways*

Pick-up: time from diagnosis to first offered genetic testing; referral time: time from first offered genetic testing to first pretesting counselling; lab time: time from bloodwork drawn to results reported by lab; result delay time: from when results reported to when the patient was informed of the results

*does not depict continuous time from diagnosis

1501 - Poster Session
The ovarian cancer message isn’t getting out: Using Google search data to gauge ovarian cancer awareness
S. Bhidea, A. Collada, A.B. Reida, C.D.T. Jacksonb, E. Hoppc and J. Nakayama. aCase Western Reserve MacDonald Women’s Hospital, Cleveland, OH, USA, bTheo. Wyess David, Ltd., Cleveland, OH, USA, cUniversity Hospital of Cleveland, Cleveland, OH, USA

Objective: Google answers billions of search queries every day with a U.S. market share of almost 80%. Changes in query volume serve as a proxy of public interest. Unlike surveys, in which participants may feel compelled to answer in what is perceived to be the “correct” way or to be swayed by the question itself, individuals are incentivized to ask Google exactly what they are interested in to get the best answer. In this study, we analyzed trends in public interest in ovarian cancer awareness month and its impact on ovarian cancer-related terms.

Methods: The Google Health API was used to provide the scaled proportion of all searches from May 2012 to October 2017 for ovarian cancer-related terms and August 2010 to 2018 for terms specific to ovarian cancer awareness month. Sampling of the entire United States was performed weekly with 30 replicates. Information on individual search terms was obtained in eight categories (e.g., cancer type, surgery, genetic) related to ovarian cancer. The most frequent searches in each category and those terms related to ovarian cancer awareness month were then individually analyzed.
**Results:** Ovarian cancer awareness month did not increase in search frequency in the categories related to ovarian cancer symptoms, prevention, diagnosis, surgery, genetic testing, or concern for the disease. The frequency of the search terms “ovarian cancer” and “ovarian cancer awareness” did respond to awareness month. There was a spike in interest each year during awareness month compared to the preceding month (12- to 73- and 0- to 7.8-fold increase, respectively). For both terms, peak interest was in 2012 and has declined progressively each year since then. From 2014 to 2016 peak interest was reached in the week before the start of awareness month. See Figure 1.

**Conclusion:** For the last 5 years, ovarian cancer awareness month has been progressively less successful in generating search-related interest. It was completely ineffective in most categories studied. Messaging around ovarian cancer awareness needs to change to reach a broader audience.

Fig. 1.

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**1502 - Poster Session**

**SPECT/CT and intraoperative gamma-probe mapping for endometrial cancer are insufficient for bilateral sentinel node detection**

**O. Tal, E. Grinstein, E. Ben Shem, O. Peled and T. Levy. E. Wolfson Medical Center, Holon, Israel**

**Objective:** The aim of this study was to evaluate success of preoperative SPECT/CT and intraoperative gamma probe in identifying sentinel lymph nodes (SLN) in endometrial cancer (EC).

**Method:** From January 2015 to July 2018, a total of 66 women with EC were included in the study. All patients received cervical injections of radiolabeled filtered Tc-99m albumin nanocolloid at the 3 and 9 o’clock positions (deep and superficial), approximately 20 hours prior to surgery. A SPECT/CT study was performed 1 hour after injection. Thereafter, laparoscopic SLN identification and removal was executed, followed by hysterectomy and bilateral salpingo-oophorectomy.

**Results:** The median age of patients was 64.15 years (range 47.75–84.1 years), with a median BMI of 32.65 kg/m² (20.8–49.78 kg/m²). Most patients (80.3%) had endometrioid histology. A median of 1 lymph node was detected on each side (right, 0–7; left, 0–9). Most SLNs on the right were found over the right external iliac vein and obturator fossa (21 lymph nodes each), while most SLNs on the left were found over the left external iliac vein (28 nodes in total). In 9 patients (13.6%) metastases were found in the sentinel nodes. The detection rate by both SPECT/CT and gamma probe was 93.9%. SPECT/CT was able to detect bilateral SLNs in 74.24% of patients. However, during laparoscopy, bilateral detection by gamma probe was successful in only 65.15%. One-sided SLN detection was achieved in 28.8% during laparoscopy, necessitating complete lymph node dissection of the other side in these patients. The concordance between SPECT/CT and intraoperative gamma probe for bilateral SLN detection was 27.3%. High BMI (>32 kg/m²) was found to be a significant factor associated with failure of bilateral detection ($P = 0.012$).

**Conclusion:** Although cervical injection of Tc-99m results in a total high detection rate of SLNs, the rate of bilateral mapping by gamma probe is disappointing. SPECT/CT can be helpful for SLN location. However, bilateral SLN detection should be improved by adding other mapping methods.
Objective: Both rural and public hospitals care for vulnerable patients with various barriers to care. Yet these hospitals may face distinctly different systems factors influencing the management of cancer patients. We sought to examine characteristics of rural hospitals and public hospitals and identify their relationship to perioperative uterine cancer outcomes.

Method: The New York Statewide Planning and Research Cooperative System database was used to identify hospitals at which women with a diagnosis of uterine cancer received a hysterectomy from 2000 to 2015. Rural hospitals met 2014 state criteria for critical access hospitals, sole community hospitals, and safety net hospitals in rural counties with high rates of uninsured patients. Public hospitals met 2014 state criteria for county- or municipality-run services. Primary outcomes included overall morbidity, inpatient mortality, perioperative complications, and prolonged length of stay. Generalized linear mixed models with Poisson distribution and log link were developed to estimate the adjusted risk ratio of primary outcomes across hospital type while accounting for hospital and surgeon clustering and observed confounders.

Results: Over the study period, 46,298 uterine cancer patients received care at 219 hospitals. There were 29 (15%) rural hospitals and 19 (9.8%) public hospitals caring for 1,013 (2.2%) and 5,086 (11%) patients, respectively. Over time, the proportion of patients cared for at rural hospitals decreased significantly from 5% (129 patients) in 2000 to 0.5% (19 patients) in 2015 ($P < 0.001$). Controlling for age, race, and comorbid conditions, there was no statistical difference in the rate of overall morbidity for rural hospitals (aRR = 0.76, 95% CI 0.43–1.34) or public hospitals (aRR = 0.96, 95% CI 0.83–1.10) compared to other state hospitals. No statistical difference was observed for either perioperative complications or prolonged length of stay. While the inpatient mortality rate was similar for public hospitals compared to other hospitals in the state (aRR = 1.23, 95% CI 0.78–1.95), it was higher risk at rural hospitals (aRR = 4.03, 95% CI 1.02–15.97). See Figure 1.

Conclusion: Fewer women with uterine cancer are undergoing hysterectomies at rural hospitals, possibly reflecting a practice shift in referral patterns to centralize cancer care. While outcomes at public hospitals are similar to those at other centers, perioperative mortality is higher at rural hospitals.

![Fig. 1. Percentage of uterine cancer patients treated at rural and public hospitals in New York](image-url)
1504 - Poster Session
The Affordable Care Act leads to an increase in early-stage diagnosis and treatment within 30 days of diagnosis for women with ovarian cancer
A.J.B. Smith and A.N. Fader. Johns Hopkins School of Medicine, Baltimore, MD, USA, Johns Hopkins Hospital, Baltimore, MD, USA

Objective: The 2010 Affordable Care Act (ACA) expanded access to insurance and care for many Americans. Our objective was to evaluate the impact of the ACA on stage at diagnosis and time to treatment for women with ovarian cancer.

Method: We utilized a difference-in-differences (DD) approach to assess stage at diagnosis and time to treatment before and after the 2010 ACA among women ages 21–64 years compared to women 65 years and older. We used the National Cancer Data Base with the 2004–2009 surveys as the pre-reform years and the 2011–2014 surveys as the postreform years. Outcomes were analyzed for women overall and by insurance type, adjusting for patient race, living in a rural area, area-level household income, education level, Charlson comorbidity score, distance traveled for care, Census region, and care at an academic center.

Results: A total of 35,842 ovarian cancer cases pre-reform and 37,145 postreform were identified for women 21–64 years compared with 28,895 cases pre-reform and 30,604 postreform for women 65 years and older. The ACA was associated with increased early-stage diagnosis for women 21–64 years compared to women 65 and older with ovarian cancer (DD = 1.7%, P for trend = 0.001). In addition, the ACA was associated with more women receiving treatment within 30 days of ovarian cancer diagnosis (DD = 1.6%, P < 0.001). Specifically, among women with public insurance, the ACA was associated with a significant improvement in stage at diagnosis and receipt of treatment within 30 days of diagnosis (DD = 2.5%, P = 0.003, and DD = 2.5%, P = 0.006). Improvements in stage at diagnosis and time to treatment were seen across race, income, and education groups.

Conclusion: Under the Affordable Care Act, women with ovarian cancer were more likely to be diagnosed at an early stage and receive treatment within 30 days of diagnosis. As stage and treatment are major determinants of survival, these gains under the ACA may have long-term impacts on women with ovarian cancer.

1505 - Poster Session
Preparation for gynecologic oncology fellowship during obstetrics and gynecology residency training: Incoming fellows’ perspectives
A.M. Saiz, A.L. Shepherd-Littlejohn, H. Chen and G.S. Leiserowitz. UC Davis Medical Center, Sacramento, CA, USA, Winthrop University Hospital, Mineola, NY, USA, UC Davis Comprehensive Cancer Center, Sacramento, CA, USA

Objective: We sought to assess the perceptions of incoming gynecologic oncology fellows on how obstetrics and gynecology residency prepared them for subspecialty training.

Method: A previously validated questionnaire, used to survey gynecologic oncology fellowship program directors, was modified and distributed to all incoming first-year gynecologic oncology fellows. Distribution was via email, and commercially available survey software was used. The fellows were identified using a contact list provided by the Society of Gynecologic Oncology. The 25-item survey contained questions about fellows’ surgical experience, their perceived ability to function independently both in the operating room and in other care settings, and their research experience. A Likert scale was used for responses. Standard descriptive statistical methods were used to analyze survey data.

Results: Thirty-five first-year fellows completed the survey, for a response rate of 52.2%. In the surgical domains, fellows reported being most experienced and most comfortable with laparoscopic hysterectomy (Figure 1). Over 80% of respondents had performed 30 or more laparoscopic hysterectomies in residency. Despite reporting being the least comfortable with robotic hysterectomies, 48.6% of fellows had performed 16 or more cases. The majority of fellows (88.6%) felt mostly or very comfortable evaluating and managing postoperative complications, but 57.1% reported feeling at most only somewhat comfortable discussing surgery and chemotherapy with patients. Most fellows reported formal research experience during residency, largely limited to written abstracts. Only 25.7% of respondents had presented more than 2 oral research presentations. Most (68.6%) rated their understanding of basic statistics as poor or fair, and 57.2% reported their ability to formulate a research project and collect and analyze data as poor or fair.
Conclusion: Incoming gynecologic oncology fellows report being underprepared for advanced subspecialty training in certain aspects of surgery and oncologic counseling as well as independent research. In comparison to the perception of fellowship program directors, a greater percentage of fellows reported feeling overall prepared for autonomous surgical practice. In light of the Accreditation Council for Graduate Medical Education (ACGME) changing guidelines with respect to surgical training and research curricula, appropriate preparation for fellowship training and independent practice remain important areas of education research.

Fig. 1.

1506 - Poster Session
Changing patterns in care settings for surgical management of ovarian and uterine malignancies
J. Sheu and Y.C. Lee. SUNY Downstate, Brooklyn, NY, USA

Objective: Literature has demonstrated improved survival and outcomes when surgery for gynecologic malignancy is performed at referral centers. Subsequently, there have been recommendations for centralization of surgical treatment toward high-volume or tertiary centers to optimize these benefits. In light of these data, we seek to investigate changing patterns of care in the last decade by assessing trends in location of surgical treatment of ovarian and uterine cancer between the years 2007 and 2014.

Method: The National Inpatient Sample (NIS) years 2007 and 2014 database was queried to identify all admissions coded for uterine cancer with hysterectomy and ovarian cancer with bilateral salpingo-oophorectomy. These observations were then subset by regions and hospital sizes. Size determination, per the NIS description of data elements, was based on bed number categories specific to each region. \(\chi^2\) tests were used to evaluate the changes in admission distribution between these two periods of time.

Results: A total of 13,828 admissions were included in the analysis, 8,562 in 2007 and 5,266 in 2014. In the Northeast, there was a significant increase in cases at medium-sized hospitals \((P < 0.01)\) and decrease at small hospitals \((P < 0.01)\). The Midwest cases increased in medium-sized hospitals \((P = 0.01)\). More surgeries in the South and West were performed in small (both \(P < 0.01\)) and medium-sized (both \(P < 0.01\)) hospitals, and fewer in large hospitals \((P < 0.01\) and \(P = 0.02\), respectively). All other changes in case distribution between 2007 and 2014 were not statistically significant (Table 1).

Conclusion: Despite recommendations for centralization of gynecologic oncology surgical management, a decreasing percentage of cases is being performed at large hospitals, particularly in the South and West. These findings underscore the importance of adequate gynecologic oncology services in small and medium-sized hospitals.
Table 1.

<table>
<thead>
<tr>
<th>Region</th>
<th>Hospital Bedsize</th>
<th>2007 N (%)</th>
<th>2014 N (%)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Northeast</td>
<td>Small</td>
<td>388 (17.79)</td>
<td>128 (11.18)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>331 (15.18)</td>
<td>278 (24.28)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>1,462 (67.03)</td>
<td>739 (64.54)</td>
<td>0.15</td>
</tr>
<tr>
<td>Midwest</td>
<td>Small</td>
<td>172 (10.22)</td>
<td>104 (8.85)</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>284 (16.87)</td>
<td>242 (20.60)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>1,227 (72.91)</td>
<td>829 (70.55)</td>
<td>0.17</td>
</tr>
<tr>
<td>South</td>
<td>Small</td>
<td>239 (8.67)</td>
<td>205 (11.77)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>443 (16.07)</td>
<td>481 (27.61)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>2,075 (75.26)</td>
<td>1,056 (60.62)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>West</td>
<td>Small</td>
<td>61 (3.14)</td>
<td>144 (11.96)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>402 (20.71)</td>
<td>189 (15.70)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>1,478 (76.15)</td>
<td>871 (72.34)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

1507 - Poster Session
Delays in definitive treatment for locally advanced cervical cancer: An analysis of disparities among a South Florida population between a university cancer center and a safety net hospital
L. Portelancea, S.E. Jordana, L. Quinterob, C. Maliakala, J.M. Pearsona, B.M. Slomovitzb, M. Huangc, M.P. Schlumbrecht and A.H. Wolfson. aUniversity of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, bNew York Medical College, Valhalla, NY, USA

Objective: According to a recently published National Cancer Data Base (NCDB) analysis, expected time to treatment initiation (eTTI) for patients diagnosed with locally advanced cervical cancer (LACC) is 44.3 days. Our study was designed to characterize the eTTI for a patient population diagnosed with LACC and treated in a South Florida cancer center serving a multiracial population, and to seek disparities between the patients treated at the university cancer center (UCC) and the safety net hospital (SNH).

Method: Using an Institutional Review Board-approved cervical cancer databank, adult women diagnosed with LACC between December 2012 and June 2017 and treated with definitive radiation therapy (RT) or chemoradiation therapy (CRT) were identified. Estimated time to treatment initiation was defined as days from diagnostic biopsy to start of RT or CRT, and was calculated for the entire patient population. A subanalysis was then done using a Student t test to compare eTTI for patients treated at the UCC versus the SNH. Interval from initial diagnosis to first consultation with a radiation oncologist or a gynecological oncologist, time to completion of workup, race, ethnicity, and insurance funding status were also collected for comparison.

Results: A total of 102 patients were identified. Sixty-two (61%) patients were treated in the SNH and 40 (39%) patients in the UCC. Nine (9%) patients were Caucasian, 11 (11%) were African-American, and 82 (80%) were Hispanic. Estimated time to treatment initiation for the entire cohort was 61 (4–180) days. In the subanalysis of eTTI between institutions, time to treatment initiation was significantly longer for patients treated in the SNH than for patients treated in the UCC (68 vs 55 days, P < 0.05).

Conclusion: While a NCDB analysis showed that eTTI for patients diagnosed with LACC is 44.3 days, our analysis of the eTTI in a South Florida cancer center was significantly longer (55 days). In the NCDB analysis, non-Hispanic white women had shorter eTTI compared to non-Hispanic black and Hispanic women (38.1, 45.2, and 49.4 days, respectively). Interventions to decrease eTTI need to be implemented to better serve our uniquely diverse population. This exercise provided important information that will be used to reduce the disparities existing within our catchment area.
Innovations that Improve Surgical Quality, Outcomes, Including Toxicity, and Recovery

1508 - Poster Session
'Present on admission': Reducing catheter-associated urinary tract infections in gynecologic oncology patients with universal intraoperative screening
M. Brackmann\textsuperscript{a}, J.A. Ebott\textsuperscript{b}, R. Gutfreund\textsuperscript{b}, K. McLean\textsuperscript{b}, R.K. Reynolds\textsuperscript{c} and S. Uppal\textsuperscript{d}, \textsuperscript{a}Michigan Medicine, Ann Arbor, MI, USA, \textsuperscript{b}The University of Michigan Hospitals, Ann Arbor, MI, USA, \textsuperscript{c}University of Michigan, Ann Arbor, MI, USA, \textsuperscript{d}University of Michigan Health Systems, Ann Arbor, MI, USA

Objective: The Centers for Medicare and Medicaid Services defines catheter-associated urinary tract infection (CAUTI) as a hospital-acquired condition. However, the proportion of "present on admission" urinary tract infections (POA-UTI) in patients with gynecologic malignancies is unknown. The objective of this study was to determine both the rate of POA-UTI in this patient population and the effect of treating POA-UTIs on CAUTI rates.

Method: This is a subset analysis of a prospective cohort study from October 1, 2016, to March 31, 2018, during which our gynecologic oncology division sent urine cultures on all patients at the time of sterile Foley catheter placement during surgery as part of a study investigating risk factors for postoperative urinary retention (n = 193). For this study group, those with urine cultures positive for >1,000 colony-forming units were treated with antibiotics. As a comparison routine care group, we used 168 patients who underwent gynecologic oncology surgery from April 1, 2018, to July 16, 2018, in whom no urine cultures were sent unless the patient had symptoms. Data were abstracted from patient charts and compared using χ² tests.

Results: There were no demographic or clinical differences between the groups. There was a 6.7% (13/193) rate of POA-UTI in the study group. The rate of CAUTI in the routine care group was 11.3% (19/168); in the study group, it was 5.2% (10/193) (P = 0.033). Thus, routinely collecting an intraoperative catheterized urine culture and treating culture-positive patients resulted in a 54% reduction in CAUTIs, demonstrating that more than half of CAUTIs were, in fact, pre-existing infections. By following the study group protocol, we estimate only 1 additional antibiotic exposure per 200 patients.

Conclusion: Our policy of using an intraoperative catheterized urine culture for screening for UTI in all patients undergoing a gynecologic oncology surgery led to a 54% reduction in CAUTIs. This approach did not lead to significant additional antibiotic exposure. By screening and treating this at-risk patient population at the time of catheter placement in the operating room, there is the potential to significantly reduce CAUTI rates. This management approach in turn has important implications for both patient outcomes and hospital reimbursement.

1509 - Poster Session
Outcomes after sentinel lymph node procedure in patients with previous excision of vulvar squamous cell carcinoma
A.L. Nica\textsuperscript{a}, A.L. Covens\textsuperscript{b,c}, D. Vicus\textsuperscript{b,c}, R. Kupets\textsuperscript{b,d,e}, R.J. Osborne\textsuperscript{e}, M. Cesari\textsuperscript{b} and L.T. Gien\textsuperscript{b,f,g}, \textsuperscript{a}University of Toronto, Toronto, ON, Canada, \textsuperscript{b}University of Toronto, Toronto, ON, Canada, \textsuperscript{c}Sunnybrook Regional Cancer Centre, Toronto, ON, Canada, \textsuperscript{d}Cancer Care Ontario, Toronto, ON, Canada, \textsuperscript{e}Sunnybrook Cancer Center/University of Toronto, Toronto, ON, Canada, \textsuperscript{f}Sunnybrook Odette Cancer Center, Toronto, ON, Canada, \textsuperscript{g}Institute for Clinical Evaluative Sciences, Toronto, ON, Canada

Objective: Sentinel lymph node (SLN) metastasis is the most important prognostic factor in patients with vulvar squamous cell carcinoma (SCC). Previous excision of the vulvar tumor may alter the accuracy of the SLN biopsy. The purpose of this study was to assess outcomes after SLN biopsy in patients who had previous excision of the vulvar tumor.

Method: This was a retrospective study of patients at a single institution with primary vulvar cancer, clinically negative nodes, and vulvar tumors <4 cm treated with surgical excision who had SLN biopsy (2008–2015). Patient and tumor characteristics, as well as recurrence rates and patterns, were collected from hospital records.

Results: There were 106 cases of concomitant wide local excision (WLE) and SLN biopsy and 24 cases in which patients had previous vulvar surgery. Median follow-up was 31 months. The SLN biopsy was positive in 27 (25%) primary surgery cases and in 2 (8%) cases of scar re-excision. Patients who had previous tumor excision were more likely to be younger (P = 0.001) and have a smaller tumor (P = 0.002) and smaller depth of invasion (P = 0.02). In the wide local excision of the scar specimen, 11 patients (46%) had no residual disease left; 8 patients (33%) had only VIN III; 4 patients (17%) had carcinoma in situ with
focal invasion; and 1 patient (4%) had invasive carcinoma within the second specimen, with clear margins by 4 mm. There were no groin recurrences in patients with previous vulvar tumor excision and negative SLN biopsy.

**Conclusion:** These data suggest SLN biopsy is feasible and safe in patients who have had previous vulvar surgery. Prior excision of the vulvar tumor does not seem to have an impact on the capacity of the SLN biopsy to accurately reflect nodal status.

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**1510 - Poster Session**

**Correlation of prospective comprehensive geriatric assessment to overall survival of gynecologic oncologic patients**

N. Michaan, S.Y. Park and M.C. Lim. 
*Li Maternity Hospital - Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, National Cancer Center Korea, Goyang-si, South Korea*

**Objective:** We aimed to investigate the correlation of prospective comprehensive geriatric assessment (CGA) tests to overall survival among elderly gynecologic oncologic patients.

**Method:** All elderly gynecologic oncologic patients >70 years had prospective CGA before treatment. CGA included the following tests: instrumental activities of daily living (IADL), modified Barthel index (MBI), mini-mental state examination (MMSE), geriatric depression scale (GDS), mini-nutritional assessment (MNA), risk of falling (ROF), and medication use. A total CGA score was also calculated. For all tests, median scores were calculated and set as cutoff values. Survival analysis, using Kaplan-Mayer estimator and log rank test, was done for patient groups below and above the cutoff values. Univariate as well as multivariate analysis was done to evaluate the association between each variable and survival.

**Results:** Between April 2011 and May 2017, 120 elderly patients had prospective CGA. Mean patient age was 76.4 ± 5 years. Seventy-nine patients had ovarian cancer; 14 had uterine cancer; 17 had cervical cancer; and 10 had other gynecologic malignancies. No correlation was found between age, BMI, and cancer type or disease stage to overall survival. Patients who were elected for surgery had significantly longer overall survival (*P* = 0.013, HR = 0.30–0.87). Patients with scores below cutoff values of MBI, IADL, MMSE, MNA, and overall CGA score had significantly lower overall survival (*P* = 0.001, *P* = 0.007, *P* = 0.019, *P* = 0.008, *P* = 0.012, respectively). This remained significant in univariate analysis for all variables and in multivariate analysis (except for MMSE).

**Conclusion:** Gynecologic oncologic patients with lower CGA scores on several dimensions have significantly lower overall survival, regardless of cancer type or disease stage. These tests allow evidence-based, objective assessment of the elderly patient and can be used in clinical practice for treatment planning.

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**1511 - Poster Session**

**The use of indocyanine green fluorescence angiography for colorectal anastomoses in cytoreductive surgery for ovarian carcinoma**

*University of Toronto, Toronto, ON, Canada, Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada*

**Objective:** Real-time intraoperative assessment of anastomotic perfusion with indocyanine green fluorescence angiography (ICG-FA) is a recent technique that has been associated with a lower risk of anastomotic leak in the general surgery literature. No studies to date have evaluated its use in patients with gynecologic malignancies. Our objective was to describe feasibility and safety of the use of ICG-FA by reporting our initial experience incorporating this tool into routine surgical practice.

**Method:** A retrospective cohort study of patients who underwent colorectal resection as part of cytoreductive surgery for ovarian cancer between November 1, 2017, and July 30, 2018 was conducted. Demographic and surgical variables, including factors known to affect anastomotic healing, were collected. ICG was administered intravenously, and a near infrared imaging system (Pinpoint, Novadaq, Canada) was used to visualize colorectal perfusion and the anastomotic staple line.

**Results:** ICG-FA was used in 18 consecutive patients. There were 18 left-sided resections (including 16 low anterior resections), 3 right-sided resections, and 2 small bowel resections. Sixteen end-to-end and 4 side-to-side anastomoses were assessed with ICG-FA. Nine patients underwent diverting ileostomy. The median age was 36 (range 17–75) years and median BMI was 23.7 (range 15.2–34.3). ICG-FA allowed complete visualization of anastomotic perfusion in all cases. ICG-FA resulted in change in operative plan for one patient (anastomotic revision and diverting ileostomy). There were no allergic reactions to ICG. There were no postoperative anastomotic leaks. See Table 1.
Conclusions: ICG-FA enables objective and accurate intraoperative assessment of anastomotic perfusion. It can be used with other risk assessment strategies to guide operative decision making in gynecologic oncology. Further prospective research is warranted.

Table 1. Demographic and surgical variables

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>36 (range 17-75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, range)</td>
<td>36 (range 17-75)</td>
</tr>
<tr>
<td>Body mass index (median, range)</td>
<td>23.7 (range 15.2-34.3)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1 smoker, 2 ex-smokers</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
</tr>
<tr>
<td>Previous radiation therapy</td>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Surgery</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Cytoreductive surgery</td>
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</tr>
<tr>
<td>Primary</td>
<td>12</td>
</tr>
<tr>
<td>Interval</td>
<td>4</td>
</tr>
<tr>
<td>Secondary debulking</td>
<td>2</td>
</tr>
<tr>
<td>Colorectal procedures</td>
<td></td>
</tr>
<tr>
<td>Left-sided resection, low anterior resection</td>
<td>18, 16</td>
</tr>
<tr>
<td>Right-sided resection</td>
<td>3</td>
</tr>
<tr>
<td>Small bowel resection</td>
<td>2</td>
</tr>
<tr>
<td>Diverting ileostomy</td>
<td>9</td>
</tr>
<tr>
<td>Diverting colostomy</td>
<td>1</td>
</tr>
<tr>
<td>Anastomoses assessed with ICG</td>
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<tr>
<td>End-to-end</td>
<td>16</td>
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<tr>
<td>Side-to-side</td>
<td>4</td>
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</tbody>
</table>

1512 - Poster Session

Intraperitoneal chemotherapy improves oncologic outcome in stage IIIC epithelial ovarian cancer patients with miliary subtype

B.L. Manning-Geistab, J.O. Schorgec, W.B. Growdond, M.G. del Carmen4, R.M. Clark4, M.G. Mutoef, U.A. Matulonisg, N.S. Horowitzf, R.S. Berkowitzf and M.J. Worley Jr.h,e. aMassachusetts General Hospital, Boston, MA, USA; bBrigham and Women’s Hospital/Harvard Medical School, Boston, MA, USA; cTufts Medical School, Boston, MA, USA; dMassachusetts General Hospital/Harvard University, Boston, MA, USA; eDana-Farber Cancer Institute, Boston, MA, USA; fBrigham and Women’s Hospital/Harvard University, Boston, MA, USA

Objective: To examine the effects of intraperitoneal (IV/IP) chemotherapy on oncologic outcomes in patients undergoing primary debulking surgery (PDS) for stage IIIC epithelial ovarian/fallopian tube/primary peritoneal carcinoma (EOC) with miliary subtype.

Method: Medical records of patients with stage IIIC EOC undergoing PDS between January 2010 and July 2015 were reviewed. Patient demographics, operative and treatment characteristics, residual disease volume, presence of miliary subtype, and survival data were collected. Patients with suboptimal residual disease (>1 cm) were excluded.

Results: Of 176 patients who underwent optimal cytoreduction for stage IIIC EOC, 93 (52.8%) had miliary subtype. Of patients with miliary disease, 46 (49.5%) underwent IV/IP chemotherapy, while 47 (50.5%) underwent IV chemotherapy alone. Patients who underwent IV/IP chemotherapy had a lower median age (63.1 vs 66.0 years, \( P < 0.04 \)) and median BMI (25.2 vs 26.6, \( P < 0.05 \)) than patients who underwent IV chemotherapy alone. However, there were no significant differences in median Charlson comorbidity index or histology subtype between patients who underwent IV/IP chemotherapy versus those who underwent IV chemotherapy alone. Among patients with miliary disease, the rate of complete surgical resection was similar when comparing those who received IV/IP to those receiving IV alone (26.1% vs 12.8%, \( P = 0.57 \)). Postoperative
Complications were similar when comparing IV/IP chemotherapy to IV chemotherapy alone. When evaluating oncologic outcomes, there was a 10-month increase in progression-free survival (PFS) (23 vs 13 months, \( P = 0.004 \)) and a 45-month increase in median overall survival (OS) (83 vs 38 months, \( P = 0.0003 \)) in patients with miliary subtype undergoing IV/IP chemotherapy versus IV chemotherapy alone. See Figure 1.

**Conclusion:** IV/IP chemotherapy was associated with significantly increased PFS and OS in patients with miliary subtype.

### Fig. 1. Survival in patients with military-subtype Stage IIIC EOC

**1513 - Poster Session**

**Perioperative blood transfusion impacts neither morbidity nor mortality in patients undergoing interval debulking surgery for advanced stage ovarian cancer**

B.L. Manning-Geist\(^{a,b}\), S. Alimena\(^{a,b}\), A. Goodman\(^{c}\), M.G. del Carmen\(^{c}\), N.S. Horowitz\(^{d,e}\), M.G. Muto\(^{d,e}\), R.M. Clark\(^{c}\), W.B. Growdon\(^{c}\), R.S. Berkowitz\(^{d,e}\) and M.J. Worley Jr.\(^{d,e}\) \( ^{a}\)Massachusetts General Hospital, Boston, MA, USA, \( ^{b}\)Brigham and Women’s Hospital/Harvard Medical School, Boston, MA, USA, \( ^{c}\)Massachusetts General Hospital/Harvard University, Boston, MA, USA, \( ^{d}\)Brigham and Women’s Hospital/Harvard University, Boston, MA, USA, \( ^{e}\)Dana-Farber Cancer Institute, Boston, MA, USA

**Objective:** To examine the effects of perioperative red blood cell transfusion (PRBCT) on morbidity and mortality in patients with high-grade epithelial ovarian/fallopian tube/primary peritoneal cancer (EOC) undergoing interval debulking surgery (IDS).

**Method:** Records of patients with stage IIIC–IV EOC managed with neoadjuvant chemotherapy and IDS between January 2010 and July 2015 were reviewed. Demographics, operative characteristics, residual disease status, and outcome data were collected. The association of PRBCT with morbidity and oncologic outcome was evaluated.

**Results:** Of 270 patients, 136 (50.4%) received PRBCT. In those who received PRBCT versus those who did not, median preoperative hemoglobin was 10.3 g/dL versus 10.9 g/dL (\( P = 0.001 \)), and median estimated blood loss (EBL) was 400 mL versus 200 mL (\( P < 0.0001 \)). There were no significant differences in PRBCT based on patient age, Charlson comorbidity index, or tumor stage. Using a standardized surgical complexity score, patients with more complex surgeries were more likely to receive PRBCT (\( P = 0.01 \)). After controlling for surgical complexity, PRBCT was not associated with increased risk of intraabdominal infection (OR = 7.1, 95% CI 0.9–59.7, \( P = 0.07 \)), wound complications (OR = 1.6, 95% CI 0.8–3.3, \( P = 0.20 \)) or venous thromboembolism/pulmonary embolism (VTE/PE) (OR = 2.0, 95% CI 0.5–8.3, \( P = 0.34 \)). Median progression-free survival (PFS) in patients who underwent PRBCT versus those who did not was 12.0 and 14.8 months, respectively. Median overall survival (OS) in patients who underwent PRBCT versus those who did not was 41.9 and 52.0 months, respectively. After adjusting for age, stage, and residual disease in a multivariable model, PRBCT was not associated with decreased PFS (HR = 1.2, 95% CI 1.0–1.6, \( P = 0.09 \)) or OS (HR = 1.3, 95% CI 0.9–1.8, \( P = 0.16 \)).
Conclusion: Among patients undergoing IDS, rates of intraabdominal infection, wound complications, and VTE/PE are similar, regardless of receiving PRBCT. PRBCT does not have an impact on PFS or OS.

1514 - Poster Session
Compliance with preoperative glucose screening and effects of carbohydrate loading on hyperglycemia among gynecologic oncology patients enrolled in an enhanced recovery after surgery (ERAS) pathway
S. Alimena, M.F. Anderson and K.M. Elias
Massachusetts General Hospital, Boston, MA, USA, Brigham and Women’s Hospital/Brigham and Women’s Hospital, Boston, MA, USA, Dana-Farber Cancer Institute, Boston, MA, USA

Objective: The goal of this study was to determine rates of screening and treatment for preoperative hyperglycemia, rates of hyperglycemia after carbohydrate loading, and rates of postoperative complications with preoperative hyperglycemia.

Method: A cohort study was performed with gynecologic oncology patients in an enhanced recovery after surgery (ERAS) pathway at one metropolitan institution. Data regarding preoperative carbohydrate loading with Clearfast®, preoperative glucose testing, pre- and postoperative insulin administration, and complications were collected. Preoperative hyperglycemia was defined as glucose ≥140; per protocol, insulin was indicated for glucose ≥180. Multivariate logistic regressions (adjusted for BMI and smoking) compared complication rates among those with and without preoperative hyperglycemia.

Results: A total of 335 patients were included, and 241 patients (71.9%) had a preoperative glucose recorded. Of patients with recorded glucose values, 42 patients (17.4%) were hyperglycemic with glucose ≥180, but only 4 were treated with insulin preoperatively. There was a trend toward increased glucose after Clearfast® use (mean glucose 144.0 ± 61.0 with Clearfast® vs 121.4 ± 37.3 without, t = −1.81, P = 0.071). In multivariate regression, preoperative hyperglycemia was not associated with increased rates of any complication, infectious complications, or hyperglycemia-related complications, although diabetic patients were significantly more likely to have any complication (OR = 3.00, 95% CI 1.14–7.89, P = 0.026) or an infectious complication (OR = 3.80, 95% CI 1.11–12.99, P = 0.033) independent of glucose value.

Conclusion: Compliance with universal preoperative glucose screening and treatment of glucose ≥180 is suboptimal. Carbohydrate loading may increase preoperative glucose values, although this does not appear to have an impact on postoperative complication rates. Diabetes is an independent risk factor for postoperative complications.

1515 - Poster Session
Lymphovascular space invasion as an independent predictor of lymph node status at a single academic institution
L.K. Berry, A. Drohan, E.M. Green, L.M. Harbin, A. Wahlquist, M.F. Kohler and W.A. Graybill
Medical University of South Carolina, Charleston, SC, USA, Medical University of South Carolina, Mount Pleasant, SC, USA

Objective: The treatment of uterine cancer is largely determined by stage and prognostic factors. Lymphovascular space invasion (LVSI) is considered a risk factor for uterine cancer, but it is currently not classified as an independent predictor for lymph node status. This has been suggested in prior studies, but given variations in the pathologic diagnosis of LVSI among pathology departments, it has been difficult to prove. Our objective was to review all uterine cancer cases at a single academic institution to determine whether LVSI can serve as an independent predictor of lymph node status.

Method: Eligible patients diagnosed with uterine carcinoma between 1988 and 2017 were identified from a single academic institution uterine cancer database. A retrospective chart review was performed to assess differences in LVSI status, lymph node metastasis (LN metastasis), histologic type (type 1 = endometrioid, type 2 = clear cell, carcinosarcoma, papillary serous), FIGO stage, and recurrence rates.

Results: A total of 937 patients were identified. Of these patients, 192 (20%) had LVSI. Of those with LVSI, 68 (35%) had LN metastasis on final pathology. With regard to type of uterine cancer, there were 573 (62%) type 1 and 198 (21%) type 2. Of the type 2 uterine cancers, 34% had LVSI, and of those, 42% had LN metastasis. With regard to the type 1 uterine cancers, of grade 1, 21/319 (7%) had LVSI with 5/21 (23%) with LN metastasis; grade 2, 23/138 (17%) had LVSI with 10/23 (43%) with LN metastasis; and grade 3, 23/33 (70%) had LVSI with 12/23 (52%) with LN metastasis. There were 174 (12%) patients with documented recurrence. Of those who recurred, 82 (47%) had LVSI. There were 116 (12%) patients with LN metastasis; of those, 68 (59%) had LVSI. See Table 1.
Conclusion: Uterine cancer patients who were LVSI positive were significantly more likely to have LN metastasis than LVSI negative patients (36% vs 6.5%, \(P < 0.0001\)). Patients with uterine cancer whose final pathology was noted to have LVSI were significantly more likely to have recurrence than those without LVSI (44% vs 12%, \(P < 0.0001\)). Based on this study’s findings, it may be reasonable to use LVSI as an independent predictor of LN metastasis in our academic institution. This is further supported by our finding that recurrence is less likely in those without LVSI. Additional multicenter studies should be undertaken before concrete recommendations can be made.

Table 1.

<table>
<thead>
<tr>
<th>Recurrence</th>
<th>LVSI Negative</th>
<th>LVSI Positive</th>
<th>(P&lt;0.0001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>651</td>
<td>104</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>92</td>
<td>82</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LN Metastasis</th>
<th>LVSI Negative</th>
<th>LVSI Positive</th>
<th>(P&lt;0.0001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>690</td>
<td>121</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

1516 - Poster Session
Factors associated with successful bilateral sentinel lymph node identification with indocyanine green (ICG) fluorescence in women with endometrial and cervical cancer

J. Gelissen, E. MacDuffie, J. Emerson, K.M. Robison and C. Raker. Women & Infants Hospital, Brown University, Providence, RI, USA

Objective: To identify factors associated with successful bilateral sentinel lymph node mapping with ICG.

Method: We performed a retrospective cohort study at a single academic center. Charts were reviewed from July 2013 to May 2016. Women were included who had either endometrial or cervical cancer and underwent a hysterectomy with attempted SLN dissection. The standard SLN technique was used with injection of 2 mL of 0.5 mg/mL ICG tracer into the cervix at 3 and 9 o’clock to a depth of 1 cm after anesthesia induction. Demographic and clinical characteristics were compared between those who had bilateral detection of at least one SLN and those who had only unilateral or no SLN detection.

Results: There were 278 cases included, 259 performed for endometrial cancer and 19 for cervical cancer. Mean subject age was 62 years (SD = 11.7). Of endometrial cases, 82% were stage I, 2.7% stage II, 14.5% stage III, and 0.8% stage IV. Endometrial histologic subtypes were 83.8% endometrioid, 3.1% clear cell, 5.8% serous, 1.2% carcinosarcoma, and 6.2% “other.” Among cervical cancers, 89.5% were stage I and 10.5% were stage III. Histology of cervical cancer cases was 63% squamous cell, 32% adenocarcinoma, and 5% adenosquamous carcinoma. Bilateral mapping success was significantly more likely in younger women (mean age 60.8 vs 64.7 years, \(P = 0.0054\), Table 1) and premenopausal women (\(P = 0.042\)). There was no difference in bilateral mapping success when endometrial and cervical cancers were compared (\(P = 0.621\)). There was no difference in mapping based on BMI, stage, grade, depth of invasion, histology, lymphovascular space invasion, tumor size, or tumor location (Table 1).

Conclusion: Failure of bilateral SLN mapping is associated with older age and postmenopausal status in women undergoing hysterectomy for endometrial or cervical cancer. Given the recent findings of the 2017 FIRES trial, concluding that SLN mapping can safely replace lymphadenectomy in endometrial cancer, it is important to understand the factors associated with mapping failure. This will allow providers to better counsel patients preoperatively, and plan for the potential need for full lymphadenectomy during initial surgery.

Table 1. Factors associated with successful bilateral sentinel lymph node mapping
<table>
<thead>
<tr>
<th>Variable</th>
<th>Failure</th>
<th>Success</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (y)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>64.67 (9.73)</td>
<td>60.84 (12.37)</td>
<td>0.0054</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>35.32 (8.64)</td>
<td>33.45 (9.4)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>76 (31.54)</td>
<td>165 (68.46)</td>
<td>0.35</td>
</tr>
<tr>
<td>Black</td>
<td>2 (33.33)</td>
<td>4 (66.67)</td>
<td></td>
</tr>
<tr>
<td>Other/Multiracial</td>
<td>13 (44.83)</td>
<td>16 (55.17)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latina</td>
<td>6 (37.5)</td>
<td>10 (62.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Non-Hispanic/Latina</td>
<td>84 (32.43)</td>
<td>175 (67.57)</td>
<td></td>
</tr>
<tr>
<td><strong>Menopausal status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>7 (18.42)</td>
<td>31 (81.58)</td>
<td>0.042</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>83 (35.32)</td>
<td>152 (64.68)</td>
<td></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrioid adenocarcinoma</td>
<td>67 (30.88)</td>
<td>150 (69.12)</td>
<td>0.53</td>
</tr>
<tr>
<td>Clear cell</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>5 (33.33)</td>
<td>10 (66.67)</td>
<td></td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>2 (66.67)</td>
<td>1 (33.33)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14 (40)</td>
<td>21 (60)</td>
<td></td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>69 (30.4)</td>
<td>158 (69.6)</td>
<td>0.059</td>
</tr>
<tr>
<td>II</td>
<td>4 (57.14)</td>
<td>3 (42.86)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>15 (38.46)</td>
<td>24 (61.54)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>2 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>49 (35)</td>
<td>91 (65)</td>
<td>0.21</td>
</tr>
<tr>
<td>2</td>
<td>18 (23.68)</td>
<td>58 (76.32)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19 (34.55)</td>
<td>36 (65.45)</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor location</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fundus</td>
<td>75 (35.21)</td>
<td>138 (64.79)</td>
<td>0.13</td>
</tr>
<tr>
<td>Lower uterine segment</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Uterus-Lower uterine segment</td>
<td>8 (21.05)</td>
<td>30 (78.95)</td>
<td></td>
</tr>
<tr>
<td>Cervix</td>
<td>5 (26.32)</td>
<td>14 (73.68)</td>
<td></td>
</tr>
<tr>
<td><strong>Lymphovascular space invasion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>71 (33.65)</td>
<td>140 (66.35)</td>
<td>0.65</td>
</tr>
<tr>
<td>Yes</td>
<td>19 (30.16)</td>
<td>44 (69.84)</td>
<td></td>
</tr>
<tr>
<td><strong>Depth of invasion (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>(n = 85)</td>
<td>15 (0-100)</td>
<td>(n = 169)</td>
</tr>
<tr>
<td>(n = 169)</td>
<td>15 (0-100)</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor size - final (cm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Includes 0 if not detectable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>(n = 91)</td>
<td>3 (0-10.5)</td>
<td>(n = 187)</td>
</tr>
<tr>
<td>(n = 187)</td>
<td>3 (0-11)</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>30 (33.33)</td>
<td>60 (66.67)</td>
<td>0.89</td>
</tr>
<tr>
<td>&lt;= 2 cm</td>
<td>61 (32.45)</td>
<td>127 (67.55)</td>
<td></td>
</tr>
</tbody>
</table>
1517 - Poster Session
Comparison of posterior rectal dissection techniques during rectosigmoid colon resection as part of cytoreductive surgery in patients with epithelial ovarian cancer: Close rectal dissection versus total mesorectal excision
S.J. Chang, J.H. Son, T.W. Kong, J. Paek and H.S. Ryu. Ajou University School of Medicine, Suwon, South Korea

Objective: The rectosigmoid colon is the bowel segment most frequently resected during cytoreductive surgery for ovarian cancer. Compared with colorectal cancer, ovarian cancer seldom accompanies deeper invasion to the surrounding mesorectal tissue. The aim of this study was to evaluate the clinical outcomes of close rectal dissection (CRD) compared with the total mesorectal excision (TME) as the technique of posterior rectal dissection procedure during rectosigmoid colectomy as part of cytoreductive surgery in patients with epithelial ovarian cancer.

Method: We retrospectively reviewed medical records of 163 patients who received posterior rectal dissection for rectosigmoid resection including low anterior resection or subtotal colectomy in ovarian cancer surgery from 2006 to 2018. The TME technique was performed mainly by colorectal surgeons and the CRD technique by an experienced gynecologic oncology surgeon preserving the mesorectal tissue and vascular supply. Patients were divided into the TME group and the CRD group. Clinical characteristics including perioperative outcomes were analyzed.

Results: A total of 163 ovarian cancer patients received rectosigmoid colon resection; 142 (87.1%) patients had low anterior resection, and 21 (12.9%) had subtotal colectomy. The median age was 56 years, and 140 (85.9%) patients had FIGO stage III–IV disease. Rectosigmoid colectomy was performed at the time of primary debulking surgery, interval debulking surgery, and secondary/tertiary debulking surgery in 95 (58.3%), 61 (37.4%), and 7 (4.3%) patients, respectively. Among the patients, 87 (53.4%) received CRD and 76 (46.6%) received TME as the technique of posterior rectal dissection. In both groups, severity of the disease and status of residual disease were not statistically different (FIGO stage, \( P = 0.390 \), residual disease, \( P = 0.412 \)). However, postoperative anastomotic leakage (\( P = 0.045 \)) and postoperative prolonged ileus (>7 days, \( P = 0.055 \)) were higher in the TME group. The length of hospital stay was longer in the TME group (\( P = 0.096 \)).

Conclusion: TME is not necessary for rectosigmoid colon resection in ovarian cancer surgery. Considering the perioperative outcomes, CRD may be an alternative technique with less perioperative morbidity and equivalent oncologic outcomes.

1518 - Poster Session
A comparison of postoperative morbidity in open versus robotic-assisted interval debulking surgery for epithelial ovarian cancer patients following neoadjuvant chemotherapy

Objective: Neoadjuvant chemotherapy (NACT) is a commonly used treatment strategy for advanced epithelial ovarian cancer (EOC) in poor surgical candidates or women with unresectable disease. Minimally invasive surgery has been shown to improve clinical outcomes compared to laparotomy in the surgical management of malignant adnexal tumors in other settings. However, there are limited data regarding the robotic approach (RA) for interval surgical debulking (IDS) compared to laparotomy (OA). Thus, we compared 30-day postoperative complications in EOC patients undergoing OA versus RA IDS after NACT.

Method: EOC patients treated with 3–6 cycles of NACT with platinum/taxane chemotherapy followed by IDS from 2014 to 2017 at a single tertiary care center were included in this retrospective cohort study. Demographic and clinical data were abstracted from medical records. Surgical complications were defined using the Clavien-Dindo Classification (CDC). Statistical analyses were performed using \( \chi^2 \), Wilcoxon rank-sum, and Student \( t \) tests.

Results: Overall, 207 EOC patients were identified with the study cohort comprising 50 patients undergoing NACT with IDS. Of these, 13 (26.0%) underwent RA and 37 (74.0%) underwent OA. In the OA group, 48.6% (18/37) had at least 1 postoperative complication compared to 7.7% (1/13) in the RA group (\( P = 0.01 \)). In the RA group, the single complication occurrence was bacteremia (CDC grade II). In the OA group, the most common complication was ileus requiring NG placement (5/37, 13.5%, CDC grade II), and the most severe required ICU admission and surgical take-back (2/37, 5.4%, CDC grade IVb). Operative EBL was less in the RA group (159.2 mL vs 311.4 mL, \( P = 0.05 \)), as well as rate of transfusion (15.4% vs 59.5%, \( P = 0.02 \)). Length of stay was shorter in the RA group (1.4 days vs 5.2 days, \( P < 0.001 \)). There was no significant difference in readmission (1 vs 7, \( P = 0.61 \)) or ICU admission (0 vs 3, \( P = 0.70 \)) between the RA and OA groups.
Conclusion: For EOC patients undergoing IDS after NACT, a robotic approach was associated with reduced perioperative risk versus laparotomy when comparing 30-day postoperative complications, operative EBL, rate of transfusion, and length of hospital stay. In appropriately selected patients, robotic-assisted IDS may be a safe surgical option for patients undergoing NAC.

1519 - Poster Session
Hysterectomy at the time of risk-reducing surgery for patients with BRCA mutations
S. Gordhandas, K.D. Vasquez, M.P. Ruiz, N. Talukdar, T.A. Caputo, K.M. Holcomb, M.K. Frey and E. Chapman-Davis; aWeill Cornell Medical College, New York, NY, USA, bNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, cWeill Cornell Medicine, New York, NY, USA

Objective: Risk-reducing salpingo-oophorectomy (RRSO) is standard management for women with BRCA1/2 mutations; however, the role of concurrent hysterectomy (CH) remains controversial. Shu et al. published the largest study addressing endometrial cancer among BRCA carriers in 2016, suggesting an increased risk of serous uterine cancer in women with BRCA1 mutations. Currently, there is no official recommendation for CH with RRSO; however, many practitioners offer this combined procedure. We sought to review our institutional experience with RRSO and CH.

Method: Data were abstracted from the medical record for all patients at a single institution with BRCA1 and BRCA2 mutations undergoing RRSO between 2003 and 2018. Univariate tests were applied based on variable distribution, and associations between categorical variables were evaluated by χ² tests or Fisher exact tests as appropriate for category size.

Results: One hundred fifty-five patients underwent RRSO (BRCA1 81, 53%; BRCA2 71, 45%; BRCA1 and BRCA2 3, 2%). Thirty-six patients underwent CH at time of RRSO (23%). The median age at time of RRSO was 48 years (range 33–73 years). Patients undergoing CH were significantly younger than those undergoing RRSO alone (45 vs 49.5, P = 0.01). Seventy-two patients (46%) had a history of breast cancer (42% of patients with breast cancer had CH vs 50% of patients without breast cancer who had CH, P = 0.45). CH was more common among women with BRCA1 mutations versus BRCA2 mutations (31% vs 14%, P = 0.02). Uterine cancer risk reduction was the most common indication for CH (13, 36%) (Figure 1). Following the 2016 publication, CH was significantly more common compared to prior, 43% versus 18%, respectively (P = 0.006).

Conclusion: Despite lack of official recommendation for CH among BRCA1 carriers, CH for uterine cancer risk reduction is becoming more common over time. With improved uptake of genetic testing resulting in identification of an expanding population of BRCA1/2 carriers coupled with a growing emphasis on cancer risk-reduction strategies, data on the oncologic benefits and safety of CH are critical.

Fig. 1. Reason for hysterectomy
**1520 - Poster Session**  
Optimizing gynecologic surgery for the morbidly obese patient with a surgical safety pathway

*The University of Texas Southwestern Medical Center, Dallas, TX, USA, New York University School of Medicine, New York, NY, USA*

**Objective:** Obesity is a significant risk factor for perioperative morbidity and mortality. Outcomes can be improved with standardized protocols including preventive measures and specialized surgical equipment and personnel. We sought to evaluate the outcomes of a surgical safety protocol for all patients with a body mass index (BMI) of ≥40 undergoing planned gynecologic surgery.

**Method:** The high BMI pathway (HBP) was developed by a multidisciplinary team of gynecologic oncologists (GO), anesthesiologists, and ancillary surgical and nursing staff based on the most current recommendations from the literature and instituted as a quality improvement project. It was implemented for all morbidly obese patients undergoing planned surgery by a GO. Patients who underwent robotic hysterectomies (RH) on the HBP from 2016 to 2018 were compared with consecutive historical controls who had RHs from 2014 to 2015 prior to HBP implementation. Standard two-sided statistical analyses were performed.

**Results:** Of the 80 patients who successfully completed surgery on the HBP, 55 patients (68.8%) underwent RH and were included in this analysis. These patients were compared to 48 historical controls prior to HBP initiation. There were no significant differences in patient factors or perioperative times between pre- and post-HBP groups (Table 1). Since implementing HBP, there were fewer anesthesia-related complications (ARC) in HBP patients after RH compared to pre-HBP patients (0.0% vs 12.5%, *P* = 0.02). Among the control patients with ARC, two had respiratory distress requiring pharmacologic intervention, two had increased postoperative nausea and vomiting, and two had intractable postoperative pain. There was also an increase in same-day discharges among patients who underwent RH (65.5% vs 41.7%, *P* = 0.03), but no difference in hospital readmission rates. There were no differences in intraoperative and 30-day postoperative complications.

**Conclusion:** A HBP to improve perioperative safety for morbidly obese patients undergoing RH resulted in fewer ARCs and increased rates of same-day discharge without increasing perioperative times or intraoperative and postoperative complications.

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>HBP (n = 55)</th>
<th>Pre-HBP (n = 48)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range, years)</td>
<td>58.0 (26-78)</td>
<td>60.5 (26-87)</td>
<td>0.4</td>
</tr>
<tr>
<td>BMI, median (kg/m²)</td>
<td>45.3 (40.2-64.5)</td>
<td>43.8 (40.0-64.3)</td>
<td>0.2</td>
</tr>
<tr>
<td>ASA score (n, %)</td>
<td>9 (16.4%)</td>
<td>17 (35.4%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cancer diagnosis (n, %)</td>
<td>35 (63.6%)</td>
<td>31 (64.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>OR setup time, median (range, minutes)</td>
<td>44.0 (10.0-74.0)</td>
<td>43.5 (15.0-87.0)</td>
<td>0.4</td>
</tr>
<tr>
<td>Operating time, median (range, minutes)</td>
<td>175.0 (45.0-444.0)</td>
<td>182.0 (61.0-379.0)</td>
<td>0.8</td>
</tr>
<tr>
<td>Anesthesia time, median (range, minutes)</td>
<td>226.5 (79.0-505.0)</td>
<td>250.0 (121.0-433.0)</td>
<td>0.2</td>
</tr>
<tr>
<td>Total OR time, median (range, minutes)</td>
<td>243.0 (89.0-542.0)</td>
<td>248.0 (118.0-441.0)</td>
<td>0.6</td>
</tr>
<tr>
<td>Conversion to laparotomy (n, %)</td>
<td>1 (1.8%)</td>
<td>2 (4.2%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Intraoperative complications (n, %)</td>
<td>3 (5.5%)</td>
<td>1 (2.1%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Anesthesia complications (n, %)</td>
<td>0 (0.0%)</td>
<td>6 (12.5%)</td>
<td>0.02</td>
</tr>
<tr>
<td>30-day postoperative complications (n, %)</td>
<td>10 (18.2%)</td>
<td>9 (18.8%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Same-day discharge</td>
<td>36 (65.5%)</td>
<td>20 (41.7%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

BMI: body mass index  
HBP: high BMI pathway  
ASA: American Society of Anesthesiologists  
OR: operating room

Table 1. Demographic and surgical characteristics of the study population
Clinical outcomes of patients with endometrioid ovarian cancer

Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: To evaluate patient characteristics, surgical/adjuvant treatment strategies, and oncologic outcomes of a large, single-institution cohort of patients diagnosed with primary endometrioid epithelial ovarian cancer (EEOC).

Method: We identified all patients treated for EEOC at our institution between January 2002 and September 2017 who either underwent initial surgery at our institution or presented to our institution within 3 months of initial surgery. Data were abstracted from medical records. All cases were reviewed by an expert gynecologic pathologist. Appropriate statistical methods were applied.

Results: We identified 212 patients; all underwent primary surgery. Median age at diagnosis was 52 years (range 20–88 years). Disease stage distribution was as follows: stage I, n = 145 (68%); stage II, n = 47 (22%); stage III/IV, n = 0 (9%). Endometriosis was seen on pathology in 128 patients (60%). Seventy-five (35%) patients had a synchronous endometrioid endometrial cancer, of which 80% were stage IA. Complete surgical staging was performed in 101 (48%) patients, and 181 (85%) and 148 (70%) patients underwent pelvic and paraaortic lymphadenectomy, respectively. Eight (5%) patients had positive pelvic lymph nodes, and 6 (4%) had positive paraaortic lymph nodes. Nearly all patients (n = 176, 97%) underwent complete gross resection. Postoperative chemotherapy was administered in 123 (60%) patients, while 56 (28%) had no additional treatment. The 5-year PFS rate was 83% (95% CI 76.6–87.8), and the 5-year OS rate was 92.7% (95% CI 87.7–95.8). On survival analysis, age, stage, and full surgical staging were associated with improved 5-year PFS, but only younger age at diagnosis was associated with improved 5-year OS (P < 0.001). Compared to observation alone, chemotherapy did not improve 5-year PFS or OS for patients with stage I disease (HR = 1.15, 95% CI 0.46–2.9; HR = 1.19, 95% CI 0.3–4.83, respectively). See Figure 1.

Conclusion: Outcomes for patients with EEOC are favorable. In this cohort, age, stage, and full surgical staging were associated with improved 5-year PFS. There was no benefit of chemotherapy for patients with stage I disease.
Site of residual disease does not predict recurrence patterns in epithelial ovarian cancer patients undergoing primary debulking surgery

B.L. Manning-Geist, A. Greer, A.A. Gockley, A. Melamed, R.S. Berkowitz, N.S. Horowitz, M.G. del Carmen, W.B. Growdon and M.J. Worley Jr.

Massachusetts General Hospital, Boston, MA, USA, Brigham and Women’s Hospital/Brigham and Women’s Hospital/Brigham and Women’s Hospital/Massachusetts General Hospital/Boston, MA, USA, Harvard Medical School, Boston, MA, USA, Dana-Farber Cancer Institute, Boston, MA, USA, Harvard University, Boston, MA, USA, Massachusetts General Hospital/Brigham and Women’s Hospital/Brigham and Women’s Hospital/Brigham and Women’s Hospital/Boston, MA, USA
Objective: To examine the effect of residual disease volume on timing and pattern of recurrence among patients with advanced-stage epithelial ovarian/fallopian tube/primary peritoneal carcinoma after primary debulking surgery (PDS) and adjuvant chemotherapy.

Method: Medical records of patients with FIGO stage IIIC and IV epithelial ovarian/fallopian tube/primary peritoneal carcinoma undergoing PDS between January 2010 and July 2015 were reviewed. Patient demographics, operative characteristics, anatomic site of residual disease and recurrent disease, as well as outcome data, were collected. Categorical variables were compared with the Fischer exact test, and continuous variables were compared with the rank sum test.

Results: Of 240 patients who underwent PDS, median age was 63.4 years (range 29.7–85.0 years). The majority of patients (83.8%) had stage IIIC disease, and serous histology was most common (76.7%). After PDS, 94 (39.2%) had complete surgical resection (CSR); 41 (17.1%) had ≤1 cm of residual disease confined to a single location (≤1 cm SL); 67 (27.9%) had ≤1 cm of residual disease in multiple locations (≤1 cm ML); and 38 (15.8%) were suboptimally (SO) debulked. Patients with CSR or ≤1 cm SL were significantly more likely to recur after 12 months or not at all, compared to patients with ≤1 cm ML (80.9% and 73.2% vs 58.2%, \( P = 0.035 \)). There were no significant differences in site of recurrence (\( P = 0.095 \)) or presence of ascites at recurrence (\( P = 0.105 \)) when CSR, ≤1 cm SL, and ≤1 cm ML were compared. Overall, 64.9% of patients undergoing CSR recurred in a single site compared to 50.0% of patients with ≤1 cm SL and 44.8% of patients with ≤1 cm ML; however, this difference did not maintain statistical significance (\( P = 0.09 \)).

Conclusion: After PDS, the PFS interval was longer in patients with CSR or ≤1 cm SL residual disease. Patients with CSR tended to recur in a single anatomic location rather than in multiple locations; however, this did not reach statistical significance.

1523 - Poster Session
Use of bowel preparation does not reduce postoperative infectious morbidity following minimally invasive or open hysterectomies
E. Kalogera, H.K. Van Houten, L.R. Sangaralingham, B.J. Borah and S.C. Dowdy. Mayo Clinic, Rochester, MN, USA

Objective: Bowel preparation (BP) is a controversial element within enhanced recovery protocols, and literature investigating its efficacy in gynecologic surgery is scarce. Our aim was to determine whether mechanical bowel preparation (MBP) alone, oral antibiotics (OA) alone, or a combination is associated with decreased rates of surgical site infections (SSI) or anastomotic leaks (AL) compared to no bowel preparation following benign or malignant hysterectomy.

Method: We identified women who underwent hysterectomy between January 2006 and July 2017 using OptumLabs, a large U.S. commercial health plan database. Inverse propensity weighing was used separately for benign and malignant groups to balance baseline characteristics. Primary outcomes of 30-day SSI, AL, and major morbidity were assessed using multivariate logistic regressions that adjusted for race, Census region, household income, diabetes, and other unbalanced variables following propensity weighting.

Results: A total of 224,687 hysterectomies (benign 186,299, malignant 38,388) were identified. Median age was 45 years for the benign and 54 years for the malignant cohort. Type of surgery was as follows: benign, laparoscopic/robotic 27.2%, laparotomy 32.7%, vaginal 40.2%; and malignant, laparoscopic/robotic 28.8%, laparotomy 47.6%, vaginal 23.6%. Bowel resection was performed in 0.4% of the benign and 2.8% of the malignant cohort. Type of bowel preparation was as follows: benign, none 93.8%, MBP only 4.6%, OA only 1.1%, MBP plus OA 0.5%; and malignant, none 87.2%, MBP only 9.6%, OA only 1.8%, MBP plus OA 1.4%. Use of BP did not result in decreased SSI, ALs, or major morbidity following benign or malignant hysterectomy (Table 1A). Among malignant abdominal hysterectomies, there was no difference in the rates of infectious morbidity between MBP alone, OA alone, or MBP plus OA compared to no BP (Table 1B).

Conclusions: BP does not protect against SSI or major morbidity following benign or malignant hysterectomy, regardless of surgical approach, and may be safely omitted.
Compliance with a sepsis care pathway and its impact on morbidity and mortality in gynecologic oncology patients


Objective: To evaluate the implementation of a hospital-wide sepsis care pathway and a rapid response team (code sepsis) on the outcomes of gynecologic oncology patients.

Method: All gynecologic oncology patients who had a code sepsis initiated from October 2016 to May 2018 were included in this retrospective chart review. The code sepsis bundle includes an order set and evaluation by a rapid response team to facilitate prompt initiation of treatment. All patients who had a code sepsis were automatically reported to the QI team. Their records were reviewed by the sepsis coordinator to monitor if and when each component of the order set was performed, and feedback was provided to the managing team. Three- and 6-hour bundle elements include cultures, lactic acid, broad-spectrum antibiotics, fluid resuscitation, and short-interval reassessment. Code sepsis is triggered by any clinical suspicion of sepsis and can be initiated by physicians or nursing staff. In addition, qSOFA or early warning score in association with concern for infection are also utilized to trigger a code sepsis. A qSOFA score is calculated with a score ≥2 and concern for infection, triggering an automatic code sepsis. The qSOFA score assigns 1 point for respiratory rate >22, systolic blood pressure <100, and altered mental status. Incidence of code sepsis, compliance with bundle elements, and observed to expected (O:E) mortality rate were evaluated.

Results: There were 1,236 admissions during the study period. Overall the rate of code sepsis was low, with 77 patients (6.2%) triggering the evaluation. Of these, 81.2% had a clear source of infection identified by either culture or imaging study. The most commonly identified sources were urosepsis (40.3%), bacteremia (22.1%), pneumonia (16.9%), and intra-abdominal infection (15.6%). Of all patients, 83.1% had sepsis present on admission, and nearly half were admitted through the emergency department. Compliance with sepsis bundle elements was high (>75%) for all elements except for the 6-hour reassessment, which was 48.1% (Table 1). The O:E for mortality was 0.06.

Conclusion: In this study, compliance with code sepsis bundle elements was high, and 80% of patients who triggered a code sepsis evaluation had a source identified. O:E mortality in this group of gynecologic oncology patients with sepsis was extremely low.
1525 - Poster Session
Surgical morbidity associated with learning curve of sentinel lymph node technique in early stage cervical cancer treatment
G. Accorsi, R. Reis, R. Schmidt, L. Nobrega, A.C.M. Beolchi, M.A. Vieira and C. Andrade. aHospital de Câncer de Barretos - Fundação Pio XII, Barretos, Brazil, bBarretos Cancer Hospital, Barretos, Brazil

Objective: It is still common for some institutions with a low volume of oncological cases to avoid introducing the use of sentinel lymph node (SLN) technique in cervical cancer treatment, mainly because of fear of increased morbidity related to the technique. Our objective is to determine the morbidity of introducing the SLN technique during the learning curve.

Method: All patients stage IA2 to IB2 cervical cancer managed with surgical procedure from May 2013 to January 2018 were included. Groups were compared according 30-day morbidity and detection rate using Mann–Whitney and Fisher exact tests; statistical significance was \( P < 0.005 \). All the data recovered were stored in the REDCAP database.

Results: We identified 149 patients; 55 patients underwent LDN plus SLN and 94 LDN only. There was no difference between the groups regarding surgical time, blood loss, and hospital stay. Intraoperative lesions occurred in 13.8% and 12.7% \(( P = 0.84)\) in the LDN and LDN plus SLN, respectively. Thirty-day complications also show no significant difference (14.9% vs 14.5%, \( P = 0.95)\). However, the overall incidence of lower limb-lymphedema (LLL) was 23.6% for LDN plus SLN and 5.4% LDN only (OR = 5.4, \( P = 0.002\), 95% CI 1.82–16.2, \( P < 0.001\)). During our learning curve we identified at least one lymph node in 96.4% (53) of the patients. From 110 mapped hemi-pelvis, 84.5% (93) had a stained lymph node. Only 2.8% had metastases to lymph nodes, and all were detected only by SLN. There were no false negative results. See Table 1.

Conclusion: There was no statistical difference in intraoperative lesions or 30-day complications during the period of sentinel biopsy learning curve. But it is interesting to note an increased risk for LLL during the addition of sentinel biopsy. And sentinel biopsy shows an excellent accuracy in detect lymph node metastasis.

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**Table 1. Sepsis Bundle Adherence**

<table>
<thead>
<tr>
<th>Component</th>
<th>Percent Completed</th>
</tr>
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<tbody>
<tr>
<td>Code Sepsis bundle initiated</td>
<td>84.4%</td>
</tr>
<tr>
<td>1st lactic acid</td>
<td>84.4%</td>
</tr>
<tr>
<td>Broad-spectrum antibiotics</td>
<td>89.6%</td>
</tr>
<tr>
<td>Blood/urine cultures</td>
<td>75.3%</td>
</tr>
<tr>
<td>IV fluid bolus</td>
<td>81.8%</td>
</tr>
<tr>
<td>6-hour reassessment</td>
<td>48.1%</td>
</tr>
<tr>
<td>Source identified</td>
<td>81.2%</td>
</tr>
</tbody>
</table>
Results: Among 460 women meeting inclusion criteria, 365 had mFI scores of 0–1, 62 had scores of 2, and 33 had scores of 3+. Mean age was 63.9 years. Overall mean time from surgery to chemoinitiation was 37.9 days. The number of days between surgery and chemoinitiation increased with increasing frailty, with 36.5 days for the not frail group, 38.8 days for the moderate frailty group, and 53.8 days for the high frailty group ($P = 0.001$). Time to chemoinitiation of 42 days or more was experienced by 23% of the not frail, 27% of the moderate frailty, and 64% of the high frailty groups ($P < 0.001$). The mean overall survival was 47.7 months in the not frail group and 46.8 months in the moderate frailty group, but only 33.2 months in the high frailty group ($P = 0.041$). See Figure 1.

Conclusion: High Modified Frailty Index scores lead to a delay between surgery and chemotherapy initiation. Ability to predict delays in chemoinitiation could allow oncologists to consider neoadjuvant chemotherapy, prehabilitation before surgery and improved preoperative counseling in high-risk patients.

Fig. 1. Kaplan-Meier Time to Chemoinitiation
operation time (238.7 ± 53.9 minutes vs 259.8 ± 56.6 minutes, P < 0.01), less bleeding (113.3 ± 98.2 ml vs 174.4 ± 126.7 ml, P < 0.01), more lymph nodes harvested (32.8 ± 11.1 vs 30.8 ± 10.4, P = 0.028), shorter catheterization time (10.2 ± 8.8 days vs 16.0 ± 16.2 days, P < 0.01), and lower incidence of postoperative hydronephrosis (2.3% vs 6.0%, P = 0.044). Compared with the LRH group, the NPS-LRH group was favorable in term of lower incidence of long-term frequent urination (4.9% vs 13.8%, P < 0.01), urge incontinence (0.5% vs 6.7%, P < 0.01), bladder sensation loss (0.8% vs 4.6%, P = 0.028), and straining to void (7.3% vs 12.8%, P = 0.063). The incidence of constipation in the NPS-LRH group was significantly lower than that in the LRH group (4.9% vs 10.7%, P = 0.029). There was no significant difference in disease-free survival (P = 0.769) and overall survival between the two groups (P = 0.973). See Figure 1.

Conclusion: As a simplified Type C1 procedure, NPS-LRH is safe and feasible, and improves postoperative function of bladder and rectum.
60% and 32% of the time, respectively, while upper abdominal was done 68% and 51% of the time, respectively. Estimated blood loss (median 600 mL PDS, 300 mL IDS) and operative time (median 362.5 minutes PDS, 268 minutes IDS) were both higher for PDS ($P < 0.001$, for both).

**Conclusion:** Patients undergoing IDS after NACT require bowel surgery over a third of the time and upper abdominal surgery over half of the time. The need for radical surgical resection is not obviated by NACT; thus advanced surgical skills must be maintained.

**Fig. 1.** Frequencies of specific procedures performed at the time of PDS and IDS for women with advanced stage epithelial ovarian cancer (*denotes statistical difference).

**1529 - Poster Session**

**Increased surgical volume and complexity are associated with an improved complete gross resection rate while maintaining patient safety for women undergoing primary surgical treatment of ovarian cancer**

O.T. Filippova¹, K. Long Roche⁵, B. Maddy⁶, O. Zivanovic⁵, G.J. Gardner⁵, Y. Sonoda⁵, D.S. Chi⁵ and V. Broach⁵, ⁶Memorial Sloan Kettering Cancer Center, New York, NY, USA, ⁵Weill Cornell Medical College, New York, NY, USA

**Objective:** To evaluate the trends in surgical complexity and morbidity among women undergoing primary debulking surgery (PDS) for advanced-stage ovarian cancer.

**Method:** All women who underwent PDS for stage IIIC or IV epithelial ovarian cancer at our institution between 2005 and 2017 were included. Patients were grouped by calendar year of PDS. Outcomes of interest were obtained via medical record review: total number of PDS cases per year, complete gross resection (CGR) rate (CGR/total PDS), rate of grade 3+ surgical complications (complications/total PDS), estimated blood loss (EBL), operative time, and length of hospital stay (LOS). Trends were assessed via linear trendlines and square of the correlation coefficient ($R^2$). The $R^2$ represents the fit of the trendline to the data.

**Results:** Over 12 years, 1,040 patients were identified and included. **Figure 1** represents the trends in the outcomes of interest, as well as linear trendlines and $R^2$. The number of PDS per year steadily increased ($R^2 = 0.79$) between 2005 ($n = 43$) and 2017 ($n = 112$). The CGR rate also steadily increased ($R^2 = 0.92$), from 14% in 2005 to 81% in 2017. Since 2010, the rate of neoadjuvant chemotherapy has stayed stable, about 30%. EBL data were only reliably available since 2011, but remained stable (600 mL in 2011 and 775 mL in 2017, $R^2 = 0.08$). Operative time increased during the study period ($R^2 = 0.72$), from 3.6
hours in 2005 to 6.5 hours in 2017. Despite increased surgical complexity to obtain CGR during the study period, the rates of surgical complications (19% in 2005, 11% in 2017, $R^2 = 0.38$) and hospital stay (8 days in 2005, 7 days in 2017, $R^2 = 0.12$) have not increased.

**Conclusion:** The complexity and extent of surgical resection has increased over the past decade without compromising surgical morbidity. Increased volume and experience are associated with improved CGR rates and enhanced patient safety and recovery.

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**Fig. 1.** Trends in PDS characteristics between 2005 and 2017 – CGR rate (%), rate of grade 3 or higher surgical complications within 30 days (%), total number of PDS per year, as well as respective linear trendlines and $r^2$ values (dashed lines represent $r^2$ values <0.7).

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**1530 - Poster Session**

**Comparison of perioperative and demographic variables among exceptional and poor responders ovarian cancer patients managed with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC)**


**Objectives:** Analysis of demographic, surgical, and perioperative characteristics of patients with advanced epithelial ovarian cancers (EOC) was used to identify predisposing factors and determine correlations between neoplastic behavior and survival outcomes.

**Methods:** Review of a retrospective database of patients with advanced EOC who underwent cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) was carried out. Inclusion criteria were histopathologic proven advanced-stage EOC, CRS/HIPEC performed by the same surgical team, residual disease <2.5 mm, and ≥6 months follow-up. Patients were divided based on treatment, CRS/HIPEC or neoadjuvant chemotherapy followed by CRS/HIPEC. All patients received adjuvant chemotherapy. Median overall survival (OS) was calculated for each group; the upper quartile defined
exceptional responders and the lowest quartile, poor responders. Survival analysis was calculated by Kaplan-Meier estimates. Demographic, surgical, and perioperative variables were analyzed using χ², Fischer test, or MUT.

**Results:** Forty-six patients were included, yielding exceptional (n = 11) and poor (n = 11) responders. Median OS for the exceptional responders was not reached, while it was 1.4 years for poor responders (P = <0.001) (Figure 1). Median PFS was 3.1 years and 1.2 years, respectively (P = 0.054). No differences in race, age, BMI, genetic mutations, smoking status, preoperative tumor markers, albumin, or C-reactive protein were noted. Poor responders had a higher incidence of histopathologically confirmed ovarian cancer (P = 0.035), rather than primary peritoneal or fallopian tube cancer. Peritoneal Cancer Index, completeness of cytoreduction score, positive lymph node status, and length of surgery had no statistical value. No significant difference was observed in surgical complications, readmissions, recurrence, or patient status.

**Conclusion:** Demographic, surgical, or perioperative characteristics do not appear to influence the neoplastic behavior of this cohort of EOC responders. Pathophysiology may be affected by molecular or genetic processes; this has yet to be determined. Molecular profiling should be considered to triage patients who will benefit from surgical management, which we intend to perform.

**Fig. 1.** Kaplan-Meier survival estimation of exceptional and poor responders

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**1531 - Poster Session**

**Electrolyte and hematological abnormalities in patients with advanced epithelial ovarian cancers treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) or neoadjuvant chemotherapy plus CRS/HIPEC**


**Objective:** To compare hematological abnormalities, electrolyte derangements, and readmission rates in patients with epithelial ovarian cancers (EOC) initially treated with either cytoreductive surgery and hyperthermic intraperitoneal chemotherapy CRS/HIPEC or neoadjuvant chemotherapy plus CRS/HIPEC.

**Method:** Review of a retrospective database of patients with advanced EOC who were initially treated with CRS/HIPEC (n = 21) or neoadjuvant chemotherapy plus CRS/HIPEC (n = 20) was carried out. Variables analyzed included presence of anemia, leukocytosis, thrombocytosis, hyponatremia, hypokalemia, hypocalcemia, and nutritional status as measured by albumin, in the following periods: preoperative, 24 hours postoperative, and 1 week, 1 month, and 2 months postoperative. Readmissions within 2 months were compared. Survival analysis was calculated from the day of the procedure to the last day of follow-up. Variables were analyzed using the dichotomous χ² test, and survival was calculated based on Kaplan-Meier estimates.

**Results:** Patients developed similar laboratory abnormality patterns, regardless of treatment (Table 1). Anemia, leukocytosis, and hypocalcemia developed at 24 hours postoperative. At 1 week postoperative, anemia and hypocalcemia persisted, and at 1 and 2 months postoperative, only anemia remained. The presence of anemia in the preoperative period was statistically significant in the neoadjuvant plus CRS/HIPEC group (P = 0.002). Readmission rates were equal in both groups. Patients who
received neoadjuvant chemotherapy plus CRS/HIPEC were more likely to be readmitted with small bowel obstructions. Median PFS was 40.8 months in the CRS/HIPEC group and 11.8 months in the neoadjuvant chemotherapy plus CRS/HIPEC group \((P = 0.005)\). Overall survival did not show a statistically significant difference \((P = 0.953)\); however, there was a trend favoring the CRS/HIPEC group.

**Conclusion:** Patients treated with neoadjuvant chemotherapy plus CRS/HIPEC are not at a higher risk of bone marrow toxicity or electrolyte imbalances. Readmission due to small bowel obstruction might be related to microscopic residual disease and may have an impact on the OS and PFS of these patients.

**Table 1.** Comparison of laboratory results in patients with CRS/HIPEC vs Neoadjuvant Chemotherapy plus CRS/HIPEC

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1532 - Poster Session

**Fistula formation in cervical cancer patients treated with bevacizumab: Pharmacovigilance after GOG 240**


**Objective:** Bevacizumab (BEV) is an effective adjunct therapy for women with recurrent/metastatic cervical cancer, but was associated with a 15% rate of fistula formation in the pivotal phase III study. Use of BEV has increased since FDA approval for this indication. We sought to evaluate the incidence, possible risk factors, and outcomes associated with fistula development in women with cervical cancer receiving BEV outside of a clinical trial.

**Method:** This retrospective cohort study included women with recurrent/metastatic cervical cancer treated with BEV at 1 academic institution between 2005 and 2015. Women with fistulae present prior to BEV initiation were excluded. The primary outcome was development of fistula or perforation. Univariate and multivariate analyses were used to identify independent factors predictive of fistulae using a Cox regression model.

**Results:** A total of 103 women who received BEV were analyzed, and 19 (18.4%) developed fistulae, 11 vesicovaginal and 9 rectovaginal. There were 96 patients (93%) who received radiation prior to treatment with BEV. Fourteen (14%) and 90 (87%) patients received BEV for primary and recurrent treatment, respectively. Median BEV treatment length was 71 days (range 1–1,402 days). There was no difference in age, stage, race, BMI, pre-existing hypertension, pelvic disease, smoking status, or performance status between patients who did and did not develop fistulae. On univariate analysis, chronic kidney disease was associated with fistula development (10.5% vs 0%, \(P = 0.03\)). There was no correlation between fistula formation and BEV dose, length of BEV treatment, number of BEV cycles, radiation treatment dose or intent, recurrence site, or treatment for primary versus recurrent cancer. Of the 19 patients who developed fistulae, 5 were continued on BEV after fistula diagnosis. Increasing dose of BEV \((P = 0.12)\) and current smoking \((P = 0.06)\) had nonsignificant trends to earlier fistula formation. When adjusted for stage and time to recurrence, fistula development was significantly associated with longer overall survival \((HR = 2.5, 95\% CI 1.1–5.4)\).

**Conclusion:** The rate of fistula formation in our nonstudy population was similar to that found in GOG 240. Chronic kidney disease was the only risk factor significantly associated with fistula development. Fistula development was associated with longer OS and should be investigated further.

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1533 - Poster Session

**Utilization of epidural analgesia at time of hysterectomy for gynecologic malignancies: An analysis of the American...**
**Objective:** The adverse effects of epidural analgesia in gynecologic oncology patients have not been well characterized. This study aims to identify the rate of 30-day complications following epidural use in these patients.

**Method:** A retrospective cohort study was conducted utilizing the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. Women ≥18 years who underwent hysterectomy for a gynecologic malignancy from 2014 to 2016 were included. Using a calculated propensity score derived from a multiple logistic regression model to control for confounding factors, women who received epidural analgesia (EA) were matched in a 1:2 ratio with patients who did not receive EA. \( \chi^2 \) and independent t tests were used to compare the cohorts.

**Results:** A total of 16,702 patients were identified who underwent a hysterectomy for a gynecologic malignancy. A total of 855 patients (5.1%) received both general anesthesia and an epidural for analgesia. The 1:2 propensity-matched samples included 1,710 patients in the non-EA group. Patient characteristics between propensity-matched EA and non-EA groups were similar. There was no difference in operative time between the groups (183 vs 189 minutes, \( P = 0.105 \)). Overall 30-day complication rate was higher in EA groups (56.8% vs 52.3%, \( P = 0.03 \)). However, when complication rates for individual major complications were compared, only the rate of blood transfusion was higher in the EA group (28.9% vs 26.3%, \( P = 0.04 \)). There were no significant differences in rate of pneumonia, UTI, DVT, or PE between groups. Length of stay was statistically significantly longer in the EA group compared to the non-EA group (5.6 days vs 5.0 days, respectively, \( P = 0.02 \)).

**Conclusion:** EA is associated with a higher 30-day complication rate and longer hospitalization. However, when analyzed individually, only the proportion of patients requiring blood transfusions was higher in the EA than in the non-EA group. The use of epidural analgesia at time of hysterectomy for a gynecologic malignancy continues to be a safe option for perioperative pain management. Its impact on hospital length of stay needs to be considered.

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**1534 - Poster Session**

**Safety of same day discharge for minimally invasive hysterectomy for endometrial cancer**

A. Praiss\(^a\), L. Chen\(^b\), C.M. St. Clair\(^c\), A.I. Tergas\(^d\), F. Khoury Collado\(^e\), J.Y. Hou\(^f\) and J.D. Wright\(^a,b\). \(^a\)Columbia University, New York, NY, USA, \(^b\)Columbia University College of Physicians and Surgeons, New York, NY, USA, \(^c\)New York-Presbyterian/Columbia University Medical Center, New York, NY, USA

**Objective:** Same-day discharge is increasingly common for women who undergo minimally invasive (MIS) hysterectomy. For women with endometrial cancer, there are limited data describing the safety of same-day discharge. We examined the trends and outcomes of same-day discharge for women with endometrial cancer who underwent MIS hysterectomy.

**Method:** The National Surgical Quality Improvement Program database was used to identify patients who underwent MIS hysterectomy based on endometrial cancer from 2011 to 2016. The cohort was limited to women discharged on the day of surgery/postoperative day (POD 0) or POD 1. Multivariate models were used to examine clinical, demographic, and procedural characteristics associated with discharge on POD 0. Multivariate models were also developed to examine the association between same-day discharge and readmission.

**Results:** A total of 133,615 patients who underwent minimally invasive hysterectomy were identified, including 12,892 (87.6%) discharged on POD 1 and 1,828 (12.4%) discharged on POD 0. The rate of same-day discharge rose from 5.6% in 2011 to 16.3% in 2016 (\( P < 0.001 \)). In a multivariate model, more recent year of surgery was associated with same-day discharge (Table 1). Older women, those with COPD, and women with hypertension on medications were less likely to have a same-day discharge. Similarly, obese women were 15% less likely to have a same-day discharge than normal weight women (RR = 0.85, 95% CI 0.75–0.97). In contrast, Hispanic women versus white (RR = 1.61, 95% CI 1.35–1.92) and those who underwent lymphadenectomy (RR = 1.17, 95% CI 1.07–1.29) were more likely to have a same-day discharge. The readmission rate was 2.3% in those women discharged on the day of surgery compared to 3.1% in women discharged on POD 1 (\( P = 0.051 \)). In a multivariate model there was no association between same-day discharge and readmission (RR = 0.99, 95% CI 0.71–1.38). Among women discharged on POD 0, a longer operative time and the occurrence of a perioperative complication were associated with readmission.
**Conclusion:** Same-day discharge for MIS hysterectomy for endometrial cancer is increasing. In selected patients there is no increased risk of readmission with same-day discharge.

Table 1.

<table>
<thead>
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<th>Variable</th>
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<td>Mortality</td>
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<td>Age</td>
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<tr>
<td>Weight</td>
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<td>Race</td>
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</tr>
<tr>
<td>Education</td>
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*Significant at 0.05.*

Logistic regression model for predictors of MIS hysterectomy discharge, adjusted for age, race, education, and weight.

Table 1. Multivariate analysis of predictors of same-day discharge for MIS hysterectomy for endometrial cancer. Results are presented as OR and 95% CI in parentheses. Significant p-values are indicated in bold. MIS, minimally invasive surgery; LND, lymph node dissection; BMI, body mass index; ASA, American Society of Anesthesiologists score; NAC, neoadjuvant chemotherapy; NED, no evidence of disease; DCS, discharge criteria score; OMS, operative time; OMS, operative time.

<table>
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<th>Predictor</th>
<th>OR (95% CI)</th>
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<td>Age</td>
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<tr>
<td>Race</td>
<td>0.74 (0.51, 0.87)</td>
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<tr>
<td>Education</td>
<td>0.87 (0.51, 0.83)</td>
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<tr>
<td>Weight</td>
<td>0.35 (0.35, 0.65)</td>
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</table>

*Significant at 0.05.*
**1535 - Poster Session**

**Prediction of perioperative complications after robotic-assisted radical hysterectomy for cervical cancer using the modified surgical Apgar score**

Y.T. Kim, J.W. Kim and G.H. Lee. **Yonsei University College of Medicine, Seoul, South Korea**

**Objective:** Although there has been marked development in surgical techniques, there is no easy and fast method of predicting complications in minimally invasive surgeries. We evaluated whether the modified surgical Apgar score (MSAS) could predict perioperative complications in patients undergoing robotic-assisted radical hysterectomy.

**Method:** All patients with cervical cancer undergoing robotic-assisted radical hysterectomy at our institution between January 2011 and May 2017 were included. Their clinical characteristics were retrieved from their medical records. The surgical Apgar score (SAS) was calculated from the estimated blood loss, lowest mean arterial pressure, and lowest heart rate during surgery. We modified the SAS considering the lower blood loss typical of robotic surgeries. Perioperative complications were defined using a previous study and the Clavien-Dindo classification and subdivided into intraoperative and postoperative complications. We analyzed the association of perioperative complications with low MSAS.

**Results:** A total of 138 patients were divided into 2 groups: with \( n = 53 \) and without \( n = 85 \) complications. According to the Clavien-Dindo classification, 49 perioperative complications were classified under grade I (73.1%); 13 under grade II (19.4%); and 5 under grade III (7.5%); and 0 under both grade IV and grade V. Perioperative complications were significantly associated with surgical time \( (P = 0.026) \). The MSAS had a correlation with perioperative complications \( (P = 0.047) \). The low MSAS \( (\text{MSAS} \leq 6, n = 52) \) group had significantly more complications \( (40, 76.9\%, P = 0.01) \). Intraoperative complications were more correlated with a low MSAS than were postoperative complications \( (1, 1.2\%, \text{vs} 21, 40.4\%, P < 0.001; 13, 15.1\%, \text{vs} 25, 48.1\%, P = 0.29, \text{respectively}) \). We also analyzed the risk-stratified MSAS in 3 subgroups: low (MSAS, 7–10), moderate (MSAS 5–6), and high risks (MSAS, 0–4). The prevalence of intraoperative complications significantly increased as the MSAS decreased \( (P = 0.01) \).

**Conclusion:** This study was consistent the concept that the intuitive and simple MSAS might be more useful in predicting intraoperative complications than in predicting postoperative complications in minimally invasive surgeries, such as robotic-assisted radical hysterectomy for cervical cancer.

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**1536 - Poster Session**

**ERAS interactive audit system (EIAS) gynecologic oncology project: Audit of international surgical practice informs perioperative care**

L. Wijka, B. Pacheb, A.D. Altmanc, L.L. Williamsd, K.M. Eliase, J. McGeef, T. Wellsg, K.M. Holcombh, C. Achtarib, O. Ljungqvista, S.C. Dowdy1 and G. Nelsonj. **aÖrebro University Hospital, Örebro, Sweden, bLausanne University Hospital, Lausanne, Switzerland, cWinnipeg Health Sciences Centre, Winnipeg, MB, Canada, dCentennial Medical Center, HCA Healthcare, Nashville, TN, USA, eBrigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA, fLondon Health Sciences Centre, London, ON, Canada, gRoyal Alexandra Hospital, Edmonton, AB, Canada, hWeill Cornell Medical College, New York, NY, USA, iMayo Clinic, Rochester, MN, USA, jTom Baker Cancer Centre, Calgary, AB, Canada**

**Objectives** To evaluate the influence of compliance to enhanced recovery after surgery (ERAS) gynecologic/oncology guideline elements on postoperative outcomes following elective surgery in an international cohort.

**Method:** The study comprised 2,101 patients undergoing elective gynecologic/oncology surgery between January 2011 and November 2017 in 10 hospitals across Canada, the United States, and Europe. Patient demographics, surgical/anesthesia details, and ERAS protocol compliance elements (pre-, intra- and postoperative phases) were entered into the ERAS Interactive Audit System (EIAS). Surgical complexity was stratified according to the Aletti scoring system (low vs medium/high). The following covariates were accounted for in the analysis: age, BMI, smoking status, presence of diabetes, ASA class, FIGO stage, preoperative chemotherapy, radiotherapy, operating time, surgical approach (open vs minimally invasive), and intraoperative blood loss. The primary endpoints were hospital length of stay (LOS) and complications. Negative binomial regression was used to model LOS as a function of compliance score and covariates.

**Results:** Patient demographics were median age 55 years, 35.5% obese (BMI >35 kg/m²), 15% smokers, and 26.7% ASA Class III–IV. Final diagnosis was malignant in 49% of patients. Laparotomy was used in 75.9% of cases (the remainder underwent minimally invasive surgery). The majority of cases (86%) were of low complexity (Aletti score ≤3). Of those patients with ovarian cancer, 40% had a medium/high complexity surgery (Aletti score 4–11). Mean LOS overall was 2.9 days in the low
group and 6.3 days in the medium/high complexity group. Adjusted logistic regression associated higher total ERAS guideline compliance with lower odds of prolonged hospitalization in both low \((P < 0.001)\) and medium/high complexity \((P = 0.002)\) groups (see Figure 1). For every 1 unit increase in total ERAS guideline compliance score, the odds of total complications was 0.88 times lower \((P < 0.05)\) among low complexity patients.

**Conclusion:** Audit of surgical practices using EIAS demonstrates that compliance with ERAS guidelines results in a synergistic improvement in clinical outcomes. These findings suggest that ERAS principles are best implemented as a bundle, rather than as individual interventions.

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**Fig. 1.** Impact of compliance to ERAS guideline elements on length of stay in medium/high and low complexity surgery.

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**1537 - Poster Session**

**Sentinel lymph node mapping alone compared to more extensive lymphadenectomy in patients with uterine serous carcinoma**

D. Basaran\(^a\), S.F. Bruce\(^b\), J.J. Mueller\(^a\), V. Broach\(^a\), K.A. Cadoo\(^a\), R.A. Soslow\(^a\), N.R. Abu-Rustum\(^a\) and M.M. Leitao Jr.\(^a\). \(^a\)Memorial Sloan Kettering Cancer Center, New York, NY, USA, \(^b\)Abington Memorial Hospital, Abington, PA, USA

**Objective:** We sought to compare survival among patients with uterine serous carcinoma (USC) who underwent a sentinel lymph node (SLN) mapping alone to survival among those who underwent more extensive lymphadenectomy (LND).

**Method:** Patients who underwent primary surgical treatment for newly diagnosed USC at our institution between January 1, 1996, and December 31, 2017, were retrospectively reviewed. Patients were allocated to 1 of 3 cohorts: those who underwent SLN mapping alone \((n = 81)\), unilateral pelvic LND with or without SLN mapping \((\text{uniLND}, n = 38)\), or bilateral pelvic LND with or without SLN mapping \((\text{biLND}, n = 283)\). We also assessed the role of paraaortic nodal dissection (PALND). Overall survival (OS) was estimated using the Kaplan-Meier method, and curves were compared with the log rank test.

**Results:** We identified 402 patients. Median follow-up was 23 months (range 1–96 months) in the SLN, 23 months (range 4–121 months) in the uniLND, and 58 months (range 0–265 months) in the biLND cohorts. In patients with stage I–II disease \((n = 267)\), the 2-year OS rates were 96.7% (SE ± 3.3) for the SLN, 100% (SE NE) for the uniLND, and 90.5% (SE ± 2.2) for the biLND cohorts \((P = 0.99)\). The 2-year OS rate in patients with stage I–II disease who underwent a PALND was 91.2% (SE ± 2.4) compared to 93.9% (SE ± 2.4) for those who did not \((P = 0.36)\). In stage III disease \((n = 109)\), the 2-year OS rates were 74.8% (SE ± 11.0) for the SLN, 100% (SE NE) for the uniLND, and 79.9% (SE ± 4.5) for the biLND cohorts \((P=0.44)\). The 2-year OS rate in patients with stage III disease who underwent a PALND was 82.7% (SE ± 5.0) compared to 76.8% (SE ± 6.5) for those who did not \((P = 0.17)\). See Figure 1.

**Conclusion:** SLN mapping alone does not appear to compromise survival in patients with stage I–III USC. PALND was not associated with an improved OS. Extensive LND in patients with uterine-confined USC appears unnecessary.


**Objective:** Efforts to decrease the risk of cancer in the high-risk population of *BRCA1* and *BRCA2* mutation carriers have focused on risk-reducing salpingo-oophorectomy (RRSO) and bilateral mastectomies. Many *BRCA* carriers undergo multiple prophylactic surgeries during their lifetime, requiring a variety of subspecialists and multiple trips to the operating room. We sought to evaluate the role of combined surgeries (CS) and single surgeries (SS) among *BRCA* mutation carriers.

**Method:** Data were abstracted from medical records for all patients at a single institution with *BRCA1/2* mutations undergoing RRSO with or without additional gynecologic or breast-related surgeries from 2003 to 2018. SS was defined as RRSO alone, and CS was defined as RRSO with breast surgery under the same anesthesia event. Univariate analyses were performed based
on variable distribution. Associations between categorical variables were evaluated by \( \chi^2 \) or Fisher exact tests as appropriate for category size.

**Results:** A total of 155 patients were identified, 81 (53%) diagnosed with BRCA1, 71 (45%) with BRCA2, and 3 (2%) with both BRCA1 and BRCA2 mutations. Overall, 22\% (\( n = 34 \)) underwent CS, including 20\% (\( n = 16 \)) of BRCA1 patients and 25\% (\( n = 18 \)) of BRCA2 patients (\( P = 0.5 \)). The mean age at the time of CS versus SS was not different (47 vs 50 years, \( P = 0.1 \)). The most common type of CS was RRSO with breast reconstruction (Figure 1). Patients who underwent CS versus SS were significantly more likely to have a diagnosis of breast cancer (65\% vs 37\% respectively, \( P = 0.02 \)). The average surgical time was longer for CS versus SS (214 minutes vs 102 minutes, \( P < 0.001 \)). Hospital stay following surgery was longer for CS versus SS (1 day vs 0.4 day, \( P = 0.01 \)). Among the patients who underwent SS, 76\% still required more than 2 additional surgeries.

**Conclusion:** Only 22\% of BRCA carriers underwent CS in our cohort, and the majority already had a diagnosis of breast cancer. Although the surgical time was longer for CS, the overall hospital stay was relatively short. With the increasing trend toward early detection and national guidelines encouraging risk-reducing surgeries, the overall number of procedures undertaken among this group should be expected to rise. Consideration should be given to provide opportunities for CS in an effort to reduce cost and limit anesthesia exposure.

**Fig. 1.** Type of combined surgery

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**1539 - Poster Session**  
**Postoperative survival analysis of laparotomy versus robotic interval debulking in epithelial ovarian cancer patients following neoadjuvant chemotherapy**  

**Objective:** Neoadjuvant chemotherapy (NACT) is a commonly utilized strategy for primary treatment of advanced epithelial ovarian cancer (EOC) in women with unresectable disease or poor surgical candidates. Minimally invasive surgery offers several advantages, including decreased postoperative morbidity, shorter hospitalization, and faster recovery; however, there are limited published data to demonstrate that these advantages are also balanced by non-inferior survival or improved time to adjuvant chemotherapy. Thus, we sought to assess whether there is a difference in time to disease recurrence as well as time to adjuvant chemotherapy in robotic (RA) versus open (OA) interval debulking surgeries (IDS).

**Method:** We performed a retrospective review of EOC patients diagnosed and treated with 3–6 cycles of NACT with platinum and taxane chemotherapy followed by IDS from January 2014 through February 2017. Demographic, clinicopathologic, and treatment data were recorded from review of records from a single tertiary care institution. Survival analysis with Kaplan-Meier estimation with Wilcoxon rank test for significance was utilized for statistical assessment.

**Results:** Forty-seven patients met inclusion criteria from the initial cohort of 207 patients. Thirteen (28\%) underwent RA, and 34 (72\%) underwent OA IDS. In comparing the RA versus OA groups, there were nonsignificant differences in age (60 vs 64 years, \( P = 0.23 \)), rate of stage IV disease (62\% vs 44\%, \( P = 0.29 \)), rate of debulking to no gross residual (46\% vs 59\%, \( P = 0.43 \)), and rate of complete response on preoperative imaging (31\% vs 12\%, \( P = 0.12 \)). There was no difference in time to disease recurrence in the RA versus OA groups (8.9 vs 7.9 months, \( P = 0.7 \)). There was no difference in time to adjuvant chemotherapy between the two arms (29.7 vs 33.3 days, \( P = 0.97 \)).

**Conclusion:** Preliminary data suggest safety of RA IDS compared to OA IDS with no difference in time to recurrence or in time to initiation of chemotherapy. Future research should explore whether minimally invasive surgery could be used to shorten time to re-initiation of chemotherapy, which could improve oncologic outcomes.
**1540 - Poster Session**

**High intermediate risk endometrioid endometrial carcinoma: Prognostic value of isolated tumor cells and role of adjuvant therapy**


**Objective:** The aims of this study were (1) to assess the prognostic value of isolated tumor cells (ITCs) in patients with high intermediate-risk (HIR) endometrioid endometrial carcinoma (EEC) compared to node-negative disease, and (2) to assess the impact of adjuvant therapy in patients with HIR EEC who are node negative or have ITCs.

**Method:** We identified all patients surgically treated at our institution for newly diagnosed endometrial cancer from January 2009 to December 2016. Only patients with endometrioid histology who met GOG 99 HIR criteria were included. All cases had nodal evaluation. For this analysis, we selected patients with node-negative disease or with ITCs, diagnosed using H&E with or without cytokeratin staining, as well as those diagnosed with cytokeratin staining alone (CK+). Disease-specific survival (DSS) was estimated using Kaplan-Meier estimates and curves compared with log rank test.

**Results:** A total of 208 patients met inclusion criteria. The median age was 67 years (range 31–92 years). SLN mapping with or without additional lymphadenectomy was performed in 195 patients (93.7%). There were 159 patients (76.4%) who were node negative and 49 (23.6%) with ITCs identified (32 H&E, 17 CK+). Median follow-up was 33.2 months (range 0–103 months). The 3-year DSS was 95.9% (SE ±1.8) for node negative compared to 100% (SE NE) for ITCs both as a group and individually (H&E vs CK+, $P = 0.2$ and $0.3$, respectively). Of the total cohort, 20 patients (9.6%) received no further postoperative therapy. The 3-year DSS was 100% (SE NE) for these 20 cases compared to 96.7% (SE ±1.5) for those who received postoperative therapy ($P = 0.4$). Postoperative chemotherapy with IVRT and/or WPRT was used in 62 patients (29.8%), and radiation therapy (RT) (IVRT and/or WPRT) alone was used in 122 patients (58.6%). The 3-year DSS was 98.2% (SE ±1.8) for chemotherapy with or without RT compared to 96.7% (SE ±1.9) for RT alone ($P = 0.1$).

**Conclusion:** In HIR EEC, ITCs are not associated with a worse outcome. Survival in the small group of patients who received no adjuvant therapy was comparable to that of the rest of the group. The type and benefit of adjuvant postoperative therapy in HIR EEC with negative nodes or ITCs remain unclear.

**1541 - Poster Session**

**Our ideas and devices to establish stable and precise procedures in robotic radical trachelectomy for cervical cancer patients**

H. Kobayashi. *Faculty of Medicine, Kagoshima University, Kagoshima, Japan*

**Objective:** To preserve fertility of cervical cancer patients, we started abdominal radical trachelectomy (ART) in 2005 and accomplished successful surgical outcome with only 1 recurrence in almost 200 cases slightly including abdominal modified-radical or simple trachelectomy. With almost 40% of patients who attempted to conceive after their abdominal trachelectomies, almost 40% of them became pregnant. However, many cases needed artificial insemination by husband or artificial reproductive technology to be pregnant. Therefore, we started to shift ART to robotic RT (RRT), which may bring not only minimal invasiveness but also increased spontaneous pregnancy rate due to reducing postoperative adhesion.

**Method:** This study started under Institutional Review Board approval, and we performed all RRT cases as well as ART cases after receiving written informed consent.

**Results:** As intraoperative safety management in ART, we determined to confirm metastatically negative sentinel lymph node (SN) and at least 5 mm cancer-free space from the amputated edge of resected cervix. To reproduce them in RRT, as for SN detection using both tracers of radioisotope and indocyanine green (ICG), hot nodes were identified by a gamma probe through the assistant port, and bright nodes were detected by the near-infrared light camera in ‘Firefly’ system of da Vinci Xi. As for cancer-free margin, we continued direct contact of UST probe to uterine cervix from the beginning of ART, since the precise decision for cervical amputation level is so important. The same procedure was successfully accomplished even in RRT by a very small UST probe through the assistant port. Both prophylactic cervical cerclage to the ‘neocervix’ and anastomosis between preserved uterus and vagina were easily performed by the robotic system rather than conventional laparoscopy.

**Conclusion:** RRT is expected to bring less invasiveness, shorter hospitalization, and higher postoperative pregnancy rate, compared with ART. Moreover, the procedures in ART seem to be easily reproducible in RRT rather than laparoscopy.
1542 - Poster Session
Outcomes and patient perspectives following implementation of tiered opioid prescription guidelines in gynecologic surgery
G.E. Glaser\textsuperscript{a}, E. Kalogera\textsuperscript{a}, D.S. Ubl\textsuperscript{b}, E.B. Habermann\textsuperscript{b} and S.C. Dowdy\textsuperscript{a}. \textsuperscript{a}Mayo Clinic, Rochester, MN, USA, \textsuperscript{b}Mayo Clinic College of Medicine, Rochester, MN, USA

Objective: To report the impact of implementing standardized guidelines for opioid prescriptions after gynecologic surgery and describe patient perspectives before and after guideline implementation for those undergoing laparotomy for ovarian cancer.

Method: Patients undergoing gynecologic surgery for malignant or benign conditions between October 2017 and May 2018 were prescribed opioids at discharge using a tiered guideline approach (Table 1). Opioid prescriptions were converted to oral morphine equivalents (OME) and compared to consecutive historical controls (March 2017–October 2017). A subset of opioid-naïve ovarian cancer laparotomy patients was surveyed regarding postoperative opioid consumption and patient experience.

Results: A total of 624 women in the tiered guideline cohort (37 complex cytoreduction, 91 laparotomy including hysterectomy, and 496 minimally invasive surgery) were compared with 748 historical controls. Following implementation, 82.2% of prescriptions met guidelines. Mean OME prescribed decreased from 178.2 to 80.8 ($P \leq 0.0001$) with no change in opioid refills (9.0% vs 7.2%, $P = 0.24$). For the subset of 75 patients with ovarian cancer who responded to the survey (91.5% response rate), 100% of study patients and 92% of controls felt very or somewhat satisfied with pain control ($P = 0.24$), despite a post-guidelines median of 75 OME prescribed and 21.6% receiving no opioids at discharge ($P = 0.002$). The median (IQR) OMEs consumed after discharge was 15 (0–75) in the study group versus 24 (0–135) in controls, and 39% and 43% consumed no opioids, respectively. The mean time between surgery and cessation of opioid use was <1 week in both groups; there was no change in patients' perceptions of the appropriateness of their opioid prescriptions ($P = 0.51$). More than 75% of patients kept their remaining opioids rather than dispose of them.

Conclusion: Reducing prescribed opioids after gynecologic surgery using tiered guidelines according to surgical procedure did not increase opioid refills or worsen patients’ perceptions of postoperative pain. Even after laparotomy, very little opioid was required over a short duration after dismissal. The large proportion of patients who did not properly dispose of leftover opioids further highlights the need to avoid overprescribing.

Table 1. Opioid Prescribing Guidelines

<table>
<thead>
<tr>
<th>Tiers</th>
<th>Definitions</th>
<th>Prescribing Guidelines</th>
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<tbody>
<tr>
<td>Tier 0</td>
<td>• Hysteroscopy</td>
<td>• No opioids</td>
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<td></td>
<td>• No opioids used in hospital</td>
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<tr>
<td>Tier 1</td>
<td>• Minimally invasive procedures</td>
<td>• Oxycodone 5mg x 10 tablets</td>
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<td></td>
<td>• Laparotomies</td>
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<td></td>
<td>• Vulvar Procedures</td>
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<tr>
<td>Tier 2</td>
<td>• Increase to next dose level</td>
<td>• Individualize based on inpatient needs (3 times 24 hour cumulative opioid requirement day before discharge)</td>
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<tr>
<td></td>
<td>• Increased frequency of dosing</td>
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<td>• Pain consult</td>
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1543 - Poster Session
Predictors of acute hematologic toxicity in women receiving extended-field chemoradiation for cervical cancer
aThe University of Chicago Medicine, Chicago, IL, USA, bUniversity of Illinois at Chicago, Oak Park, IL, USA

Objective: Cervical cancer patients considered to be at high risk for paraaortic lymphatic involvement may receive extended-field chemoradiation (EF-CRT), with inclusion of the paraaortic region. Increased radiation to bone marrow (BM) may heighten hematologic toxicity (HT) and have an impact on timely delivery of chemotherapy and radiation. Factors (including radiation planning metrics) associated with HT in this setting have not been well-studied.

Method: This is a retrospective analysis of women treated with EF-CRT from 2012 to 2018. Patients were treated with platinum-based chemotherapy. Extended-field was defined using the superior border at the renal veins. Factors including age, BMI, race, Charlson comorbidity index (CCI), chemotherapy cycles delivered, and nadirs for white blood cell (WBC) count, absolute neutrophil count (ANC), hemoglobin (Hb), and platelet (Plt) count were obtained for each patient. BM metrics collected include V5Gy, V10, V15, V20, V25, V30, V35, V40, and V45 (where VxGy is defined as percentage of BM volume receiving x Gy). HT was defined as any grade 2+ (RTOG criteria) or grade 2+ thrombocytopenia and neutropenia (T/N). Univariate (UVA) and multivariate analysis (MVA) were performed using logistic regression; comparison of nadirs was performed using the Student t test.

Results: A total of 41 women were identified. UVA showed no significant association between HT and age, BMI, or CCI. Race (black vs other) was associated with any grade 2+ HT (OR = 10.9, 95% CI 1.2–133); V15Gy ≥ 85% was associated with grade 2+ T/N (5.1% vs 17.9%, P = 0.02, OR = 8.2, 95% CI 1.5–35). Previously described radiation metrics (V10Gy ≥ 90%, V20Gy ≥ 75%, V40Gy ≥ 37%) revealed no association with HT. On MVA including race and V15Gy, only V15Gy ≥ 85% was associated with grade 2+ T/N (OR = 8.1, 95% CI 1.4-46.9). Women with grade 2+ T/N were more likely to require chemotherapy reduction (14.6% vs 19.5%, P = 0.003). V15Gy ≥ 85% was also associated with lower WBC (2.27 vs 1.61, P = 0.043), Hb (9.23 vs 8.18, P = 0.040), and Plt nadirs (117.8 vs 83.1, P = 0.039).

Conclusion: Acute HT in patients receiving EF-CRT was associated with BM radiation dose and race but not with age, BMI, or CCI. Limiting BM V15Gy to <85% may prevent acute HT and the need for chemotherapy reduction.

1544 - Poster Session
Choosing the right preoperative imaging: Prognostic value of PET-CT compared to CT for preoperative planning in high risk histology endometrial carcinoma
J.D. St. Laurenta,b and W.B. Growdona,c.
aMassachusetts General Hospital, Boston, MA, USA, bBrigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA, cHarvard Medical School, Boston, MA, USA

Objective: GOG 0233 demonstrated positron emission tomography (PET) with computed tomography (CT) scan provided high sensitivity for detecting lymph node metastasis and peritoneal disease compared to CT alone. The objective of this study was to characterize how preoperative PET-CT associates with patient outcomes compared to CT in high-risk endometrial carcinoma.

Method: With Institutional Review Board approval, we conducted a multicenter review of all cases of epithelial endometrial cancer from January 2008 through December 2015. Clinical variables pertaining to surgical procedure, preoperative imaging modality, and further medical therapy were collected for all patients with high-risk histology (serous, clear cell, carcinosarcoma, or high-grade endometrioid). Recurrence and survival were correlated utilizing parametric and nonparametric testing. Survival was calculated utilizing the Kaplan-Meier and Cox proportional hazards methodologies.

Results: We identified 2,263 women treated for endometrial cancer, 556 with high-risk histology. A total of 88 (3.2%) underwent preoperative PET-CT compared to 110 (4.4%) who received CT alone. Use of PET-CT utilization increased from 2.4% in the 2008–2011 era to 22% in the 2012–2015 era (P < 0.001). PET-CT demonstrated FDG-avid lymph nodes, extraterine spread, peritoneal disease, or distant metastasis in 37 women (42%) compared to positive findings in 33 (30%) with preoperative CT alone. PET-CT had a PPV of 96% for nodal metastasis based on surgical staging compared to 60% for CT alone. PET-CT was associated with a sensitivity of 85% for detecting peritoneal disease compared to 40% by CT alone, although the NPV for peritoneal disease was similar at 98% and 97%, respectively. There were significantly more stage IV diagnoses (47% vs 16%, P < 0.05) in the PET-CT compared to CT group. Women with a negative PET-CT (n = 64) had longer median OS not yet reached compared to 7.2 years (HR = 2.4, P < 0.001) in the group with no preoperative imaging (n = 380).
Positive PET-CT for extra uterine disease, however, had a markedly worsened OS (2.9 years, HR = 7.6/3.1, P < 0.001) compared to both groups (Figure 1).

Conclusion: Compared to CT alone, PET-CT offered robust prognostic information and was associated with a higher sensitivity for detecting peritoneal disease with a high negative predictive value for lymph node metastasis when used for preoperative staging of high-risk histology endometrial carcinoma.

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1545 - Poster Session
Obstetric outcomes after abdominal radical trachelectomy (ART) for early-stage cervical cancers: A retrospective analysis of 341 cases in China
X. Li and X. Wu. Fudan University Shanghai Cancer Center, Shanghai, China

Objective: We sought to report the obstetric outcomes of young patients undergoing abdominal radical trachelectomy (ART) for the treatment of early-stage cervical cancers in China.

Method: We retrospectively reviewed 341 patients with stage IA–IB1 cervical cancer who underwent ART between April 2004 and September 2017 in China.

Results: Of the 341 patients who underwent ART, 325 had their fertility preserved. There were 200 women (61.5%) who did not plan to get pregnant after ART, 85.0% of them because of childbearing before surgery (55.0%) or being unmarried (30.0%). Among 125 women who attempted to conceive, 23 achieved a total of 26 pregnancies. Seventy-four patients had infertility problems; 35 conceived with assisted reproductive technologies, and 13 of them succeeded. Cervical stenosis (22, 25.9%) and fallopian tube obstruction (18, 21.2%) were the most frequent causes of fertility treatment after surgery. Among patients who conceived, 3 patients had first-trimester miscarriage and 5 patients had second-trimester miscarriage. Two women elected to have pregnancy termination, and 1 was currently pregnant. A total of 15 pregnancies reached the third trimester, and 80% of them ended at more than 36 weeks of gestation. Among 13 cases of miscarriages and preterm births, 7 occurred in patients without cerclage placed. In 10 cases of full-time birth, 8 patients had cerclage placed.

Conclusion: The majority of patients did not attempt to conceive or experienced infertility after ART in China. Assisted reproductive technology should be encouraged to improve the fertility rate. Cerclage is effective in the prevention of miscarriage and preterm labor.

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1546 - Poster Session
The value of incremental standardization for patients undergoing large bowel resection within an established enhanced recovery after surgery (ERAS) pathway
Objective: To investigate whether incremental standardization within an established enhanced recovery after surgery (ERAS) pathway further decreases postoperative ileus and length of stay (LOS) among patients undergoing large bowel resection (LBR) for gynecologic cancer.

Method: A modified ERAS pathway targeting accelerated bowel function, including use of a standardized bowel regimen for patients with and without LBR, postoperative chewing gum, and alvimopan for LBR was adopted division-wide. Consecutive patients undergoing complex cytoreductive surgery under the modified ERAS (November 2017–April 2018, n = 64) were compared to historic controls treated under the original ERAS pathway (July 2013–June 2014, n = 121). The χ², Wilcoxon rank sum, and Levene tests for comparison of variances were utilized.

Results: Patient characteristics were comparable between cases under the modified ERAS and historic controls with the exception of a higher proportion of LBR in ERAS cases (46.9% vs 29.8%, P = 0.021). A higher proportion of ERAS cases had bowel function return on postoperative day 1 (32.8% vs 19%, P=0.036). Although overall ileus rates were comparable between ERAS cases and historic controls (17.2% vs 19.8%, P = 0.66), when focusing on patients undergoing LBR, there was a significant decrease in ileus rates in ERAS cases compared to historic controls (13.3% vs 36.1%, P = 0.035). Among LBR patients, mean LOS was not significantly lower in ERAS cases compared to historic controls (6.3 vs 7.7 days, median 6 days for both groups, P = 0.29); however, ERAS cases had a statistically significant decrease in LOS variability compared to historic controls (IQR 5–7 vs 5–10.5 days, P = 0.014). Postoperative morbidity after LBR was significantly lower in ERAS cases (36.7% vs 63.9%, P = 0.028). No anastomotic leaks were observed in either group.

Conclusion: Within an established ERAS pathway, further optimization of perioperative care for patients with gynecologic cancer undergoing LBR resulted in additional reductions in time to return of bowel function, lower rates of postoperative ileus, and fewer complications. Variation in LOS among the study cohort was also reduced, demonstrating the value of standardization and continuous improvement.

1547 - Poster Session
Efficacy of TAP blocks following ovarian cancer surgery
S.P. Bisch, S.J. Glaze, A. Cameron, J. Nation and G. Nelson. aTom Baker Cancer Centre, Calgary, AB, Canada, bUniversity of Calgary, Calgary, AB, Canada

Objective: The aim of this study was to characterize the magnitude and duration of effect of transversus abdominis plane (TAP) blocks on postoperative opioid use in ovarian cancer cytoreductive surgery.

Method: All patients undergoing ovarian cancer cytoreductive surgery under an enhanced recovery after surgery (ERAS) protocol from November 2016 to June 2017 were assessed. Data on patient demographics, type of block used, surgical characteristics, and outcomes were abstracted from the ERAS Interactive Audit System and the electronic health record. Opioid use was abstracted from the electronic health record and converted to morphine equivalent daily dose (MEDD in milligrams of IV morphine equivalent). Mean opioid use between 24 and 48 hours postoperatively was analyzed using multiple linear regression modelling correcting for type of block and use of an epidural.

Results: From November 2016 to June 2017 49 patients underwent cytoreductive surgery for ovarian cancer. Twenty-nine of these patients received surgical TAP blocks prior to fascial closure. Mean opioid use from 24 for 48 hours was reduced by 62% among patients with TAP blocks compared to no regional analgesia (15.9 mg vs 25.58 mg MEDD, P = 0.0316). From 48 to 72 hours opioid use was decreased by 56% for patients with TAP blocks compared to no TAP block (8.58 mg vs 15.23 mg MEDD); however, this number was no longer statistically significant (P = 0.2683). There was no difference in mean opioid use from 0 to 24 hours postoperatively.

Conclusion: In patients on an ERAS protocol, TAP blocks significantly decrease opioid use at 24–48 hours postoperatively following cytoreductive surgery for ovarian cancer. This effect persists beyond 48 hours but is no longer statistically significant.

1548 - Poster Session
Pelvic exenteration for gynecologic malignancies: Experiences of National Cancer Center Korea
H.K. Chang, W.K. Shin, H.J. Yoo, M.C. Lim, S. Kang, S.S. Seo and S.Y. Park. aNational Cancer Center Korea, Goyang-si, South Korea, bChungnam National University, Daejeon, South Korea
Objective: We sought to determine survival in patients with gynecologic malignancies after pelvic exenteration (PE) for curative management.

Method: Between July 2001 and December 2016, a total of 136 patients who underwent PE for gynecologic malignancies at our single institution were included retrospectively. Clinical status and demographic information were obtained by medical records. We had analyzed 61 patients with recurrent cervical cancer who underwent PE in 2012; however, we reanalyzed with the large sample size.

Results: PE was performed with 136 patients with gynecologic malignancies (123 cervical cancer, 13 vaginal cancer). Median age was 56 years (range 25–75 years), and median interval to PE since primary diagnosis was 20 months (range 1–300 months). Types of PE were total PE (83 cases, 61%), anterior PE (48 cases, 35%), and posterior PE (5 cases, 4%). Postoperative complications occurred in 76 cases (56%). Median OS and disease-free survival (DFS) were 40 months (range 26–74 months) and 27 months (range 14–57 months), respectively. The 5-year OS and DFS were 43% and 39%, respectively. Median follow-up was 33 months. Affecting factors for OS were resection margin status, pelvic sidewall involvement, and rectal involvement. See Figure 1.

Conclusion: The 5-year OS was encouraging, although the rate of postoperative complications was high. Despite improvements in surgical apparatus, survival outcomes have not significantly improved since 2001. Further investigation and another strategy are needed for better survival outcomes.

1549 - Poster Session
Surgical approach for interval debulking after neoadjuvant chemotherapy for treatment of advanced-stage ovarian cancer
K.B. Dugan\textsuperscript{a}, B. McNamara\textsuperscript{b}, L. Lu\textsuperscript{c}, B. Litkouhi\textsuperscript{d}, M. Azodi\textsuperscript{e}, P.E. Schwartz\textsuperscript{e}, E.S. Ratner\textsuperscript{e}, G. Menderes\textsuperscript{a} and D.A. Silasi\textsuperscript{a}, \textsuperscript{a}Yale University School of Medicine, New Haven, CT, USA, \textsuperscript{b}UCSF School of Medicine, San Francisco, CA, USA, \textsuperscript{c}Yale School of Public Health, New Haven, CT, USA

Objective: The aim of this study was to evaluate surgical and oncologic outcomes, particularly PFS, in patients who had interval debulking surgery (IDS) performed by laparoscopy compared to those who underwent laparotomy.

Method: This was a retrospective matched cohort study of patients who underwent IDS from 2013 to 2017 at our institution. Laparoscopy and laparotomy cases were identified, and matching variables were coded. Controls (laparotomy) were matched to cases (laparoscopy) by an investigator blinded to outcome. Patients were matched on 6 covariates: age group, tumor
Results: There were 24 laparoscopy IDS cases matched on the 6 specified parameters to 24 laparotomy IDS cases. The median surgical date was earlier for the laparotomy cases, and median follow-up time for disease-free patients was 46 versus 19 months ($P = 0.005$). Mean CA-125 at diagnosis was higher, but not statistically so, for the laparotomy group (2,022 vs 1,573, $P = 0.62$) as well as at the time of IDS (97 vs 27, $P = 0.37$). Laparotomy cases were more likely to have residual disease at IDS (83% vs 58%, $P = 0.06$). Median PFS was longer for patients undergoing laparotomy for IDS (35.5 vs 19.5 months, $P = 0.06$). Mean time to initiation of adjuvant chemotherapy was the same (37.7 vs 37.9 days). See Figure 1.

Conclusion: There was a large trend toward increased PFS in women who underwent laparotomy for IDS, although this did not achieve statistical significance. This may reflect a less extensive abdominal survey and dissection in laparoscopy or a confounder not controlled for in this analysis. Patients who underwent laparoscopic IDS did not initiate adjuvant chemotherapy earlier, which has been considered a benefit of minimally invasive debulking. Additional cases are being included as follow-up time becomes sufficient, and updated survival data for current cases will allow stronger conclusions to be drawn.

![Progression Free Survival After Interval Debulking Surgery](image)

**Fig. 1.**
**Objective:** Despite expense and high failure rates, thoracic epidurals (TEs) have been the favored modality for loco-regional analgesia on enhanced recovery after surgery (ERAS) protocols because of their presumed superiority in mitigating pain and the surgical stress response. However, these factors have not been well-quantified for ERAS patients managed without TEs. We conducted a pilot study to characterize the surgical stress biomarker profile and clinical outcomes of gynecologic oncology patients on an ERAS protocol using surgical site infiltration with liposomal bupivacaine (LB) in lieu of TEs.

**Method:** Twelve consecutive patients undergoing open abdominopelvic surgery were prospectively enrolled. Saliva and blood were collected preoperatively and daily postoperatively (saliva between 8 and 11 p.m.). ELISAs were used to measure salivary cortisol and serum IL-6, TNF-α, CRP, and syndecan-1. Syndecan-1 is a marker of endothelial glycocalyx degradation due to volume overload. Relevant clinicodemographic data were compared between the study cohort and FY17 ERAS patients with TEs (n = 113). Wilcoxon rank sum and Student t tests were used for analyses.

**Results:** The study cohort was equally balanced for benign and malignant gynecologic conditions. Median age and BMI were 50 years and 29.4 kg/m², respectively. Median length of stay (LOS) was 2.5 days and was significantly lower than that for FY17 ERAS patients with TEs (6 days, \( P < 0.01 \)). Mean total MME through postoperative day (POD) 3 was 150.8 and was significantly lower than that for FY17 ERAS patients with TEs (494.3, \( P < 0.05 \)). Mean pain scores ranged from 3.4 to 4.3 across POD 0–3 and were comparable to those for FY 2017 ERAS patients with TEs (3.3–4.5). Baseline (BL) salivary cortisol and serum IL-6, CRP, and syndecan-1 did not significantly differ between study cohort patients with and without cancer. Patients with cancer had significantly higher median (BL) TNF-α (22.4 vs 15.3, \( P < 0.05 \)). No significant time-dependent changes in TNF-α were detected. Cortisol and IL-6 peaked on POD 0 and returned to BL on POD 1 and 3, respectively. CRP and Syndecan-1 peaked on POD 1 and 2, respectively, with return to BL by POD 4 (Figure 1).

**Conclusion:** Surgical site infiltration with LB may be a valuable alternative to TE for gynecologic oncology patients on ERAS protocols. Time-dependent changes in surgical stress biomarkers are detectable, objective, and a potentially useful tool for evaluating the biologic impact of ERAS interventions, and are being prospectively validated in a randomized trial of LB versus TE.

Fig. 1.
**1551 - Poster Session**

**What are the risk factors for lymphocyst formation after endometrial cancer staging?**

G. Baiocchi, E. Drizlionoks, P.M. Brandao, H. Mantoan, L.Y. Kumagai, L. Badiglian-Filho and C.C. Faloppa. *A.C. Camargo Cancer Center, São Paulo, Brazil*

**Objective:** The aim of this study was to determine the risk factors for lymphocyst development after endometrial cancer surgical staging.

**Method:** We analyzed a series of 281 patients treated at AC Camargo Cancer Center from January 2013 to May 2018 who had sentinel node (SLN) mapping with cervical injection of blue dye (*n* = 241) or indocyanine green (*n* = 40). Patients with high-risk tumors (high-grade or deep myometrial invasion) also had systematic pelvic with or without paraaortic node lymph node dissection (LND).

**Results:** Median age was 60 years. Fifty-eight (20.6%) patients had open and 223 (79.4%) minimally invasive surgeries. Seventy-two (25.6%) patients had pelvic lymph node dissection (LND), 82 (29.2%) pelvic with paraaortic LND, and 127 (45.2%) only SLN. The overall SLN detection rate was 87.9%, and bilateral 66.5%. Median pelvic and paraaortic LN dissected was 23.5 and 16, respectively. A total of 236 (84%) had endometrioid tumors; 63 (22.4%) had deep myometrial invasion; and 61 (21.7%) had lymphovascular space invasion. There were overall 33 (11.7%) positive SLN cases. Twenty-six (9.3%) cases had lymphocyst diagnosed during follow-up, 2 (8%) were bilateral, and 7 (28%) were symptomatic (pain or pelvic discomfort). Of those, 4 (16%) cases required percutaneous drainage. Patients who received only SLN mapping, pelvic LND, and pelvic with paraaortic LND had lymphocyst in 2.4%, 15.3%, and 14.6% of cases, respectively. Nonendometrioid histology (17.8% vs 7.6%, *P* = 0.046), deep myometrial invasion (17.5% vs 6.9%, *P* = 0.023), and systematic LND (14.9% vs 2.4%) were related to higher risk of lymphocyst formation. Age, ASA, obesity, and open surgery were not associated with higher risk of lymphocyst formation. However, in multivariate analysis only systematic node dissection (pelvic with or without paraaortic LND) maintained as an independent variable to lymphocyst development.

**Conclusion:** Our data suggest that lymphocyst develops even after only SLN mapping and lymph node dissection remain as the main risk factor for lymphocyst formation.

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**1552 - Poster Session**

**Gasless single port laparoscopic adnexal surgery with a new abdominal wall retractor**

B.W. Kim and M.K. Kim. *aInternational St. Mary’s Hospital, Incheon, Korea, Republic of [South], bCHA Gangnam Medical Center, CHA University, Seoul, South Korea*

**Objective:** Conventional laparoscopy requires pneumoperitoneum with CO₂ insufflation to get operation field. However, CO₂-insufflated pneumoperitoneum increases intra-abdominal pressure and has several adverse effects including shoulder pain and postoperative nausea vomiting (PONV). Gasless laparoscopy is an alternative method to reduce complications arising from CO₂ pneumoperitoneum. In this study, we investigated the feasibility of gasless single-port laparoscopic ovarian surgery with a new abdominal wall retractor.

**Method:** This study included 30 patients with benign ovarian tumor. We developed a new and simple abdominal wall retractor, which was clamped to Omni tract retractor or Thompson retractor. Operative outcomes including operation time, bleeding volume, postoperative wound pain, and shoulder pain were evaluated.

**Results:** All operations were performed successfully without conversion to gas laparoscopy and laparotomy. Mean retractor setup time from umbilical incision was 8 minutes, and mean operation time was 61 minutes. Ovarian tumors included 12 dermoid cysts, 9 serous cystadenoma, 6 endometrioma, 3 mucinous cystadenoma, and ovarian surgeries were 24 ovarian cystectomies and 3 salpingo-oophorectomies. Mean estimated blood loss was 83 mL. Mean wound site and shoulder pain VAS pain score at postoperative 24 hours were 3.6 and 1.3, respectively.

**Conclusion:** Our new abdominal wall retractor for gasless single-port laparoscopy provided easy setup and proper operation field for laparoscopic ovarian surgery.
**Impact of postoperative chemotherapy in patients with comprehensively staged uterine serous carcinoma**


**Memorial Sloan Kettering Cancer Center, New York, NY, USA, Abington Memorial Hospital, Abington, PA, USA**

**Objective:** The aim of this study was to evaluate the survival effect of chemotherapy among patients with uterine serous carcinoma (USC).

**Methods:** Patients who underwent primary surgical treatment for newly diagnosed USC at our institution between January 1, 1996, and December 31, 2017, were retrospectively reviewed. Surgical treatment included staging surgery with nodal assessment using either sentinel lymph node (SLN) mapping alone or conventional lymphadenectomy with or without SLN mapping. The FIGO 2009 staging system was used. OS was estimated using the Kaplan-Meier method, and curves were compared with the log rank test.

**Results:** A total of 402 patients were identified. Median follow-up time was 43.5 months (range 0–265 months). Ninety-one patients (22.6%) had adjuvant chemotherapy (CT) alone; 166 (41.3%) had CT plus intravaginal radiotherapy (IVRT); 43 (10.7%) had CT plus external beam radiation therapy (EBRT); 41 (10.2%) had IVRT alone; 16 (4.0%) had EBRT alone; and 43 (10.7%) did not receive any adjuvant therapy. In patients with stage I–II disease ($n = 267$), the 4-year OS rates were 84.9% (SE ±2.9) for patients who received CT ± RT ($n = 177$), and 88.6% (SE ±4.1) for those who did not receive any chemotherapy ($n = 90, P = 0.89$). Patients with stage I–II disease and positive peritoneal cytology ($n = 30$) had significantly worse 4-year OS than patients with negative washings ($n = 226, 76.1\%, SE \pm 8.7, vs 86.7\%, SE \pm 2.6, P = 0.042$). However, the 4-year OS rate was 86% (SE ±3.1) for CT compared to 88.1% (SE ±4.6, $P = 0.76$) for no CT for those with negative washings in early-stage disease. For stage III disease, the 4-year OS rate for those who received CT was 56.8% (SE ±5.5) compared to 23.9% (SE ±14.5) for those who did not ($P = 0.04$). See Figure 1.

**Conclusion:** Adjuvant CT with or without RT was not associated with an OS benefit in patients with surgically staged USC confined to the uterus and/or cervix (stage I–II). Positive peritoneal cytology had a statistically significant negative effect on survival outcomes in early-stage USC. CT with or without IVRT/EBRT seems to offer an OS benefit in patients with stage III USC.
Overall survival of patients with early stage (stage I/II) USC according to adjuvant treatment

![Graph showing overall survival](image)

log rank: $p=0.89$

Overall survival of patients with Stage III USC according to adjuvant treatment

![Graph showing overall survival](image)

log rank: $0.04$

Fig. 1.
Removal of positive pelvic sentinel lymph nodes without additional lymphadenectomy does not compromise pelvic side wall control in patients with endometrial cancer

aMemorial Sloan Kettering Cancer Center, New York, NY, USA, bCedars-Sinai Medical Center, Los Angeles, CA, USA, cThe Norwegian Radium Hospital, Oslo, Norway

Objective: The aim of this study was to evaluate whether pelvic side wall (PSW) control is compromised by removal of positive sentinel lymph nodes (SLNs) alone compared with SLN and additional lymph node dissection (SLN + LND) in patients with stage IIIIC1 endometrial cancer.

Method: All patients with endometrial cancer who underwent staging including SLN mapping at our institution from January 2007 to December 2016 were identified. Only patients with FIGO stage IIIIC1 endometrial cancer without extra-uterine disease (adnexal, vaginal, or parametrial involvement) were included. PSW control was defined as absence of nodal recurrence in the ipsilateral hemipelvic iliac or obturator regions. Appropriate statistical tests were employed.

Results: Of 151 patients who met inclusion criteria, a positive SLN was identified in 197 hemipelvises. A median of 2 SLNs (range 1–8) were removed; a median of 1 (range 1–3) was positive. In 60/197 (30%) hemipelvises with a positive SLN, a concurrent LND was performed, with a median of 3 (range 1–20) additional nodes removed. The SLN-only and SLN + LND hemipelvises groups did not differ in clinicopathologic characteristics, adjuvant RT (126/137, 92%, vs 50/60, 83%, respectively, $P = 0.071$), and adjuvant chemotherapy (114/137, 83%, vs 54/60, 90%, respectively, $P = 0.216$). The SLN + LND group had more open procedures (9/137, 7%, vs 18/60, 30%, respectively, $P = 0.00001$), and a longer median follow-up (37.2 months, range 8.0–115.5, vs 60.3 months, range 6.9–135.3, respectively, $P < 0.0001$). PSW recurrences did not differ between the SLN-only group (5/137, 3.6%) and the SLN + LND group (2/60, 3.3%, $P = 0.912$). There was also no difference between the SLN-only and SLN + LND groups in 3-year PSW recurrence-free survival (96.1% vs 95.7%, $P = 0.866$, respectively, Figure 1), 3-year overall recurrence-free survival (74.3% vs 77.2%, respectively, $P = 0.555$), or 3-year disease-specific survival (88.8% vs 92.4%, respectively, $P = 0.835$).

Conclusion: Our data suggest that removal of a positive SLN without additional lymphadenectomy is safe and does not have an adverse impact on PSW recurrence or oncologic outcomes in patients with endometrial cancer receiving appropriate adjuvant therapy.

Fig. 1. Pelvic sidewall progression-free survival
**1555 - Poster Session**

**Role of diagnostic laparoscopy in deciding primary treatment in advanced-stage ovarian cancer**
Y.S. Chung, J.Y. Lee, E.J. Nam, S.W. Kim, Y.T. Kim and S. Kim. *Yonsei University College of Medicine, Seoul, South Korea*

**Objective:** We sought to investigate whether preoperative diagnostic laparoscopy can prevent futile primary debulking surgery (PDS) by predicting optimal cytoreduction (residual disease < 1 cm) in patients with advanced-stage ovarian cancer.

**Method:** We retrospectively analyzed 307 patients with advanced-stage ovarian cancer from January 2010 to September 2017. According to the use of diagnostic laparoscopy, we stratified patients into 2 groups. In 121 patients, laparoscopy was used to guide selection of PDS or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS), and in 186 patients, primary treatment was decided by CT or surgeon’s discretion. The primary outcome was futile PDS or the rate of non-HGSC patients who underwent NAC/IDS.

**Results:** In the decision by laparoscopy group (group 1), 37 (30.6%) of 121 patients underwent PDS versus 112 (60.2%) of 186 patients in the decision by CT or surgeon’s discretion group (group 2). Futile laparotomy (residual disease >1 cm) occurred in 1 (3%) of 121 patients in group 1 versus 19 (17%) of 186 patients in group 2 (P = 0.02). The rate of patients who underwent NACT with non-HGSC was higher in group 2 than group 1 (13.5% vs 6.0%, P = 0.051). However, there were no significant differences in postoperative morbidity and radical surgery rate. Kaplan-Meier analysis showed no between-group differences in PFS or OS (P = 0.218 and 0.482, respectively).

**Conclusion:** Diagnostic laparoscopy is an effective tool for selecting patients in whom PDS will be successful in achieving <1 cm of residual disease. Therefore, diagnostic laparoscopy should be considered in the diagnostic workup of women with ovarian cancer to guide treatment selection for either PDS or NACT/IDS.

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**1556 - Poster Session**

**Mapping the robotic hysterectomy learning curve and reestablishing surgical training metrics**
K.H. Kim and T.B. Turner. *University of Alabama at Birmingham, Birmingham, AL, USA*

**Objective:** The most common robotic training curricula in the United States currently entail completion of an online module followed by dry lab training with standardized exercises, such as manipulating needles with robotic needle drivers. This training occurs once a year, at the beginning at the academic year, and typically lasts between 30 and 60 minutes for each resident. Likert scale-based assessments are used for evaluation, generally limited to amount of time and subjective proficiency in the training task. There are no procedure-specific tasks or training. Although simulation training is increasing, there is little use of it. We sought to create a simulation-based curriculum with objective measurements of trainee progress and map the trainee learning curve to allow for deficit-specific teaching.

**Method:** The pilot curriculum was based on a high-fidelity procedural hysterectomy simulation performed every 3–4 months. Each simulation episode had one-on-one teaching. As learners progressed through the curriculum, they increasingly built upon previous skills and performed increasingly more advanced simulation and techniques, while minimizing skill decay. The robotic platform was used to measure all movements within Cartesian coordinates, the number of clutches, instrument collisions, time to complete the simulated hysterectomy, and unintended injuries during the procedure.

**Results:** The pilot curriculum was well-received by all trainees. Objective metrics recorded throughout the year improved nearly universally. More senior residents demonstrated superior capabilities compared to junior residents, as expected. The majority of residents (29/32) were able to complete an entire simulated hysterectomy in the allotted 30-minute training session period by the end of the year.

**Conclusion:** This program establishes learning curves based on objective data points using a risk-free simulation platform. The curves can then be used to evaluate trainee skill level and tailor teaching to specific objective deficiencies. Plans are being implemented to expand this training program to all surgical specialties that utilize robotic surgery. The pilot curriculum will be tailored to the unique needs of each surgical discipline’s residency training.
**1557 - Poster Session**

**Prediction of optimal surgical outcomes with radiologic images using deep learning artificial intelligence**
A.M. Newton, J.N. Mattson, M.J. Goodheart, D.P. Bender, M. Rajput, M. McDonald, Y.A. Lyons, H.D. Reyes and J. Gonzalez-Bosquet. *University of Iowa Hospitals and Clinics, Iowa City, IA, USA, Gynecologic Oncology, Iowa City, IA, USA*

**Objective:** At present, there is no universally accepted objective method for predicting which patients will reach optimal cytoreduction after primary debulking surgery for high-grade serous ovarian cancer (HGSC). Our objective was to predict which patients will obtain optimal surgical outcomes in advanced-stage HGSC using preoperative radiologic images processed with convolutional neural networks and artificial intelligence.

**Method:** An initial prediction model was created using 178 patients with pretreatment radiographic imaging studies of the abdomen. A total of 122 of these patients had an optimal cytoreductive surgery outcome, and 56 of these patients were suboptimal. An optimal cytoreductive surgery outcome was defined as a composite variable including <1 cm gross residual disease at the time of surgery, patient survival of at least 90 days after surgery, and ability to receive chemotherapy within 2 months after surgery. We abstracted, selected, and formatted more than 44,000 CT scan axial abdominal/pelvic images from patients with optimal outcomes, and more than 17,000 from patients with suboptimal outcomes. Deep convolutional neural networks (CNN) were used with GoogLeNet and Caffe frameworks with the help of NVIDIA DIGITS (Deep Learning GPU Training System) to create a prediction algorithm. Subsequently, a group of 102 HGSC patients was used for validation of the algorithm. Seventy-one of these patients had optimal and 31 had suboptimal outcomes. Performances of resulting models in the validation set were evaluated using the area under (AUC) the receiver operator curve (ROC).

**Results:** The initial prediction model using the deep learning algorithm had an accuracy of more than 99% in predicting optimal or suboptimal surgical outcomes. This result was not as robust when the model was subsequently validated with more than 33,000 separate images. On validation, the best model had an AUC of 72%, with an accuracy of 63% and a negative predictive value of 82%. The threshold for this model was established for a sensitivity of 80%.

**Conclusion:** Preoperative images processed with deep learning artificial intelligence may have a role in predicting optimal surgical outcomes in patients with HGSC. There remains a need for optimization of model creation and validation methods before clinical application.

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**1558 - Poster Session**

**Minimally invasive interval debulking surgery in ovarian cancer (MIID-SOC): A prospective pilot study**
A.B. Costales, S.N. Shah, S. Ricci, H. Mahdi, P.G. Rose and C.M. Michener. *Cleveland Clinic, Cleveland, OH, USA, The Cleveland Clinic Foundation, Cleveland, OH, USA*

**Objective:** Neoadjuvant chemotherapy (NACT) and interval debulking surgery (IDS) have been shown to have similar survival rates compared to primary surgery. The objective of this study is to implement, evaluate, and further investigate the role of minimally invasive surgery in patients undergoing interval debulking following neoadjuvant chemotherapy in patients with advanced ovarian cancer (AOC).

**Method:** This is a prospective pilot study, currently accruing 50 consecutively identified patients, since December 19, 2017, who have AOC and have achieved at least a partial response. Each patient underwent an initial laparoscopic evaluation followed by primary surgeon-dictated surgical approach, either continue laparoscopically (MIS) with placement of a hand port for manual palpation or convert to a laparotomy. Preoperative patient factors, imaging scoring systems, as well as intraoperative scoring systems, are being used to determine a possible cohort amenable to a laparoscopic interval approach. We present preliminary data from the initial 12 patients who have participated in this clinicaltrials.gov registered study (No. NCT03378128); see Table 1.

**Results:** Three patients had a MIS IDS. The number of cycles prior to IDS was 3 in 50% and 4 in 50%, with 50% having received dose dense paclitaxel and carboplatin (other regimens: standard dosing carboplatin/paclitaxel 17%, carboplatin/paclitaxel/bevacizumab 25%, and carboplatin/docetaxel 8%). Comparing MIS to open, as expected, median operative time, blood loss, and length of stay were less in the MIS group (189 vs 268 minutes, 100 vs 500 mL, 1 vs 4 days, respectively). One patient in the MIS group and 4 in the open cohort received hyperthermic intraperitoneal chemotherapy following IDS. Median computed preoperative image scoring systems were lower in those who had a MIS approach compared to those who underwent a laparotomic approach (Suidan score 3 vs 4 and Bristow 4 vs 7.5, respectively). Median-modified
Conclusion: Further prospective investigations are needed to identify a patient cohort amenable to a minimally invasive interval debulking approach. We are continuing to accrue patients and following oncologic outcomes in this study.

Table 1. Demographics of the 12 study patients

<table>
<thead>
<tr>
<th>Age at diagnosis in years Mean [min-max]</th>
<th>67.5 [55-77]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>African-American</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>BMI</td>
<td>26.68 kg/m2 [15.5-30.1]</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Serous - epyey</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Serous - uterine</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>I/D</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>I/V</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>RvR</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Neoadjuvant regimen</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant carboplatin/paclitaxel</td>
<td>6 (59%)</td>
</tr>
<tr>
<td>Standard dosing carboplatin/paclitaxel</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Carboplatin/paclitaxel/potaxuzamab</td>
<td>3 (29%)</td>
</tr>
<tr>
<td>Carboplatin/docetaxel</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Number of cycles prior to interval debulking</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6 (59%)</td>
</tr>
<tr>
<td>4</td>
<td>6 (59%)</td>
</tr>
<tr>
<td>Number of days since last adjuvant/chemotherapy prior to surgery</td>
<td>24 [13-35]</td>
</tr>
<tr>
<td>Median [min-max]</td>
<td></td>
</tr>
<tr>
<td>Preoperative CA 125 level</td>
<td>119U/mL [7-274]</td>
</tr>
<tr>
<td>Median [min-max]</td>
<td></td>
</tr>
<tr>
<td>Prior laparotomy</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 2. Scoring system based on surgical approach for patients who had an optimal interval debulking

<table>
<thead>
<tr>
<th>Scoring system</th>
<th>Minimally invasive</th>
<th>Laparotomic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prespective</td>
<td>Sudan et al.</td>
<td></td>
</tr>
<tr>
<td>Mean/ Median [min-max]</td>
<td>3.7/ 3 [1.7] (n=5)</td>
<td>5/4 [1.7] (n=5)*</td>
</tr>
<tr>
<td>Brustow et al.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean/ Median [min-max]</td>
<td>4/4 [3.5] (n=3)</td>
<td>9/ 75 [3.15] (n=5)*</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>Fagotti et al.</td>
<td></td>
</tr>
<tr>
<td>Mean/ Median [min-max]</td>
<td>1/1/2 [0.2] (n=3)</td>
<td>3.25/3 [2-6] (n=4)</td>
</tr>
</tbody>
</table>

1559 - Poster Session
The modified early warning score in gynecologic oncology inpatients: A quality improvement project
K.V. Grettea, G. Mantellb, N.L. Jonesa, J.Y. Piercena, R.P. Rocconi and J.M. Scalicia. aMitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, bUniversity of South Alabama, Mobile, AL, USA

Objective: The modified early warning score (MEWS) was developed to identify acute patients by subtle changes in vital signs that predict future deterioration. We adopted MEWS to improve communication and reduce acute events requiring emergent intervention.

Method: MEWS was derived from previous reports and adapted to the gynecologic oncology service at a single institution. MEWS scores were retroactively applied to vital signs recorded by nursing on inpatients over a 3-month period. The clinical course of all patients with a MEWS score of >5 was reviewed to determine the congruence of the score to patient outcomes. Action algorithms based on MEWS score were established, and physician and nursing teams educated in their use. After implementation, MEWS scores were recorded with each vital sign set. Data collection is ongoing but was evaluated 1 month after implementation to assess completion and accuracy.

Results: Vital signs of 50 inpatients were reviewed prior to implementation, and a MEWS score was calculated. Eleven (22%) would have scored 5 or greater. Of these, 2 (18%) experienced clinical deterioration, and 1 required intensive care unit (ICU) transfer. Seven (46%) had disease-related morbidities, including metastasis, pulmonary embolus, uncontrolled hypertension, sepsis, and blood loss anemia. Two (18%) had isolated vital sign abnormalities in the immediate postoperative period that resolved spontaneously. After implementation, data from 32 patients were reviewed. MEWS was completed on 67% of vital assessments and was accurate in 91%. No acute events or ICU transfers were noted with scores <3 (n = 19, 59%), NPV = 100%. Of 13 patients with scores >3, 6 (46%) developed sequelae of a new or comorbid condition (PPV = 64%). After implementation, no patients deteriorated to a level requiring urgent/emergent ICU transfer. See Table 1.
Conclusion: Despite the complexity of gynecology/oncology patients, MEWS scoring accurately stratifies patients at risk for acute events with an NPV of 100%.

Fig. 1.

1560 - Poster Session
Timing of postoperative Foley catheter removal from robotic-assisted radical hysterectomy in patients with early-stage cervical cancer

Objective: Types II or III radical hysterectomy with bilateral pelvic lymphadenectomy is the preferred method of primary treatment for early-stage cervical cancer (CC) (stage 1A1–1B1). Prolonged use of a Foley catheter postoperatively due to high rate of lower genitourinary tract dysfunction (8%–80%) is common practice for suspected autonomic nerve injury with dissection. The CDC category 1B recommendations include the expeditious discontinuation of a Foley catheter to decrease the risk of catheter-associated urinary tract (CAUTI) in the postoperative period.

Method: This was a retrospective chart review of patients enrolled in a database with early-stage CC and treated from January 2010 to December 2017 with types II or III robotic-assisted radical hysterectomy (RARH). Foley catheters were routinely placed at the beginning of procedure. Patients were stratified into either having a prolonged physician-indicated Foley catheter (PIFC) or removal and awaiting spontaneous void (SV) postoperatively. Statistical analyses were performed using Fisher exact tests. All tests were evaluated using 0.05 as the statistical significance value with SPSS version 21 statistical software.

Results: Ninety-seven patients were identified with mean age 47.5 ± 13.1 years and BMI 29.2 ± 6.3 kg/m². Nine of 51 (17.6%) cases were stage 1A for those with PIFC, and 11/46 (24%) were stage 1A for SV. Of 97 patients, 46 (47.4%) had a discontinuation of Foley prior to discharge, mean length of stay 1.1 ± 0.41 days. Of 46 patients, 27 (58.6%) were able to spontaneously void and did not require replacement of a Foley. Of those 27 patients, none were readmitted or brought to the office for Foley reinsertion. There was no statistical difference in the rate of bladder injuries, ureter injuries, or voiding dysfunction between those with a PIFC and those with SV. Controlling for stage (1A vs 1B) in cases with SV, there was no statistical difference in the rate of bladder injuries, ureter injuries, or voiding dysfunction. Recurrence rate was 7/97 (7.2%). Patients were more likely to have recurrent disease in those cases who were sent home with a PIFC than those with SV ($P = 0.013$).

Conclusion: Early discontinuation of a Foley catheter may be offered to postoperative patients on day 1 from a RARH for early-stage CC without having an impact on the rates of long-term complications and would decrease the risk of CAUTI.

1601 - Poster Session
Identical recurrence rates after radical hysterectomy, regardless of modality, for primary treatment of early-stage cervical cancer
S.B. Holloway and J.S. Lea. The University of Texas Southwestern Medical Center, Dallas, TX, USA
**Objective:** A recent prospective trial showed that MIS radical hysterectomy was associated with a significantly higher risk for recurrence than open radical hysterectomy (RH). However, laparoscopic radical hysterectomy (LRH) for early-stage cervical cancer has been shown to be a feasible surgical procedure that is associated with a lower surgical morbidity compared to open RH. We sought to examine the recurrence rates and sites of recurrence among women with early-stage cervical cancer who underwent a radical hysterectomy by either laparoscopic or open approach at our institution.

**Method:** Patients with stage IA1–IB2 cervical cancer who underwent primary surgical management with either open RH or LRH from 2005 to 2017 were identified. Patient demographics and clinical-pathologic data were abstracted from medical records. Exclusion criteria were neuroendocrine carcinoma, node positive cervical cancer, and immunosuppression. The remaining cases were analyzed for disease recurrence outcomes. The χ² test was used for statistical analysis.

**Results:** We identified 214 women with early-stage cervical cancer, of whom 173 met inclusion criteria. Of the latter, 146 had open RH and 27 had LRH. Median follow-up was 5 years. Median pathologic tumor size was 2.5 cm for open RH and 2.0 cm for LRH cases. Nine percent of women who underwent an open RH and 11% of women who underwent a LRH had disease recurrence (P = NS). Fifty-seven women met criteria for recurrence (intermediate risk) and underwent adjuvant radiation therapy. Of these patients, 46 had an open RH and 11 had an LRH. Of the 116 remaining low-risk women, 5% who underwent RH and 0% who underwent LRH had disease recurrence (P = NS). All 3 women with disease recurrence who underwent a LRH had tumors larger than 2 cm and pelvic recurrence only. Of the 13 women treated with open RH, approximately 50% had both distant and local recurrence.

**Conclusion:** Women with intermediate-/low-risk early-stage cervical cancer who were treated with LRH had a similar disease recurrence rate when compared to women who underwent an open RH. All patients who were treated with LRH and recurred had tumor size greater than 2 cm and local recurrence.

**1602 - Poster Session**

**Decrease in narcotic use after initiation of an advanced surgical recovery program**

L.P. Geisler, N. Seeley and K.J. Manahan. *Cancer Treatment Centers of America, Newnan, GA, USA*

**Objective:** To determine the differences in opioid use (IV and total) in the postoperative period and 90 days after surgery for patients undergoing radical complete debulking for ovarian cancer before and after initiation of an advanced surgical recovery program

**Method:** Medical records were examined for the last 50 patients undergoing radical complete debulking for ovarian cancer before initiation of the program and for the first 75 patients after the initiation of the program. Only patients not on narcotics before surgery were included. No patients were knowingly excluded. Opioid amounts were converted to morphine equivalents (ME). Demographics, use of opioids before surgery, and prolonged use of narcotics (≥90 days after surgery) were also collected.

**Results:** Mean pre-initiation IV (71.2 ME, 95% CI 33.1–109.3) and total (85.8 ME, 95% CI 42.0–129.6) opioid use were significantly higher before initiation of the ASURE® program than after (IV, 4.2 ME, 95% CI 1.0–7.9, and total, 21.9 ME, 95% CI 15.5–28.3). This correlates with a 94.1% decrease in IV narcotic use and 74.5% decrease in total narcotic use. At 90 days after surgery, the continued use of narcotics decreased from 6% to 1.3% (P < 0.001) after initiation of the program. The mean age and BMI before initiation (50.2 years, 95% CI 47.5–52.0; 29.7 kg/m², 95% CI 28.6–30.9) and after initiation (51.5 years, 95% CI 49.6–53.4; 31.1 kg/m², 95% CI 30.2–31.9) were not significantly different.

**Conclusion:** After initiation of an advanced surgical recovery program designed to decrease narcotic use, there were significant decreases both in postoperative opioid use and in chronic opioid use at 90 days.

**1603 - Poster Session**

**Changes in length of stay and 30-day readmission rates after starting an advanced surgical recovery program**

L.P. Geisler, N. Seeley and K.J. Manahan. *Cancer Treatment Centers of America, Newnan, GA, USA*

**Objective:** Advanced surgical recovery programs have been initiated at many institutions to improve quality and enhance patient safety. The objective of this study was to determine whether length of stay in days (LOS) and 30-day readmission rates changed after implementation of the program.
Method: Medical records were examined for the last 50 patients undergoing radical complete debulking for ovarian cancer before and first 75 patients after the beginning of the program. No patients using opioids before surgery were included. No patients were knowingly excluded. Demographics, length of postoperative stay in days (LOS), and 30-day readmission rates at any hospital were collected. Two-tailed statistical tests were employed.

Results: The mean age and BMI before the program (50.2 years, 95% CI 47.5–52.0; 29.7 kg/m², 95% CI 28.6–30.9) and after the program started (51.5 years, 95% CI 49.6–53.4; 31.1 kg/m², 95% CI 30.2–31.9) were not significantly different. There were no differences in radical procedures required for complete cytoreduction between the groups including bowel resections, diaphragm stripping/resection, liver wedge resections, or splenectomies. Mean LOS decreased from 7.1 days (95% CI 5.9–8.3) to 2.6 (95% CI 2.6–2.8). Similarly, the readmission rate at 30 days decreased from 14% to 0% (P < 0.001).

Conclusion: When employed in the care of patients with ovarian cancer undergoing complete cytoreductive surgery, advanced surgical recover programs can decrease LOS without increasing 30-day readmission rates.

1604 - Poster Session
Robotic surgery versus laparotomy in elderly patients with endometrial cancer: Perioperative outcome and complications
R. Eitan, L. Salman, L. Guy, A. Borovich, O. Raban, G. Sabah, A. Jakobson-Setton, E. Yeoshoua and D. Tsoref. Rabin Medical Center, Petach-Tikvah, Israel

Objective: We aimed to evaluate perioperative outcome and complications in elderly patients with endometrial cancer undergoing surgical staging with robotic-assisted laparoscopy (RAL) versus laparotomy.

Method: This was a retrospective cohort study of all elderly patients (≥70 years old) with endometrial cancer in one university-affiliated medical center (2009–2017). We compared outcome between patients undergoing RAL and those undergoing laparotomy. We excluded patients who underwent vaginal hysterectomy or conventional laparoscopy. Our primary outcome was defined as perioperative outcome and complications that included operation time, anesthesia duration, estimated blood loss, intraoperative complications (excessive blood loss, bowel or urinary tract injury), length of stay, postoperative complications (blood transfusion, surgical site infection, fever, ileus, and re-laparotomy), and rates of readmission.

Results: Overall, 125 patients met inclusion criteria: 45 (36%) had RAL and 80 (64%) underwent laparotomy. There were no differences between groups in age, BMI, stage, or histology (P > 0.05 for all). Patients undergoing RAL had significantly longer operation time (142 vs 94 minutes, P < 0.001) and anesthesia duration (194 vs 148 minutes, P < 0.001) (Table). Rates of lymph node dissection were higher in the RAL group compared to laparotomy (77.7% vs 52.5%, P = 0.006). Compared to RAL, patients undergoing laparotomy had significantly longer length of stay (7 vs 2 days, P < 0.001) with significantly higher rates of intraoperative and postoperative complications (18.7% vs 4.4%, P = 0.02, and 17.5% vs 2.2%, P = 0.001, respectively). There were no differences between groups in rates of adjuvant radiotherapy or chemotherapy (P > 0.05).

Conclusion: Elderly patients with endometrial cancer undergoing RAL are more likely to undergo oncologic staging. In spite of the potentially more morbid procedure, these patients have lower perioperative complications, with shorter hospital stay, compared to laparotomy.

Table 12. Operative and post-operative outcome
The impact of an enhanced recovery after surgery (ERAS) program on opioid use reduction in patients undergoing minimally invasive hysterectomy (MIH) in gynecology oncology

E. Weston, M. Noel, K. Douglas, K. Terrones, F. Grumbine, R.L. Stone and K. Levinson. \textsuperscript{a}Johns Hopkins School of Medicine, Baltimore, MD, USA, \textsuperscript{b}Greater Baltimore Medical Center, Towson, MD, USA, \textsuperscript{c}Johns Hopkins Medical Institutions, Baltimore, MD, USA, \textsuperscript{d}Johns Hopkins Hospital, The Kelly Gynecologic Oncology Service, Baltimore, MD, USA, \textsuperscript{e}Johns Hopkins Hospital, Baltimore, MD, USA

Objective: While data suggest that enhanced recovery after surgery (ERAS) protocols significantly reduce opioid consumption for gynecologic oncology patients undergoing exploratory laparotomies, the impact of ERAS on opioid consumption in patients undergoing minimally invasive hysterectomy (MIH) has not yet been evaluated. This study evaluated the effects of an ERAS protocol on opioid requirements in gynecologic oncology patients undergoing MIH.

Method: A retrospective review of gynecologic oncology patients undergoing MIH in the 14 months following implementation of a minimally invasive gynecology ERAS protocol was performed. Patient demographics, surgical and clinical characteristics, opioid use in morphine milligram equivalents (MME), and pain scores were compared in patients undergoing MIH in the 9-month period prior to implementation of the ERAS program. Patients with chronic opioid use or chronic pain were excluded. Student t test, $\chi^2$, Fisher exact, and Wilcoxon rank sum were used in the analysis.

Results: During the first 14 months of the ERAS program, 129 eligible patients underwent MIH. These patients were compared to 99 patients undergoing MIH in the 9 months before implementation of the ERAS protocol. There was no difference in age (median 58 years), BMI (median 31 kg/m$^2$), cancer diagnosis (52% cancer), surgical approach (43% robotic, 34% laparoscopy, 23% single incision laparoscopy), operative time (median 152 minutes), use of local anesthetic (99% received), or hospital length of stay (median 25 hours) between the groups. Following implementation of the ERAS protocol, patients received fewer intraoperative opioids (median 12.0 vs 32.0 MME, \(P < 0.0001\)) and fewer postoperative opioids (median 20.0 vs 35.0 MME, \(P = 0.02\)) while inpatient. Despite using fewer opioids, pain scores among ERAS patients were lower compared to patients undergoing MIH prior to ERAS implementation (mean 3.6 vs 4.1, \(P = 0.03\)).

Conclusion: ERAS protocols have a significant impact not only on the recovery of gynecologic oncology patients undergoing exploratory laparotomy, but also on the reduction of opioids for women undergoing MIH, in both the intraoperative and postoperative settings. Further studies are ongoing to better quantify, predict, and decrease opioid requirements in this population.

Palliative Care and Patient Reported Outcomes

Clinical outcomes using modern radiotherapy techniques in the palliative treatment of bleeding gynecological malignancies

S.W. Dutta, R.J. Taylor, K.L. Ring, K.D. Romano and T.N. Showalter. \textsuperscript{a}University of Virginia, Charlottesville, VA, USA, \textsuperscript{b}University of South Carolina, Columbia, SC, USA

Objective: To evaluate the effectiveness of palliative radiotherapy using contemporary conformal techniques for vaginal bleeding secondary to gynecologic tumors.

Method: Consecutive female patients who were referred for refractory vaginal bleeding from gynecologic cancers were identified retrospectively. Time to bleeding cessation was measured from the start of radiotherapy. Logistic regression was performed to investigate factors associated with recurrent bleeding, and Kaplan-Meier (KM) estimate was used to calculate bleeding-free survival (BFS) and overall survival (OS). Toxicities were graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Results: Between October 2015 and April 2018, 28 patients received radiotherapy to a median dose of 30 Gy (range 15–66.4 Gy) in 10 fractions (range 3–36 fractions). Median follow-up was 8 months (range 1–40 months). The majority of cases were endometrial (\(n = 18, 64\%\)). Seventeen (61%) were new primary cancers, and 11 (39%) were recurrent. Prior to treatment, 16 patients (57%) were transfusion-dependent due to bleeding. Radiotherapy volume was limited to gross tumor plus margin in
most cases \((n = 22)\), but regional nodes were included in patients treated with definitive intent \((n = 6)\). Bleeding resolved after radiotherapy in 27 patients \((96\%)\). The one patient who did not adequately respond required hysterectomy. Median time to bleeding cessation was 14 days \((\text{range 2–103 days})\). Six patients \((21\%)\) experienced recurrent bleeding at a median interval of 15 months. Median BFS was 38 months, and KM estimate at 2 years was 53\%. Median OS for the entire cohort was 20 months, and KM estimate at 2 years was 46\%. Factors not predictive of recurrent bleeding were total radiation dose, dose per fraction, and radiation technique \((P > 0.05)\), while longer follow-up was predictive \((HR = 1.2 \text{ per month}, P = 0.016)\). Two \((7\%)\) grade 3+ toxicities were observed \((vaginal\, fistula\, and\, small\, bowel\, obstruction)\).

**Conclusion:** Conformal palliative radiotherapy is highly effective at controlling vaginal bleeding secondary to gynecologic malignancies. Patients who live longer are at higher risk of recurrent bleeding, warranting additional study to find a durable treatment regimen in selected patients with favorable prognoses.

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**1607 - Poster Session**

**Symptom trajectory in women with recurrent ovarian cancer: How does symptom burden change near the end of life?**


**Objective:** The symptom burden of patients with recurrent ovarian cancer \((ROC)\) reflects the cumulative impact of treatment and progressive disease. Given the recent interest in bringing patient reported outcomes \((PROs)\) into routine clinical care, we sought to explore symptom burden as patients approach the end of life.

**Method:** Patients with ROC completed the MD Anderson Symptom Inventory–Ovarian Cancer \((MDASI-OC)\), a 27-item validated PRO instrument biweekly. Patients rated symptom severity and interference at its worst over 24 hours from 0 = “not present” to 10 = “as bad as you can imagine.” This analysis includes patients whose last MDASI-OC was completed within \(\leq 12\) months of most recent recurrence. Linear mixed effect models examined longitudinal changes in symptom burden based on whether patients were alive or died within 12 months of most recent recurrence. Models were adjusted for age, race, and income level.

**Results:** A total of \(18/87\) patients \((21\%)\) have died. Median age was 63 years; 71 patients \((82\%)\) had stage III/IV disease; 71 \((82\%)\) had serous histology; and 41 \((47\%)\) were receiving platinum-based treatment at enrollment. Median time from diagnosis was 2.8 years; median days since recurrence was 50. Groups were similar demographically and clinically. The most severe symptoms were fatigue, numbness, pain, sleep disturbance, and drowsiness. Patients who died reported worse symptom interference compared to patients who were alive at 12 months \((3.1 \text{ vs } 2.2, P < 0.0001)\), and significantly worse scores for 20 of 27 MDASI-OC items including pain, nausea, distress, shortness of breath \((SOB)\), loss of appetite, sadness, constipation \((P < 0.001–0.04)\). Lowess curves show symptom trajectories for pain, SOB, loss of appetite, and the physical subscale of symptom interference with walking, activity, and work between those alive and dead within 12 months \((Figure\, 1)\). While patients who died had consistently higher pain levels, this was in the mild range and remained stable even near the end of life. SOB, loss of appetite, and physical interference worsened near end of life compared to patients still alive.

**Conclusion:** Patients in the last 12 months of life report significantly worse symptom burden compared to others with ROC. The distinctly different symptom burden trajectories trend over months and provide insight into the utility of utilizing symptom burden trends to alert patients and clinicians to symptoms on which to focus supportive care efforts. Longitudinal
PRO data may also help guide the timing of discussions regarding when to stop active oncologic therapy.

**Fig. 1.**

1608 - Poster Session
Perceptions of palliative care and hospice services among gynecology oncology physicians
E.M. Newlin, M. Yao and C.M. Michener. Cleveland Clinic, Cleveland, OH, USA

**Objective:** We aimed to determine barriers to hospice and palliative care as perceived by gynecology oncology physicians, and to correlate personal and professional experiences with perceptions of hospice and palliative care services.

**Method:** A 60-question cross-sectional descriptive survey was sent to all full, associate, fellow in training, and candidate physician members of the Society of Gynecologic Oncology (SGO).

**Results:** A total of 1,410 SGO members were invited to participate, and 176 (12.5%) responded. Participants were asked to rate reasons to refer patients to hospice as well as barriers to hospice referral. The highest rated reason for hospice referral was “pain or symptom control” (median 3 on 1–4 scale), followed by “assistance through the dying process” (median 4). Attendings were more likely than fellows to place importance on hospice referral for “nursing support” ($P = 0.01$) and “prevention of readmission” ($P = 0.01$). The highest rated barriers to hospice referral were “difficulty predicting patient death within 6 months” (median 2 on 1–4 scale) and “physician desire to pursue additional lines of chemotherapy” (median 2), which were both more likely to be rated higher by fellows than attending physicians ($P = 0.03$ and $P = 0.01$, respectively). Fellows were also more likely than staff physicians to agree that they had a “lack of time” to discuss issues of dying and hospice care ($P < 0.01$). Respondents were also asked to describe the primary role of palliative care at their institution, choosing from pain management (31%), goals of care (18%), transition to hospice (22%), and other symptom management (29%). Respondents were more likely to associate palliative care with pain and symptom management if they were fellow physicians ($P = 0.03$) or had received end-of-life care training ($P = 0.03$). Likert scale data also differed by the fellow–attending divide, as fellows were more likely to agree that palliative care physicians were better communicators than gynecologic oncology physicians ($P = 0.01$).
Conclusion: Many perceptions of palliative care and hospice services differed along a fellow-attending divide. Forty percent of respondents thought the primary role of palliative care to be goals of care and hospice transition, highlighting a potential trend in the respondent population to late involvement of palliative care services.

1609 - Poster Session
A prospective assessment of patient preferences in ovarian cancer: What do patients value the most?
R.S. Suidan, C.C.L. Sun, K.H. Lu, S.H. Giordano and L.A. Meyer. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Discussions regarding treatment in ovarian cancer often involve the tradeoff between survival benefits and complications/toxicity. However, little is known about how patients value these different aspects. The American Society of Clinical Oncology defines value in cancer care as clinical benefit in the context of morbidity and costs. Our objective was to elucidate patient preferences in ovarian cancer and to ascertain what they value the most.

Method: From January 2017 to May 2017, 50 patients with ovarian cancer were enrolled in this prospective study. Eleven attributes related to having cancer or its treatment were assessed. Patients rated each attribute using a Likert scale from 1 (not important) to 5 (deeply important) and ranked them from the most important (1) to the least important (11). To assess preferences regarding the tradeoff between survival and complications, they were asked how many additional months of overall survival (OS) a treatment approach would have to give them if it increased the complication risk from 10% to 30%, or the risk of getting a colostomy from 1% to 10%, respectively. Appropriate statistical tests were used.

Results: The median patient age was 63 years; the majority had stage IIIC cancer (64%); and 70% had experienced a recurrence. OS was deemed the most important attribute by patients (mean ranking 2.1, mean rating 4.8/5, with 58% of patients ranking it as the most important one). This was followed by progression-free survival, physical/mental well-being, permanent complications/sequelae (i.e., permanent colostomy), return to pretreatment activities of daily living, time off treatment, and temporary complications/sequelae (Table 1). Chemotherapy schedule/type, assistance with care, cost of care, and logistical issues were the least important attributes. There were no differences in preferences between patients who recurred versus those who did not. A treatment approach that increased the major complication risk from 10% to 30% would have to yield patients an additional median OS of 6 months (range 0.25–54 months) to be acceptable. A treatment approach that increased the colostomy risk from 1% to 10% would also have to give patients an additional median OS of 6 months (range 0.25–48 months).

Conclusion: Patients with ovarian cancer value OS the most, followed by progression-free survival and physical/mental well-being. A treatment approach that increases the risk of complications or getting a colostomy would have to give patients an additional 6 months of OS to be acceptable.
Ovarian tissue cryopreservation: A fertility preservation option for gynecologic oncology patients


Objective: To report on fertility preservation outcomes utilizing ovarian tissue cryopreservation (OTC) in premenopausal women undergoing surgery for suspected gynecologic malignancy.

Method: This study was approved by the University of Pittsburgh Institutional Review Board. Data collection was completed on women undergoing OTC as part of surgery for presumed or biopsy-proven gynecologic malignancy from 2011 through 2018. Chart abstraction included patient age at fertility preservation, anti-mullerian hormone (AMH) level, type of gynecologic malignancy, and amount of tissue cryopreserved.

Results: Fifteen women undergoing surgery for presumed gynecologic malignancy had concordant harvesting of ovarian cortical tissue for cryopreservation; five additional women were consented but did not require oophorectomy. Median age at time of surgery was 31 (range 11–39) years, and median AMH level was 0.96 (range 0.22–4.52). Fourteen women did not qualify for standard-of-care oocyte cryopreservation; three women were pregnant at the time of surgery. Three patients (20.0%) had a confirmed diagnosis of malignancy (2 uterine and 1 ovarian cancer); 5 (33.3%) had an ovarian tumor of low malignant potential; and 7 (46.6%) had benign ovarian pathology. Normal ovarian tissue appropriate for cryopreservation was recovered from 13 of 15 patients (86.6%). Cortical tissue measuring approximately 2 cm × 0.5 cm was frozen in strips; the median number of strips cryopreserved per patient was 7 (range 3–30).

Conclusion: Fertility preservation via OTC is an opportunity for women undergoing surgery for presumed gynecologic malignancy to retain the option for future genetic offspring. The procedure is performed in conjunction with surgical staging and typically does not add complexity to the case. We advocate for discussion and consideration of this procedure in appropriately counseled, premenopausal gynecologic oncology patients. This approach is an option for patients who do not qualify for oocyte or embryo cryopreservation because of suspected ovarian malignancy or because of need to proceed with surgery expeditiously. Patients should be counseled about the possible need for experimental in vitro maturation because ovarian tissue transplantation may not be appropriate in the setting of prior malignancy.

Medical marijuana for palliation of symptoms in women with gynecologic cancers

A.L. Brodsky, D. Gerber, K. Lutz, E. Reece, B. Pothuri and A. Kim. *New York University School of Medicine, New York, NY, USA, bNYU Clinical Cancer Center, New York, NY, USA

Objective: The use of medical marijuana (MM) in cancer patients was legalized in New York state in 2016. Reported benefits of MM include reduction of cancer-associated pain, nausea, vomiting, fatigue, and improved appetite, as well as mitigating other side effects of cancer treatment. Tetrahydrocannabinol (THC) and cannabidiol (CBD), both components of MM, have been shown to have therapeutic benefit for cancer-related symptoms. Dosing of MM is described in terms of the THC:CBD ratio. While the general therapeutic benefits have been documented, there is a paucity of data on MM use in patients with gynecologic cancers (GC). We sought to evaluate the effect of medical marijuana for symptom management in patients with GC at our institution.

Method: We retrospectively identified women with GC using MM between May 2016 and August 2018 from the medical record. Demographic data, cancer diagnosis, dosage form, quantity, frequency, length of treatment, indication, and reported efficacy of MM were collected.

Results: We identified 34 patients using MM for a diagnosis of GC. Table 1 lists the patient characteristics and indications for MM and dosing. Median age of patients using MM was 60 years (46–78 years). Median length of treatment with MM was 189 days (11–761 days). Response to MM included 17(50%) improvement in symptoms; 3 (9%) minimal change; 10 (29%) not reported yet; and 4 (12%) unknown. Overall, among patients for whom symptom improvement was available to date, 17/20 (85%) noted improvement. Four (12%) patients reported unwanted side effects, which were euphoria, dizziness, fatigue, and paranoia. Three patients who reported side effects received MM with a 1:1 THC:CBD ratio; the other patient received a low...
THC: high CBD dosing. Only one (3%) patient ceased medical marijuana use because of untoward adverse effects. All the patients who reported an improvement in symptoms while using MM were concurrently receiving chemotherapy. Improvement in symptoms was not related to formulation, form, or length of treatment of MM.

**Conclusion:** An improvement in symptoms associated with cancer and treatment was noted in over 80% of GC patients using MM, and very few reported adverse side effects. MM is likely to be a promising treatment for pain, nausea, and anorexia in GC patients and should be considered in the armamentarium of palliative cancer treatment options.

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<th>Cancer site</th>
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<th>On chemotherapy?</th>
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<tr>
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<tr>
<td>Pain</td>
<td>22 (65%)</td>
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<tr>
<td>Nausea and Vomiting</td>
<td>16 (47%)</td>
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<td>Anorexia</td>
<td>9 (26%)</td>
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<tr>
<td>Insomnia</td>
<td>3 (9%)</td>
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<tr>
<td>Fatigue</td>
<td>2 (6%)</td>
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<td>Anxiety</td>
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<th>Dosing Ratio (THC:CBD)</th>
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<td>1:1</td>
<td>23 (68%)</td>
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<td>Low: High</td>
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<td>14 (41%)</td>
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<tr>
<td>Oral</td>
<td>9 (26%)</td>
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1612 - Poster Session
**Variation in utilization of end-of-life resources by cancer site**
V. Pleasant\(^a\), R.J. Spencer\(^b\), S. Bell\(^c\), R.K. Reynolds\(^d\), L.W. Rice\(^e\) and S. Uppal\(^f\). \(^a\)The University of Michigan Hospitals, Ann Arbor, MI, USA, \(^b\)University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, \(^c\)University of Michigan, Ann Arbor, MI, USA

**Objective:** To examine the differences in end-of-life resource utilization among patients diagnosed with gynecologic malignancies (cervical, endometrial, or ovarian) compared to the five most prevalent nongynecologic cancers (breast, colorectal, lung, pancreatic, and prostate).

**Method:** This was a cross-sectional retrospective study from the Surveillance, Epidemiology, and End Results Program (SEER)-Medicare linked database from 2008 to 2013. Consistent with previous publications, end-of-life utilization of the following were examined in the last 30 days of life: 2 or more visits to the emergency department (ED), any life-extending procedure, hospice ≤3 days, any hospice use, admission to intensive care unit (ICU), hospitalizations, terminal hospitalization (death in hospital), or chemotherapy (last 14 days).

**Results:** Gynecologic cancers had higher hospitalization rates in the last 30 days of life compared to nongynecologic cancers (52.5% vs 50.8%, \(P = 0.003\)). However, terminal hospitalization for cervical (24.7%), endometrial (28.5%), and ovarian (25.4%) cancers were similar to those for nongynecologic cancers (range 20.7%–34.3%, \(P > 0.05\)). Gynecologic cancers had lower rates of hospice utilization compared to nongynecologic cancers (14.9% vs 32.1%, \(P < 0.001\)). Specifically cervical (15.9%), endometrial (12.2%), ovarian (17.1%), and pancreatic cancer (19.5%) had a lowest utilization of hospice compared to other cancer sites (35.9%–55.9%, \(P < 0.001\) for gynecologic vs nongynecologic). More gynecologic cancer patients received chemotherapy within 14 days of death compared to patients with nongynecologic cancers (1.1% vs 0.7%, \(P < 0.001\)). This difference was likely driven by ovarian cancer patients with rates double that of other malignancies (1.7% vs 0.7%, \(P < 0.001\)). There were no differences between the rate of terminal hospitalization, ED utilization, any life-extending procedures, or ICU utilization between gynecologic and nongynecologic cancers (Table 1).

**Conclusion:** Patients with gynecologic cancers may have barriers in their care that delay or impede hospice enrollment and allow for continued medical treatments such as chemotherapy, even at the end of life. Further research in this area is necessary to identify explanations for this discrepancy for patients with gynecologic cancers.
Table 1. End-of-life care by cancer type

<table>
<thead>
<tr>
<th>End of life treatment or event</th>
<th>Gynecologic(^1) (N=9,846 cancer diagnoses)</th>
<th>Not gynecologic(^2) (N=36,702 cancer diagnoses)</th>
<th>P-value(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\geq 2) ED Visits</td>
<td>584 (5.9%)</td>
<td>2,326 (6.3%)</td>
<td>0.1393</td>
</tr>
<tr>
<td>Life extending procedure (any)</td>
<td>662 (6.7%)</td>
<td>2,651 (7.2%)</td>
<td>0.087</td>
</tr>
<tr>
<td>Hospice (\leq 3) days in length</td>
<td>413 (4.2%)</td>
<td>3,451 (9.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any hospice</td>
<td>1,466 (14.9%)</td>
<td>11,792 (32.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ICU</td>
<td>2,042 (20.7%)</td>
<td>7,890 (21.5%)</td>
<td>0.103</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>5,168 (52.5%)</td>
<td>18,646 (50.8%)</td>
<td>0.030</td>
</tr>
<tr>
<td>Terminal hospitalization</td>
<td>2,624 (26.7%)</td>
<td>9,821 (26.8%)</td>
<td>0.8292</td>
</tr>
<tr>
<td>Chemotherapy(^4)</td>
<td>106 (1.1%)</td>
<td>248 (0.7%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

(1) Includes cervical, endometrial, and ovarian cancer (2) Includes breast, colorectal, lung, pancreatic, and prostate cancer (3) Chi-square test – does not account for patients who have multiple cancer diagnoses (4) Administered 1-4 days prior to death

1613 - Poster Session
Outcomes after gastrostomy tubes for malignant bowel obstruction
C. Hoppenot\(^a\), P.N. Peters\(^b\), M. Cowan\(^a\), N.K. Lee\(^a\) and S.D. Yamada\(^a\). \(^a\)The University of Chicago Medicine, Chicago, IL, USA, \(^b\)University of California, San Francisco, San Francisco, CA, USA

Objective: To compare outcomes for patients who underwent gastrostomy tube (GT) placement for malignant bowel obstruction (MBO) from recurrent gynecologic cancer to those who were surgically or medically managed.

Method: This was a retrospective chart review of patient characteristics, inpatient interventions, and outcomes of patients admitted between 2005 and 2016 for MBO from recurrent gynecologic cancer at two institutions.

Results: A total of 180 patients were included. The majority of patients (98%) had ovarian or uterine cancer; 21% were managed with GT only: 11 surgically and 27 minimally invasively. Forty-two other patients had a laparotomy (LAP) for relief of MBO, 4 of whom subsequently needed a GT, and 100 had neither procedure (MED). Twenty GT patients (48%) required at least 1 other procedure to adjust or replace it. Eleven others had an unsuccessful attempt at GT placement. There was no difference in origin of cancer, disease status, or number of previous chemotherapy regimens between GT, LAP, or MED patients. Rates of complications were 65% for LAP and GT patients and 42% for MED patients. After discharge, GT and LAP patients had similar rates of chemotherapy (53% and 50%) and TPN use (30% and 19%, respectively), with lower rates for MED patients (41% chemo, \(P = 0.07\); 8% TPN, \(P = 0.001\)). Of GT patients 89% had a documented goals-of-care conversation, versus 62% of LAP patients and 74% of MED patients (\(P < 0.05\)). Rates of hospice, however, were similar in the GT patients (50%) and MED patients (42%) (\(P = NS\)) and lower in LAP patients (26%, \(P = 0.01\)). Median survival after MBO was similar for GT and MED patients (93 and 77 days, respectively) and longer in LAP patients (190 days, \(P < 0.001\)). One GT patient (2.7%), 8 MED patients (8%), and no LAP patients died during their MBO admission.

Conclusion: GT used for palliation of MBO symptoms is associated with a high rate (48%) of additional procedures, similar rates of chemotherapy, and no difference in survival compared to patients managed medically. These data can help inform counseling and expectations in patients admitted for MBO from recurrent gynecologic cancers. Future research, however, should focus on patient-reported outcomes and quality of life to assist in shared decision making.

1614 - Poster Session
Gastrointestinal fistula formation in cervical cancer patients who received bevacizumab
D. Gerber\(^a\), J.P. Curtin\(^b\), M. Saleh\(^a\), L.R. Boyd\(^a\), S. Lymberis\(^a\), P.B. Schiff\(^a\), B. Pothuri\(^a\) and J. Lee\(^a\). \(^a\)New York University School of Medicine, New York, NY, USA, \(^b\)The University of Texas Southwestern Medical Center, Dallas, TX, USA

Objective: The Gynecologic Oncology Group (GOG) study 240 demonstrated a 3.5-month improvement in overall survival when bevacizumab (bev) was added to a combination chemotherapy regimen. This study established a bev-containing regimen as standard therapy for women with recurrent, persistent, or metastatic cervical cancer (CC). Gastrointestinal fistula (GIF) formation is a known complication of bev, and the long-term data of GOG 240 reported that a GIF rate of 15% in women
who were treated with bev compared to 1% in the control group women. We sought to evaluate our experience with women treated with bev for CC and to identify associated risk factors for GIF formation.

**Method:** All patients who have received bev for CC from 2012 to 2018 at two academic institutions were identified, and their records were reviewed. Standard two-sided statistical analyses were performed.

**Results:** A total of 43 women were treated with a bev-containing chemotherapy regimen; among them, 34 (79.1%) were treated for CC recurrence, and the remaining were treated for metastatic disease at initial presentation or persistent disease following primary treatment. Thirty-three women (76.6%) received prior radiation therapy (RT); of these, 10 (32.3%) received external beam radiation therapy (EBRT), and 21 (67.7%) had prior EBRT and brachytherapy (BT). The median dose of bev was 15 mg/kg for both EBRT only and EBRT and BT groups. Eleven women developed GIF after bev treatment (11/43, 25.6%). All 11 (100%) had been previously treated with RT, and six (54.5%) had received EBRT plus BT. This resulted in rates of 33.3% (11/33) for GIF formation among women who received EBRT, and 28.6% (6/21) for GIF formation among women who received EBRT plus BT. The median number of bev cycles prior to GIF development was 8 (1–29), and 7 (7/11, 63.6%) received the dose of bev (15 mg/kg) as prescribed in GOG 240. See Table 1.

**Conclusion:** In our cohort of women with CC who were treated with bev, over 25% developed GIF. This is more than expected based on the 15% seen in GOG 240. Notably almost all who developed GIF had recurrent disease and were treated with prior RT. A third of women treated with RT followed by bev formed GIF, representing a considerable proportion of the cohort. GIF development and the possibility of requiring a colostomy should be a part of counseling prior to bev initiation especially in those who have had prior RT.

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>(+) Fistula (n = 11)</th>
<th>(-) Fistula (n = 32)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range, years)</td>
<td>48 (28–67)</td>
<td>52 (34–78)</td>
<td>0.4</td>
</tr>
<tr>
<td>BMI, median (range, kg/m²)</td>
<td>27.9 (17.8–44.4)</td>
<td>25.6 (16.5–44.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Stage (n, %)</td>
<td></td>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>T1/T2/T3A</td>
<td>9 (90.0%)</td>
<td>22 (71.0%)</td>
<td></td>
</tr>
<tr>
<td>T1/T2/T3B</td>
<td>1 (10.0%)</td>
<td>9 (29.0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Histology (n, %)</td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1 (11.1%)</td>
<td>6 (19.4%)</td>
<td></td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>3 (33.3%)</td>
<td>10 (31.3%)</td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>7 (63.7%)</td>
<td>23 (71.9%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Prior hysterectomy (n, %)</td>
<td></td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>6 (18.8%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11 (100.0%)</td>
<td>11 (81.3%)</td>
<td></td>
</tr>
<tr>
<td>Disease presentation (n, %)</td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Metastatic</td>
<td>1 (9.1%)</td>
<td>8 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Recurrent</td>
<td>10 (90.9%)</td>
<td>24 (75.0%)</td>
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<tr>
<td>History of radiation therapy (n, %)</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>Yes</td>
<td>11 (100.0%)</td>
<td>23 (71.9%)</td>
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</tr>
<tr>
<td>No</td>
<td>0 (0.0%)</td>
<td>10 (31.3%)</td>
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</tr>
<tr>
<td>History of brachytherapy (n, %)</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>6 (54.5%)</td>
<td>13 (59.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5 (45.5%)</td>
<td>13 (41.0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

1615 - Poster Session
**Electronic symptom monitoring with patient-reported outcomes in patients recovering from ambulatory minimally invasive gynecologic cancer surgery: A prospective pilot study**

**Objective:** To test an electronic symptom tracking platform and determine its clinical usefulness for patients undergoing ambulatory cancer surgery.
**Method:** This single-arm pilot study assessed user response of an electronic system designed to self-report symptoms among patients recovering from ambulatory surgery. Secondary endpoints included evaluation of postoperative patient-reported symptoms after surgery and patient satisfaction. An 8-item symptom inventory of pain, nausea, vomiting, shortness of breath, fever, swelling, discharge, and redness was developed. On postoperative days (POD) 2–6, all patients were asked to complete the symptom inventory. If responses exceeded defined thresholds of severity, alerts to health care providers were triggered. Postoperative symptoms, alerts, actions taken, urgent care center (UCC) visits, and hospital admissions were tracked until POD 30. Patient satisfaction was evaluated on POD 7. A patient was defined as a “responder” if at least 3 of 8 symptom items on at least 3 PODs were completed. The symptom assessment method was deemed successful if 64 of 100 patients responded.

**Results:** Of 102 patients, 97 were evaluable and 65 met criteria as “responders,” for a 67% responder rate (95% CI 57.2–75.6%). A total of 321 surveys were completed (mean, 3.7 surveys per patient; median, 4). Of these, 248 (77%) were completed in ≤2 minutes. Involving caregivers and allowing for additional symptom reporting improved the responder rate to 72% (95% CI 58.3–82.5%). Most commonly reported moderate, severe, and very severe symptoms were pain, nausea, and swelling; 71% of patients reported moderate to very severe pain on POD 2. Phone calls with review or adjustment of supportive medications were sufficient to address most symptoms. Two patients (2%) presented at the UCC before and 4 patients (4%) after POD 6; 1 patient (1%) was admitted. Most patients agreed or strongly agreed that electronic symptom tracking was helpful and easy to use and that they would recommend it to other patients.

**Conclusion:** Electronic postoperative electronic symptom tracking is feasible for patients undergoing ambulatory gynecologic cancer surgery. Symptom burden is high in the early postoperative period. Addressing patient-reported symptoms following surgery in a timely and automated manner may prevent severe downstream adverse events, reduce UCC visits and readmission rates, and ultimately improve outcomes.

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**1616 - Poster Session**

**A single-arm clinical trial investigating the effectiveness of a non-hormonal vaginal moisturizer in postmenopausal cancer survivors**


**Objective:** To assess the efficacy of a nonhormonal hyaluronic acid (HLA) vaginal gel in improving vulvovaginal estrogen-deprivation symptoms in postmenopausal women with a history of breast or endometrial cancer.

**Method:** We identified patients with a history of HR+ breast cancer treated with an aromatase inhibitor or endometrial cancer treated with surgery/radiation, with no current evidence of disease, who had completed treatment 3–60 months prior to enrollment. Assessment points were at baseline (T1), 4–6 weeks (T2), 12–14 weeks (T3), and 22–24 weeks (T4) after starting study treatment. Participants used HLA daily for 2 weeks, followed by 3 times per week until T3. Patients with no improvement in vulvovaginal symptoms or pH at T3 increased HLA use to 5 times per week. Assessments included clinical evaluation, the Vaginal Assessment Scale (VAS), the Vulvar Assessment Scale (VuAS), the Female Sexual Function Index (FSFI), and the Menopausal Symptom Checklist (MSCL).

**Results:** Of 101 patients, mean age was 55 years (range 31–78 years); 68% (n = 69) were partnered; and 60% (n = 61) reported current sexual activity. Compared to baseline (T1), VAS and VuAS scores significantly improved at T2, T3, and T4 (all \( P < 0.001 \)). In addition, VAS scores also significantly improved from T2 to T4, and VuAS scores significantly improved from T3 to T4 (both \( P < 0.01 \)). FSFI and MSCL total scores significantly improved from baseline to T2, T3, and T4 (all \( P < 0.001 \)). Of women with measurements at both T1 and T4, 51% (n = 29) felt confident about future sexual activity at T1 compared to 68% (n = 39) at T4 (\( P = 0.03 \)). Severe vaginal pH (>6.5) decreased from 26% (n = 17) at T1 to 19% (n = 12) at T4 (\( P = 0.18 \)). Presence of vestibular irritation significantly improved from 48% (n = 32) at T1 to 27% (n = 18) at T4 (\( P < 0.01 \)). Prevalence of vestibular irritation also decreased from 59% (n = 39) at T1 to 36% (n = 24) at T4 (\( P < 0.01 \)). At T3, 72% (n = 57) of patients were deemed nonresponders (no change or worsening) and increased application from 3 to 5 times per week.

**Conclusion:** HLA vaginal moisturizing gel applied intravaginally and topically to the vulva improved the vulvovaginal health and sexual function of cancer survivors in perceived symptoms and clinical exam outcomes. HLA needs to be used at a higher frequency (3 to 5 times per week) than recommended for general menopause (1 to 2 times per week) to achieve symptom relief.
Objective: We investigated the effect of self-administered guided imagery, a meditation technique used to treat stress, on perioperative distress and pain scores in women undergoing surgical management for a suspected gynecologic malignancy.

Method: We conducted a randomized, comparative, multicenter trial in patients undergoing surgical intervention by gynecologic oncologists at 2 comprehensive cancer centers between April 2015 and February 2016. A total of 130 eligible patients were randomized to receive standard care (SOC, n = 65) or standard care plus guided imagery (GI, n = 65) for managing pain and distress in the perioperative period. Distress, pain, positive affect, agency, and locus of control were measured using validated instruments at baseline, on postoperative day 1, and at the postoperative visit. Predictors of distress and pain scores were identified using multivariate logistic regression with random effects and ANOVA.

Results: A total of 100 patients completed surveys at all 3 time points (N_{SOC} = 46 and N_{GI} = 54). The study arms were balanced with respect to core demographics, disease state, and surgical characteristics. Study arm was not a predictor of overall pain or distress scores, but it did significantly predict distress in patients with procedurally confirmed malignancy (P = 0.02). As shown in the left panel of Figure 1, there was a significant interaction between timepoint and study arm (P = 0.03), where distress decreased at the postoperative visit only for those in the intervention arm. Those with lower positive affect and agency scores had higher pain and distress scores regardless of their study arm.

Conclusion: Self-administered guided imagery significantly decreased distress at the time of the postoperative visit for those undergoing surgery for a procedurally confirmed gynecologic malignancy. This nonpharmaceutical intervention may be a beneficial adjunctive strategy in a comprehensive pain management plan aimed at limiting long-term narcotic abuse.

Fig. 1. Mean distress score (left) and pain score (right) at baseline (Time 0), postoperative day 1 (Time 1), and postoperative visit (Time 2) for patients with surgically confirmed gynecologic malignancies. The control arm (0) is shown in red and the intervention in blue (1). Error bars represent standard error of the sample means.
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1618 - Poster Session
More severe financial toxicity correlated with worse quality of life in gynecologic cancer patients on treatment

Objective: Our objective was to determine the relationship between financial toxicity and quality of life (QOL) among gynecologic cancer patients receiving systemic therapy.

Method: A cross-sectional survey of women with gynecologic cancer who started a new line of systemic therapy, within the previous 2 months, was conducted over the phone or in-person at a tertiary care referral center. Comprehensive Score for Financial Toxicity (COST) was obtained on a scale of 0–44 with lower score indicating worse financial toxicity. COST <26 was used as a threshold for financial toxicity. Functional Assessment of Cancer Therapy-General (FACT-G) was obtained on a scale of 0–108 with lower score indicating worse QOL. Patient and treatment characteristics were abstracted from the medical record. Descriptive statistics, Pearson correlation coefficients, and linear regression were performed.

Results: There were 79 participants, including 54% ovarian, 24% uterine, 16% cervical, and 5% vulvar/vaginal cancer patients. The majority of participants (58%) were receiving their first line of systemic therapy. Median COST score was 23 (range 4–43), resulting in 61% of participants screening positive for financial toxicity. Median QOL scores were total FACT-G, 71 (range 38–103); physical well-being, 15 (range 4–28); social well-being, 22 (range 0–28); emotional well-being, 19 (range 4–24); and functional well-being, 15 (range 2–28). A moderate correlation was noted between COST and total FACT-G scores ($r = 0.59, \( P < 0.01 \)) with worse financial toxicity associated with worse QOL. Similarly, moderate correlations were observed between COST and emotional ($r = 0.45, \( P < 0.01 \)), functional ($r = 0.46, \( P < 0.01 \)), and physical ($r = 0.59, \( P < 0.01 \)) well-being subscale scores. No significant correlation was seen between COST and social well-being subscale scores. The presence of financial toxicity was associated on average with a 15-point decrease in total FACT-G score ($P < 0.01$) after controlling for age, race, annual household income <$40,000, insurance type (public vs private), cancer type, and line of treatment (first vs subsequent).

Conclusion: Financial toxicity is associated with a decline in QOL, supporting COST as a relevant patient-reported outcome. These findings also emphasize the impact of financial toxicity on multiple domains (emotional, functional, and physical) among gynecologic cancer patients undergoing treatment.

1619 - Poster Session
Lymphovenous anastomosis: A reasonable treatment of secondary lower extremity lymphedema arising from the treatment of gynecologic malignancies
M.J. Song¹, E.Y. Ki² and S.J. Lee³. ¹Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Dae Jeon, South Korea, ²Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea, ³St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea, Suwon, South Korea

Objective: We investigated the feasibility and efficacy of lymphatic venous anastomosis (LVA) for the treatment of lower extremity lymphedema resulting from lymphadenectomy or radiation therapy in treatment of gynecologic malignancies.

Method: Between December 2017 and July 2018, 33 patients with secondary lower extremity lymphedema underwent lymphovenous anastomosis in the groin area. Campisi staging was used for the clinical staging of lymphatic edema. All patients underwent lymphoscintigraphy to ensure accurate diagnosis of lymphatic edema. Surgery was performed on patients with a modified transport index (TI) >10 calculated by lymphoscintigraphy or patients with recurrent lymphangitis. Indocyanine green (ICG) was injected into dorsal subcutaneous space (between first and second toes) 12 hours before the operation to assess the functional lymphatic flow by ICG-lymphangiography during the LVA. Indigocarmine (blue dye) was also injected into the thigh 10 minutes before surgery. Lymphatic vessels afferent to the blue dye or ICG-stained nodes were used to perform LVA using a collateral branch of the great saphenous vein. Indocyanine green-stained lymph nodes and lymph vessels were identified with a near infrared (NIR) camera. Treatment effects were assessed using lower extremity lymphedema index (LELI) 3 months after surgery.

Results: There were 6 patients with stage II, 21 patients with stage III, 5 patients with stage IV, and 1 patient with stage IV. Five patients had recurrent lymphangitis. Mean preoperative transport index by lymphoscintigraphy was 29.2. Mean operation time was 176 minutes. Thirty-one patients achieved reduction in affected leg volume (94%). Among these cases, 15
patients showed reduction of more than 3 cm in the circumference of the lower leg. Mean volume reduction rate 3 months after surgery was 16.4% by LELI measurement. Pitting edemas were improved in all cases. See Figure 1.

**Conclusion:** Lymphovenous anastomosis is a feasible and effective surgical procedure for those struggling with lower extremity lymphedema. This approach could be a reasonable choice for the treatment of secondary lymphedema refractory to complex physical therapy.

**Fig. 1.**
**Objective:** Opioids are the first-line treatment for moderate to severe cancer-related pain. Increased awareness of opioid prescription misuse and adverse outcomes have prompted statements on their use from multiple national medical groups. In this study we characterize national-level opioid prescription patterns among gynecologic oncologists treating Medicare beneficiaries.

**Method:** The Centers for Medicare and Medicaid Services (CMS) database was used to access Medicare Part D beneficiary data (2016). All available opioid claims prescribed by gynecologic oncologists were identified. Medication type, prescription length, and other prescribing factors were recorded. Physician demographics were obtained from departmental websites and accrediting bodies. Physicians with fewer than 10 opioid claims are not included in the CMS database. Bivariate statistical analyses including $\chi^2$, Fisher exact test, and Wilcoxon rank sum test were performed to compare variables with threshold for significance set at $P < 0.05$. Linear regression modeling was also performed to examine association of gender with number of opioids prescribed.

**Results:** A total of 494 board-certified gynecologic oncologists were included in this analysis. In 2016, gynecologic oncologists wrote 23,584 opioid prescriptions for 267,824 days of treatment (average of 9.24 prescribed days per claim). The most commonly prescribed opioid was oxycodone/acetaminophen (41%). Male physicians had significantly more opioid prescription claims than females ($P < 0.01$) including after adjusting for differences in years of experience. The majority of physicians had 11–50 opioid prescription claims (68%). A minority were high-prescribing physicians with more than 100 opioid claims (11%). Of these, the overwhelming majority were male (82%) and late career (46%, >15 years since board certification). Physicians in the South had the greatest number of opioid prescription claims and significantly more than physicians in the Northeast, who had the fewest ($P < 0.01$). Mean number of opioid claims increased with increasing years of experience ($P < 0.05$). See Table 1.

**Conclusion:** Among gynecologic oncologists, there were gender-based, regional, and experience-related variations in opioid prescribing in the Medicare population in 2016. Further longitudinal studies are required to elucidate secular trends in opioid prescription practice.

**Table 1.**

<table>
<thead>
<tr>
<th>Characteristics*</th>
<th>Total Cohort (N=494)</th>
<th>Female (N=193)</th>
<th>Male (N=301)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>224 (45)</td>
<td>85 (44)</td>
<td>139 (46)</td>
<td>0.70</td>
</tr>
<tr>
<td>Midwest</td>
<td>97 (20)</td>
<td>35 (18)</td>
<td>62 (21)</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>91 (18)</td>
<td>40 (21)</td>
<td>51 (17)</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>82 (17)</td>
<td>33 (17)</td>
<td>49 (16)</td>
<td></td>
</tr>
<tr>
<td>Certified in palliative care</td>
<td>19 (4)</td>
<td>5 (3)</td>
<td>14 (5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Years since certification</td>
<td>12 (5, 21)</td>
<td>6 (3, 13)</td>
<td>17 (8, 24)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Beneficiary count†</td>
<td>27 (15, 46)</td>
<td>24 (15, 39)</td>
<td>29 (16, 52)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total claims filed for opiate prescriptions</td>
<td>33 (18, 64)</td>
<td>27 (16, 47)</td>
<td>39 (20, 72)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total number of days of opiate prescribed</td>
<td>260 (136, 596)</td>
<td>223 (129, 447)</td>
<td>285 (152, 654)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total number of days of opiate per claim</td>
<td>8 (6, 11)</td>
<td>8 (6, 12)</td>
<td>8 (6, 11)</td>
<td>0.84</td>
</tr>
<tr>
<td>Total cost for opiates prescribed (dollars)</td>
<td>459 (243, 1033)</td>
<td>420 (238, 874)</td>
<td>532 (255, 1239)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* Continuous data reported as median (interquartile range). Categorical data are presented as N (%).
† Based on 426 available observations.
1621 - Poster Session
Low knowledge of coverage benefits and insurance characteristics do not increase the risk of financial toxicity in the gynecologic cancer population

Objective: The objective of this study was to evaluate the impact of patient knowledge of coverage benefits and insurance characteristics on financial toxicity among gynecologic cancer patients actively on treatment.

Method: A cross-sectional survey of gynecologic cancer patients, who started a new line of systemic therapy within the previous 8 weeks, was conducted over the phone or in-person at a tertiary care referral center. Participants were asked to report their insurance type, premium, deductible, and out-of-pocket maximum. Financial toxicity was determined using Comprehensive Score for Financial Toxicity (COST) <26. Descriptive statistics and χ² analysis were performed.

Results: Out of 79 participants, 5 (6%) were uninsured, which left 74 patients with evaluable responses related to insurance. The majority of participants had at least some private insurance (77%) and were covered on an individual (84%) plan. Forty-seven (64%) knew their premium; the average monthly premium was $339 (range $25–$2,700). Eight (11%) participants reported their monthly premium had increased since their cancer diagnosis with an average increase of $235 (range $6–$750). Thirty-six participants (49%) knew their deductible; the average annual deductible was $4,321 (range $18–$25,000). Half of these coverage plans (53%) were considered high-deductible health plans (HDHP) based on the Internal Revenue Service definition of ≥$1,350 deductible for an individual. Twenty-two (32%) participants knew their out-of-pocket maximum; the average annual out-of-pocket maximum was $7,738 ($200–$75,000). Not knowing one’s premium, deductible, or out-of-pocket maximum was not associated with financial toxicity. Insurance type (any private vs only public insurance) or HDHP was also not associated with financial toxicity.

Conclusion: Gynecologic cancer patients receiving treatment were frequently unaware of the dollar amount for their premium, deductible, or out-of-pocket maximum; however, patients’ lack of knowledge regarding their benefits and insurance characteristics was not a significant risk factor for financial toxicity.

1622 - Poster Session
The value of financial and time costs to ovarian cancer patients when making decisions about their care
M.I. Liang, E. Funkhouser, K. Kenzik, M. Martin, W. Huh and M. Pisu. University of Alabama at Birmingham, Birmingham, AL, USA, University of Tennessee Health Science Center, Memphis, TN, USA

Objective: The objective of this study was to understand how ovarian cancer patients value financial and time costs when making decisions about their care.

Method: This was a cross-sectional survey of ovarian cancer patients diagnosed within the last 2 years who were recruited from 2 cancer centers and a statewide registry in Alabama. Phone interviews were conducted that asked participants to rate each factor from “very important” to “not very important” when making decisions about their care. Descriptive statistics and χ² analysis were performed.

Results: The response rate was 66%, resulting in 170 participants. Forty-two percent were 65 years and older, and 24% were African-American. The majority were employed (58%). Insurance coverage ranged from private insurance (48%), Medicare and/or Medicaid (42%), or uninsured (5%). There were 36 (21%) patients who stated their income was not enough to meet their basic needs along with their medical care. Patients rated the following factors as “very important” when choosing their physicians for treatment: insurance coverage (84%), cost even with insurance (66%), time away from family (52%), transportation (40%), distance (28%), and time away from work (18%). Annual household income <$25,000 was associated with higher rates of concern about costs even with insurance (79% vs 59%, P < 0.01), transportation (57% vs 34%, P < 0.01), and distance (48% vs 18%, P < 0.01). Not being able to meet basic needs along with medical care was associated with higher rates of concern for cost even with insurance (81% vs 61%, P = 0.046), time away from work (33% vs 15%, P = 0.02), and transportation (67% vs 33%, P < 0.01). Fewer patients rated the following factors as “very important” for decisions related to chemotherapy: insurance coverage (4%), time away from family (5%), transportation (1%), distance (3%), and time away from work (1%). Instead, for chemotherapy, more patients rated immediate side effects (35%), late side effects (26%), and how side effects would affect family, work, and other activities as “very important.”
Conclusion: Ovarian cancer patients strongly consider financial and time costs when choosing their physicians for cancer treatment; however, these factors were less important once patients were making decisions about chemotherapy at which time side effects were more highly valued.

1623 - Poster Session
Economic and humanistic burden associated with cervical cancer: An analysis of patient-reported outcomes in Europe (the H-EMBRACE study)
M.J. Doanea and C. Nwankwob. aKantar Health, Horsham, PA, USA, bMRL, Kenilworth, NJ, USA

Objective: Cervical cancer (CC) represents the sixth most frequent female cancer in Europe, with a total of 58,373 new cases of CC and 24,404 deaths from CC reported in Europe in 2012. This study compared demographic and patient-reported outcomes (PROs) between women with and without a diagnosis of CC in Europe.

Methods: Data were from the 2016–2018 National Health and Wellness Surveys (NHWS) conducted in the EU5 (i.e., France, Germany, Italy, Spain, and the United Kingdom). This study used cross-sectional, retrospective, internet-based survey data representative of adults across the EU5 (n = 204,600). Women who reported a diagnosis of CC were compared with women who did not report any cancer diagnosis. Bivariate analyses (i.e., χ² and t tests) assessed differences in demographics and PROs between these two groups. Humanistic outcomes included mental and physical component summary scores (MCS and PCS) of the SF-36. Economic outcomes included work productivity loss and health care resource use.

Results: Of 89,839 female respondents, 725 reported a CC diagnosis. CC respondents were less likely to be employed full-time (29.5% vs 34.4%, P < 0.05) and were older (52.2 vs 44.5 years, P < 0.05) than respondents without CC. In addition, CC respondents reported living with more comorbid conditions (0.5 vs 0.2, P < 0.05) and were more likely to be current smokers (43.6% vs 23.2%, P < 0.05). CC respondents reported significantly lower PCS scores (46.9 vs 50.8, P < 0.05) relative to respondents without CC. Among employed women, CC respondents reported greater absenteeism from work (12.3% vs 8.0%, P < 0.05) and presenteeism while at work (23.6% vs 20.3%, P < 0.05), leading to greater overall work impairment (30.8% vs 24.9%, P < 0.05). CC respondents also reported greater impairment of their daily activities (36.3% vs 26.8%, P < 0.05). Women with CC were more likely to visit any HCP (94.6% vs 86.2%, P < 0.05) and have 1 or more hospitalizations (12.7% vs 7.8%, P < 0.05) during the prior 6 months. Many of the differences between the 2 groups remained significant even when current and former smokers were excluded from analyses (Table 1).

Conclusion: CC is associated with both humanistic (e.g., health-related quality of life) and economic burden (e.g., work productivity loss and health care resource use) among women in the EU5.
Objective: The Clinical Practice Committee of the Society of Gynecologic Oncology recommends palliative care for women with advanced gynecologic cancers. Therefore, we sought to describe national trends in the utilization of palliative care among older women with uterine, ovarian, cervical, and vulvar cancer.

Method: We included women 66 years and older with stage III–IV ovarian, cervical, or vulvar cancer diagnosed from 2004 to 2013 in the linked Surveillance, Epidemiology, End Results (SEER) Medicare database. Patient demographic, cancer, and treatment characteristics were extracted. Palliative care consultation (PCC) was defined as the presence of the ICD-9 code V66.7 “Encounter for palliative care.” We calculated unadjusted and adjusted prevalence ratios for PCC using a log binomial regression model. The multivariate model included age, marital status, race, poverty level, region, Charlson comorbidity index, year of diagnosis, disease site, stage, and initial treatment variables.

Results: We identified 13,255 women diagnosed between 2004 and 2013 with uterine (n = 4,123), ovary (n = 7,597), cervix (n = 1,033), and vulva (n = 502) cancer. The overall rate of PCC was 7.4%, and this differed significantly by cancer type: uterine 6.6%, ovary 7.5%, cervix 10.5%, and vulva 6.8%. In the women who had PCC, 45.5% had an early PCC within 56 days of diagnosis. On univariate analysis, women were statistically more likely to have a PCC if they were 85 years and older, single versus married, black versus white, lower socioeconomic status, living in a western region, Charlson comorbidity index > 0, later calendar year at diagnosis (see Figure 1), stage IV at diagnosis, and absence of surgery or chemotherapy at initial diagnosis. In the fully adjusted model, only later calendar year of diagnosis, stage IV, and absence of initial or chemotherapy remained statistically significant. Women who had surgery were 49% less likely to have a PCC (P < 0.001), and women who had chemotherapy were 42% less likely to have a PCC compared to the women who did not have treatment (P < 0.001).

Conclusion: The rate of PCC in older women with advanced gynecologic malignancies is increasing, but appears to target those with the poorest prognosis. New innovations are needed to increase concurrent palliative care with standard oncology treatment to improve symptom control and quality of life.

Fig. 1.
1625 - Poster Session

Does using hormonal therapy after risk reducing salpingo-oophorectomy increase the incidence of malignancy in women with high risk genetic predisposition to cancer?


*a*Washington University School of Medicine in St. Louis, St. Louis, MO, USA, bMoffitt Cancer Center-University of South Florida, Tampa, FL, USA, cMayo Clinic, Rochester, MN, USA, dThe Ohio State University, Columbus, OH, USA, eH. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA, fThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, gThe Ohio State University College of Medicine, Columbus, OH, USA

**Objective:** The aim of this study was to assess the effect of hormone replacement therapy (HRT) on the incidence of subsequent malignancies in patients with genetic predisposition to müllerian cancers who have undergone risk-reducing salpingo-oophorectomy (RRSO) in a national cohort.

**Method:** After Institutional Review Board approval, a retrospective multicenter cohort study was performed at 4 academic institutions. Women age 18–51 years with confirmed pathogenic mutations who underwent RRSO between 1991 and 2016 were included. Patients with a prior malignancy were excluded. Clinicodemographic data were collected, and patients with no documented contact for the year prior to study end were called to confirm duration of hormone use and occurrence of secondary outcomes. HRT included any combination of progesterone or estrogen. Categorical and continuous variables were analyzed using $\chi^2$ or Fisher exact test and Student $t$ test or Kruskal-Wallis test as appropriate.

**Results:** A total of 126 patients were included with a mean age of 41.6 years and a median 6-year follow-up after RRSO. Sixty-three patients received HRT (50%), and 63 did not (50%). HRT regimens included oral estrogen ($n = 30, 47.6\%$), oral estrogen and progesterone ($n = 29, 46\%$), and vaginal estrogen ($n = 4, 6.3\%$). High-risk mutations included $BRCA1$ ($n = 74$), $BRCA2$ ($n = 49$), DNA mismatch repair defects ($n = 2$), and $RAD51$ ($n = 1$), and were not significantly different between HRT and no HRT groups. No difference in race, BMI, incidence of concurrent hysterectomy, or years since RRSO between groups was found. Patients receiving HRT were younger (39.0 vs. 44.2 years, $P < 0.01$) and more frequently underwent risk-reducing mastectomy (69.8% vs 50.8%, $P = 0.03$). There was no difference in malignancy incidence between HRT and no HRT groups ($n = 6$ vs $n = 7$, $P = 0.80$, OR = 0.84). Subsequent malignancies identified were melanoma ($n = 1$), GI ($n = 1$), breast ($n = 6$), leukemia ($n = 1$), and basal and squamous cell skin carcinomas ($n = 6$). Outcomes including osteoporosis, stroke, myocardial infarction, venous thromboembolism, and death were rare and not significantly different in both cohorts.

**Conclusion:** In this multiinstitution retrospective study, there was no significant difference in the incidence of malignancy after RRSO in patients with high-risk genetic mutations treated with HRT. Further large-scale data collection is underway to better assess long-term outcomes in this patient population.

1626 - Poster Session

Weight intervention in endometrial cancer: A pilot program


*a*University of Missouri, Columbia, MO, USA, bHunter Oncology, Columbia, MO, USA

**Objective:** Obesity is a strong risk factor for the development and persistence of endometrial cancer. Few patients receive direct physician-to-patient nutrition counseling in oncology. This study evaluates the efficacy of direct physician recommendations of a low-carbohydrate, high-vegetable, high-plant-fat diet on weight loss for 2 years following surgical staging for endometrial cancer.

**Method:** Cancer-specific nutritional guidelines were crafted into a 6-page patient handout. The guidelines suggested daily carbohydrates of 40 grams, and a shift to plant-based foods dominated by plant fats, with minimal aged cheeses and lean meat. Fasting was encouraged. Random distribution of endometrial cancer patients into 2 attending clinics created 2 patient groups. The experimental group (EG) received materials and 20 minutes of physician diet-counseling during the initial consultation. The control group (CG) received the standard of care, encouraging a healthy lifestyle and diet, with a referral to the dietitian. A retrospective chart review of all patients seen from 2014 to 2016 with a BMI $>34$ kg/m$^2$ and a diagnosis of endometrial cancer was performed. Differences in variables were compared using $\chi^2$ and one-way ANOVA.
Results: A total of 106 patients were included, 62 in the EG group and 44 controls. The average BMI at consult was 44 kg/m² and did not differ between groups, nor did age, stage, chemotherapy, or the rate of open surgery. At 6 months from consult, 39% of EG patients achieved a reduction in body weight of more than 5%, compared to 9% in the control group ($P = 0.001$). Of the 93 patients evaluable at 12 months, 29% maintained a 5% or greater weight reduction, compared to 11% for controls ($P = 0.03$). At 18 months 33% and 14% ($P = 0.04$) and at 24 months 26% and 14% (NS) of patients in EG and CG maintained a 5% reduction, respectively.

Conclusion: Direct physician-to-patient counseling with recommendations of a low-carbohydrate, high-plant-fat diet results in greater weight loss in patients with endometrial cancer compared to a traditional approach. The experimental group maintained a continued improvement over the control group for up to 2 years. This study provides a basis for evaluation of the long-term benefits of weight loss with a low-carbohydrate, high-plant-fat diet in endometrial cancer patients.

1627 - Poster Session
Power of support: The effect of peer navigation on the emotional strain and coping for women with gynecologic cancers in early survivorship
F.J. Hlubockya, L. Hassenfritzb, J.S. Kimc and N.K. Leea,b. aThe University of Chicago Medicine, Chicago, IL, USA, bUniversity of Chicago, Chicago, IL, USA

Objective: The aim of this study was to investigate the longitudinal effects of a pilot peer navigation program on the emotional strain (e.g., stress, loneliness) and ability to cope for gynecologic cancer survivors (GCS).

Method: A GCS who completed treatment 1 year prior underwent extensive training as a peer navigator and was later paired with a newly diagnosed patient initiating gynecologic cancer treatment at (1) initial diagnosis, (2) postsurgery, or (3) chemotherapy/radiation. Participant psychosocial needs were assessed at baseline (T1), 6 months (T2), and 12 months (T3) using quantitative measures including stress (Impact of Events Scale), loneliness (UCLA Loneliness Scale), and coping (Brief COPE).

Results: To date, a total of 40 participants (23 patients and 17 peer navigators) have enrolled. Patient demographics include mean age 58.7 years (41–67 years); ethnicity, 59% African-American, 40% Caucasian, and 1% Latina; and diagnosis, 71% endometrial, 28% ovarian, and 1% cervical. For peer navigators, demographics include mean age 61.8 years (range 48–80 years); ethnicity, 65% Caucasian, 30% African-American, and 5% Latina; and diagnosis, 47% endometrial, 12% cervical, and 41% ovarian. At T1, significant differences were identified between the 2 groups for overall stress (27.9 ± 2.9 vs 32.5 ± 4.7, $P = 0.04$) and loneliness (31.9 ± 4.4 vs 35 ± 6.2, $P = 0.03$) with patients reporting greater symptom severity. Peer navigators reported high utilization of emotional support coping (87.0%) and acceptance (55%), with low utilization of denial (29.5%) and self-blame (39.9%) at T1. The effect of the navigation program on patient emotional strain and coping adjustment to cancer revealed a transient difference at the 6-month follow-up, when patients reported reduction in overall: stress ($P = 0.04$), loneliness ($P = 0.002$), avoidant coping ($P = 0.001$), and denial ($P = 0.04$). No additional significant effects were observed.

Conclusion: A well-trained, experienced peer navigator may provide meaningful emotional and social support to a newly diagnosed woman with gynecological cancer. Future investigation should involve large-scale, culturally sensitive, multiinstitutional, randomized controlled trials of a peer navigator intervention for gynecologic survivors to facilitate coping.

1628 - Poster Session
Risk for anxiety and depression among individuals with ovarian cancer: The interplay between age and distress
M. Donzigera, A.K. Zaletaa, S. McManusb, J. Olsonb, R. Salani, N.K. Leea, K. Santiagoa, S. La Cavaa, M.L. Smithf, S. DeFeoa and K. Steinb. aCancer Support Community, Washington, DC, USA, bCancer Support Community, Research and Training Institute, Philadelphia, PA, USA, cThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, dUniversity of Chicago, Chicago, IL, USA, eCancer Support Community Los Angeles, Benjamin Center, Los Angeles, CA, USA, fResearch Advocacy Network, Plano, TX, USA, gOvarian Cancer Research Fund Alliance, New York City, NY, USA

Objective: With limited screening options for ovarian cancer, most women are diagnosed with advanced disease, which can have an impact on quality of life. Younger age may also be associated with distress, given fertility and relationship concerns. This study explored predictors of psychosocial distress among a community-based sample of ovarian cancer survivors.
Method: A total of 128 ovarian cancer survivors enrolled in the Cancer Support Community’s Cancer Experience Registry®. Participants provided sociodemosographics and reported cancer-related distress using CancerSupportSource®, a validated 25-item tool measuring level of concern (0–4) over 5 domains: emotional concerns (including a 4-item depression/anxiety risk screening subscale), symptom burden, body/healthy lifestyle, health care team communication (HCTC), and relationships. We examined risk for clinically significant anxiety and depression, and used logistic regression to explore associations between domains of concern and anxiety/depression risk and to determine whether associations vary by age.

Results: Participants were 86% non-Hispanic white; mean age was 57.3 years, SD = 10.9; mean time since diagnosis was 4.5 years, SD = 6.2. Thirty-four percent were metastatic, and 45% received chemotherapy, 22% radiation, and 11% hormone therapy. Fifty-five percent were at risk for clinically significant anxiety, and 37% for clinically significant depression. Relationship, body/healthy lifestyle, symptom burden, and HCTC concerns were bivariately associated with anxiety and depression risk (P < 0.001). After controlling for significant demographic/clinical variables, HCTC concerns predicted anxiety risk (R² [Nagelkerke] = 0.46, OR = 1.74, P < 0.005). In addition, the interaction between relationship concerns and age predicted anxiety risk, with the association being stronger for younger survivors (R² = 0.52, OR = 0.95, P < 0.05). HCTC concerns also predicted depression risk (R² = 0.51, OR = 1.59, P < 0.05); this did not vary by age.

Conclusion: Health care team communication concerns predict risk for clinically significant anxiety and depression in ovarian cancer survivors. In addition, relationship concerns predict anxiety risk, especially among younger survivors. Findings highlight the need for constructive patient-provider communications, focusing on relationships, sexual health, and fertility concerns.

1629 - Poster Session
Factors influencing the feasibility and safety of outpatient robotic-assisted hysterectomy for the treatment of endometrial and cervical cancers
P.C. Lima,b, T.S. Matern3 and E. Kangb. aUniversity of Nevada School of Medicine at Reno, Reno, NV, USA, bCenter of Hope, Reno, NV, USA

Objective: To identify the factors influencing the feasibility and safety of outpatient surgery for gynecologic oncology patients undergoing robotic-assisted hysterectomy for endometrial or cervical carcinoma.

Method: We performed a single-institution retrospective chart review of patients undergoing robotic-assisted hysterectomy for cervical or endometrial cancer between 2012 and 2016. Patient outcomes were measured by length of stay (LOS), which was categorized as an admit-to-discharge time of >12 hours (inpatient) or <12 hours (outpatient). Past medical history, surgical history, social history, patient demographics, intraoperative course, and postoperative events were examined as possible factors associated with LOS >12 hours. These factors were evaluated and compared using multivariate logistic regression. The rate of readmission between the inpatient and outpatient groups was compared using an independent-samples t test.

Results: Of the 254 patient charts that were reviewed, 150 (59.1%) had a LOS >12 hours and 104 (40.9%) had a LOS <12 hours. The factors that were associated with a LOS >12 hours (P < 0.05) included postoperative emesis, inadequate pain control, OR time > 180 minutes, uterine mass >150 grams, start time after 3:00 pm, past history of venous thromboembolism (VTE), age >75 years, BMI 35–39.9, and postoperative VTE formation. Of the 7 patients who were readmitted, those in the outpatient category (n = 3) were not more likely than those in the inpatient category (n = 4) to be rehospitalized (P = 0.92).

Conclusion: Robotic hysterectomy for the treatment of endometrial and cervical carcinoma in the outpatient setting is both feasible and safe, as >40% of patients were successfully treated as outpatients with no increase in readmission. Multiple risk factors were identified for extended hospitalization, offering potential for the development of a risk stratification model to improve the efficacy of outpatient robotic hysterectomy.

1630 - Poster Session
Impact of morcellation on mortality in women with unexpected uterine cancer who underwent hysterectomy and myomectomy
X. Xua, J.D. Wrightb, C.P. Grossa, H. Lin5, F.P. Boscoed, L.M. Hutchisond, P.E. Schwartza and V.B. Desaia,e. aYale University School of Medicine, New Haven, CT, USA, bColumbia University College of Physicians and Surgeons, New York, NY, USA, cYale University
Objective: To determine whether laparoscopic power morcellation is associated with increased mortality in women with occult uterine cancer who underwent a hysterectomy or myomectomy for presumed benign indications.

Method: By linking hospital discharge records from the New York Statewide Planning and Research Cooperative System to state cancer registry data, we identified women who underwent a hysterectomy/myomectomy for benign indications during the period October 1, 2003–December 31, 2013, with an unexpected diagnosis of uterine cancer within 28 days after the surgery. Disease-specific mortality was measured for each patient, along with age, race/ethnicity, stage, grade, cancer subtype, history of other cancer, comorbidity, and cancer treatment. We used laparoscopic supracervical hysterectomy/laparoscopic myomectomy (LSH/LM) as a surrogate indicator for power morcellation, as this was the standard technique used during the study period. We included supracervical abdominal hysterectomy/abdominal myomectomy (SAH/AM) and total abdominal hysterectomy (TAH) as two comparison groups, which did not involve power morcellation. We compared mortality between groups using Cox proportional hazards regression with adjustment for patient characteristics and their propensity score of undergoing different surgical approaches.

Results: Our sample included 60,230 and 889 women with occult uterine cancer who underwent an LSH/LM, SAH/AM, or TAH, respectively. Median duration of follow up was 48 months (IQR 26–78 months). Patient characteristics differed significantly across groups generally favoring the LSH/LM group. After adjusting for patient characteristics and propensity score of surgical approach, disease-specific survival did not differ significantly across the LSH/LM, SAH/AM, and TAH groups in women with occult endometrial carcinoma. However, in women with occult leiomyosarcoma, LSH/LM was associated with a significantly higher risk for disease-specific mortality compared to SAH/AM and TAH (aHR = 4.27, \( P < 0.01 \), and aHR = 5.32, \( P < 0.01 \), respectively). See Table 1.

Conclusion: Laparoscopic power morcellation did not affect disease-specific mortality in women with occult endometrial carcinoma but was associated with higher disease-specific mortality in women with occult leiomyosarcoma.

Table 1. Comparison of disease-specific mortality by surgical group in women with occult uterine cancer.
Emerging Pathologic Assessment, Treatments and Novel Therapies in Development

2101 - Poster Session
Neoadjuvant chemotherapy with taxane and platinum regimen could improve the long-term prognosis for patients with locally advanced cervical cancer
T. Wana and J. Liu. aSun Yat-Sen University, Cancer Center, Guangzhou, China, bCancer Center, Sun Yat-Sen University, Guangzhou, China

Objective: We sought to identify the long-term effects of neoadjuvant chemotherapy (NACT) with taxane and platinum-based regimen (TP) in locally advanced cervical cancer patients.

Method: A total of 330 patients with FIGO stage IB2 or IIA2 cervical cancer were retrospectively studied. These patients were treated with NACT followed by radical surgery between 2005 and 2010 at Sun Yat-sen University Cancer Center. The median follow-up period was 76 months (range 3–150 months). All enrolled patients received 1–3 cycles of platinum-based NACT. One hundred seventy-seven patients received TP regimen (group A), and 153 patients received other platinum combination regimens (group B).

Results: After NACT, patients with complete or partial response (CR or PR) were defined as responsive; the responsive rate in group A was 80.2% and in Group B 83.0%. Five-year PFS and OS was 87.5% (95% CI 84.8%–93.0%) and 93.2% (95% CI 89.3%–97.1%) in group A, and 80.0% (95% CI 73.5%–86.5%) and 83.2% (95% CI 77.1%–89.3%), respectively, in group B. The HR of recurrence and death was in favor of group A (recurrence HR = 0.51, 95% CI 0.30–0.89, P = 0.017; death HR = 0.35, 95% CI 0.17–0.70, P = 0.003). See Figure 1.

Conclusion: NACT followed by radical surgery approach is an effective alternative option for patients with stage IB2 and IIA2 cervical cancer. The taxane/platinum regimen might be one of the most effective regimens for NACT from the long-term survival observation.

Fig. 1. Progression Free Survival

2102 - Poster Session
Association between isolated tumor cells and recurrence in stage I endometrial cancer
A.M. Puech1, K.C. Strickland1, E.J. Tanner III1, T. Murdock1, G. Broadwater1, J.A. Ehrisman2, P.S. Lee2, A.A. Secord2 and L. Havrilesky3. aDuke University Medical Center, Durham, NC, USA, bJohns Hopkins Hospital, Baltimore, MD, USA
Objective: It is unclear whether isolated tumor cells (ITCs) identified in pelvic sentinel lymph nodes (SLNs) predict recurrence of early-stage endometrial cancer. We sought to identify the prognostic value of ITCs in early-stage endometrial cancer.

Method: From 2011 to 2017, patients from two institutions with stage 1 endometrial cancer who underwent surgical staging and SLN assessment were included in a retrospective case control study. Inclusion criteria were bilateral SLN mapping or unilateral SLN mapping plus contralateral pelvic lymphadenectomy. Cases comprised women who developed recurrence and were matched 1:1 to cases without recurrence. Groups were matched for age, histology, grade, depth of invasion, lymphovascular space invasion (LVSI), and adjuvant therapy. SLNs were evaluated for ITCs using an ultrastaging protocol employing H&E and cytokeratin IHC. Power analysis, assuming a baseline ITC rate of 15% and planned power of 90%, resulted in an intended n = 40 in each cohort to detect a 20% absolute difference in ITC detection rate between cases and controls.

Results: A total of 36 subjects with recurrence (cases) were identified and matched to 36 subjects without recurrence (controls). Sixty patients (83%) had endometrioid histology: 23 grade 1 (32%), 19 grade 2 (26%). Among cases, 12 (33.3%) had recurrent disease at the vaginal cuff only, 8 (22.2%) recurred in the pelvis only, and 16 (44.4%) had abdominal/distant recurrence. Median age in both groups was 66 years. Median follow-up time was 2.2 years. Median depth of myometrial invasion for controls and cases was 40% and 44%, respectively (P = 0.47). LVSI was present in 18 patients with recurrence (50%) and in 15 patients without recurrence (42%, P = 0.48). Nineteen of the controls (53%) and 16 of the cases (44%) received adjuvant treatment. ITCs were identified in 7 patients (9.7%): 3 cases (8.3%), 4 controls (11.1%, P = 0.7). All ITCs were identified in SLNs. Given the lower than expected ITC rate in both cohorts, as well as an actual n = 36 per cohort, a futility power analysis was performed, revealing a less than 5% chance that a higher ITC rate is associated with recurrence.

Conclusion: The presence of ITCs in pelvic SLNs was not associated with recurrence in stage I endometrial cancer. These findings are similar to what has been observed in breast cancer and suggest that use of IHC to detect ITCs may not be useful in guiding adjuvant therapy.

2103 - Poster Session
Quantitative computed tomography image feature analysis predicts response to immune checkpoint inhibitors in gynecologic cancers
K.G. Essela, T. Thaia, K. Dingb, W.C. Burkett Jr.a, M.E. Buechela, B. Zhenga and K.N. Moorec. aThe University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, bThe University of Oklahoma, Oklahoma City, OK, USA, cThe University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK, USA

Objective: To investigate the role of applying quantitative image (QI) feature analysis computed from computed tomography (CT) images for early prediction of tumor response to immune checkpoint inhibitors (ICPI) among patients with recurrent gynecologic cancer.

Method: We conducted a retrospective review of 56 patients with gynecologic cancer at a single institution who received an ICPI for management of recurrent disease. Each patient had CT images prior to and after the initiation of therapy. A computer-aided detection scheme was applied to segment metastatic tumors previously tracked by radiologists on CT images, and image features were computed. A QI feature pool was built, and a features selection method was applied to select optimal features; an equal-weighted fusion method was used to generate a new quantitative imaging marker for each pool to predict 6-month progression-free survival (6PFS). The prediction accuracy between quantitative imaging markers and the response evaluation criteria in solid tumors version 1.1 (RECIST) criteria and immune RECIST criteria (iRECIST) were also compared. Complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) were assessed by RECIST criteria.

Results: Of the 56 patients identified, 29 patients (51.8%) had ovarian cancer; 16 patients (28.6%) had cervical cancer; and 11 patients (19.6%) had uterine cancer. Thirty-eight patients (67.9%) received a programmed death 1 (PD-1) inhibitor; 11 patients (19.6%) received a programmed death-ligand 1 (PD-L1) inhibitor; 5 patients (8.9%) received a combination of PD-1 inhibitor and cytotoxic lymphocyte antigen-4 (CTLA-4) inhibitor; 1 patient (1.8%) received anti-cell immunoglobulin and ITIM domain protein (TIGIT); and 1 patient (1.8%) received a GITR-agonist resulting in 1 CR, 9 PR, 9 SD, and 20 PD, respectively. The area under the receiver operating characteristic curve (AUC) is 0.95 when QI feature analysis is used to predict 6PFS and 0.81 when RECIST criteria are used. The QI feature analysis resulted in a prediction accuracy level of 92.3% versus 61.5% with RECIST criteria versus 70.9% with iRECIST criteria. See Figure 1.
Conclusion: Quantitative CT image feature analysis accurately predicts response to ICPI in patients with recurrent gynecologic cancer. This technology is a promising tool for predicting the clinical benefit of ICPIs early in the course of treatment of gynecologic cancers.

Fig. 1. ROC Curves for Comparisons

2104 - Poster Session
Pathologic chemotherapy response score (pCRS) after neoadjuvant chemotherapy in advanced ovarian/peritoneal/fallopian tube cancer does not predict optimal cytoreduction or recurrence-free survival

aThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, bJames Cancer Hospital, Columbus, OH, USA, cThe Ohio State University, Columbus, OH, USA, dThe Ohio State University Medical Center, Columbus, OH, USA

Objective: We sought to evaluate a pathologic chemotherapy response score (pCRS) system in advanced ovarian/fallopian tube/peritoneal cancer at a single institution cohort as it relates to surgical cytoreduction and outcomes.

Method: Pathologic specimens of women with advanced ovarian/fallopian tube/peritoneal cancer who received NACT then interval debulking surgery (IDS) from January 2016 to December 2017 were prospectively assigned a pCRS per the AJCC/UICC/CAP protocol (January 2016); subjects were classified as pCRS1, 2, or 3. A pCRS was assigned by board-certified pathologists. Clinicopathologic data were analyzed, and recurrence data were calculated from date of diagnosis to recurrence. Optimal cytoreduction was defined as ≤1 cm residual. All patients received treatment acceptable from National Cancer Comprehensive Network guidelines during their therapy. The log rank test was used to test for differences in survival by pCRS.

Results: There were 53 subjects assigned a pCRS. The majority of patients were scored pCRS2 (58.5%), followed by pCRS1 and pCRS3 (26.4% and 15.1%, respectively). The median number of pre-IDS chemotherapy cycles was similar for pCRS1, 2, 3 (4, 3, 3.5 cycles, P = 0.82) as was CA-125 at time of diagnosis (1,407.5, 1,228.4, 818 U/mL, P = 0.68 Kruskal-Wallis). All patients with pCRS2 and 3 were high-grade serous histology. pCRS1 included 2 low-grade serous and 1 clear cell histology. Most patients underwent NACT because of disease extent. Pre-IDS CA-125 was similar among the three groups (399.54, 258.4, 52.49, P = 0.17). All patients with pCRS2 or 3 underwent optimal cytoreduction with most achieving no gross residual (77%). Of the 53 patients, only 2 had suboptimal IDS both of which were assigned CRS1 and were low-grade serous histology. Recurrence was frequent among all three groups; 78.5% of pCRS1, 74.2% of pCRS2, and 75% of pCRS3 subjects recurred.
Median recurrence-free survival was similar among the three groups at 13.2, 13.53, and 17.1 months ($P = 0.2$). Similarly, overall survival (OS) was not different; however, median OS was not reached for pCRS1 or 3.

**Conclusion:** pCRS does not predict recurrence-free survival and thus should not be used for prognostic counseling. Furthermore, most patients regardless of pCRS will undergo complete or optimal cytoreduction, and therefore this information likely does not allow for preoperative stratification for suboptimal debulking during interval cytoreductive surgery.

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**2105 - Poster Session**

**Use of low-dose whole abdominal radiation therapy (LDWART) as a chemosensitizer in combination with weekly paclitaxel for platinum-resistant ovarian cancer: Safety analysis**


*National Cancer Institute, Singapore, Singapore, Singapore, National University Cancer Institute, Singapore (NCIS), National University Hospital, Singapore, Singapore, Singapore, National University Hospital of Singapore, Singapore, Singapore, National University of Singapore, Singapore, Singapore, National University Hospital, Singapore, Singapore*

**Objective:** TP53 mutations are common in epithelial ovarian cancer. Hyperradiation sensitivity (HRS) is enhanced in cells with mutant TP53, where effective cell killing occurs even at very low doses, ~0.1 Gy, of radiation. HRS in the form of low-dose fractionated radiation therapy (LDFRT) has been associated with upregulation of several pro-apoptotic proteins in tumors, thus potentiating the efficacy of chemotherapy. We hypothesized that combining low-dose fractionated whole abdominal radiation therapy (LDWART) as a chemosensitizer with weekly paclitaxel (WP) may be feasible and safe for patients with platinum-resistant ovarian cancer and evaluated this novel therapeutic combination in a phase I study.

**Method:** This study is a single arm phase I study with 3+3 dose de-escalation design. Patients with platinum-resistant (disease progression <6 months from last platinum treatment) epithelial ovarian cancer (including fallopian tube and primary peritoneum carcinoma) with measurable intra-abdominal disease were treated with WP and LDWART at 60-cGy fractions, twice daily for two days, with a minimum of 4 hours inter-fraction interval for 6 weeks (Figure 1). The pre-planned dose levels of WP in combination with LDWART were DL1, 80 mg/m$^2$; DL2, 70 mg/m$^2$; and DL3, 60 mg/m$^2$. Safety and tolerability were assessed in all patients using the CTCAE Version 4.03.

**Results:** Six patients received study treatment at DL1. No dose-limiting toxicity (DLT) was observed in the initial 3 patients. An additional 3 patients were recruited into DL1 for further safety analysis. The most common study-related adverse events (AE) ≥ grade 3/4 observed were G3 neutropenia lasting less than 7 days (67%), G3 thrombocytopenia (17%) not associated with bleeding, and G3 anemia (17%). Other grade ≤2 AE observed were fatigue (83%), nausea (67%), peripheral neuropathy (67%), vomiting (50%), and diarrhea (50%). Six of six patients had dose interruptions, and 1 patient had a dose reduction after cycle 1 due to recurrent G3 neutropenia.

**Conclusion:** LDWART is feasible, well tolerated, and safe when used with WP at 80 mg/m$^2$ for heavily pretreated ovarian cancer patients. This RP2D dose will be used in the phase II study for efficacy and safety analysis. An additional 4 patients will be recruited to confirm safety at this dose level.
2106 - Poster Session
The learning curve of surgeon influences recurrence after robotic radical hysterectomy in stage IB cervical cancer
P.C. Lim, J. Paek and E. Kang. University of Nevada School of Medicine at Reno, Reno, NV, USA, Ajou University School of Medicine, Suwon, South Korea, Center of Hope, Reno, NV, USA

Objective: To assess the clinicopathologic prognostic factors for survival after robotic radical hysterectomy (RRH) in the treatment of stage IB cervical cancer.

Method: A retrospective study was performed on a cohort of patients who underwent robotic radical hysterectomy from March 2008 to March 2018. During this period, 82 cervical cancer patients underwent RRH by a single surgeon. Patients who had stage IA, stage II, or neuroendocrine cell type were excluded. Overall, 65 patients were enrolled in this study. We determined the recurrence rate and site of recurrence and assessed the overall survival rate. Univariate and multivariate variables such as age, types of radical hysterectomy, clinical tumor size, stage, grade, lymphovascular space involvement, parametrial and vaginal cuff involvement, operative time, blood loss, and learning curve parameters were analyzed to assess prognostic factors for survival.

Results: The overall recurrence rate was 10.8% (7/65). There were 5 recurrences in the pelvic cavity, 1 at the vaginal vault, and 1 at the spine. The overall survival rate was 94% (4/65). The median follow-up was 47 months. Multivariate analysis showed that the early period of RRH ($P = 0.027$, HR = 0.04, 95% CI 0.01–0.69) and clinical tumor size more than 3 cm ($P = 0.005$, HR = 2.68, 95% CI 1.16–6.14) were prognostic factors related to the recurrence. When patients were divided into 3 groups in order based on surgery date, the first period showed significantly higher recurrence rate (5/21, 24%) compared to both the second (2/22, 9%) and third periods (0/22) ($P = 0.040$). Although there was no significance in multivariate analysis, there was no recurrence since the uterine colpotomizer was not used. There was no predictor related to overall survival via multivariate analysis. See Figure 1.

Conclusion: The learning curve and tumor size were related to the disease recurrence after RRH. Although the utilization of colpotomizer did not show significance in the analysis, interestingly there was no recurrence when colpotomizer was omitted as part of the robotic radical hysterectomy technique. We suggest that the achievement of proficiency and appropriate patient selection are critical for prognosis after RRH in stage IB cervical cancer.

Fig. 1. Treatment Schema during LDWART
Novel targeted TRAIL-based therapy for ovarian cancer using SMAC mimetic as sensitizing agent
T.R. Buchanan Jr., J.C. Cripe, A.S. Zamorano, D.G. Mutch, M.A. Powell and D. Spitzer. Washington University School of Medicine in St. Louis, St. Louis, MO, USA

Objective: Although TNF-α related apoptosis inducing ligand (TRAIL) is highly biologically active in its recombinant form, efficacy for most TRAIL-based therapeutics is limited. Combination therapy with drugs that mimic the second mitochondria-derived activator of caspases (SMAC) have been shown to cause cell death by competitively binding to apoptosis inhibitors, overcoming TRAIL resistance by activating both intrinsic and extrinsic apoptosis pathways. We aim to show that using a modified TRAIL agent can safely and effectively cause ovarian cancer cell death more efficiently when combined with SMAC mimetics.

Method: Drugs used included TRAIL-based TR3 and modified CA-125-targeted variant, Meso64-TR3, and Sigma-2/SMAC drug conjugates SW III-123 and SW IV-134 with carboplatin as a comparison. OVCAR3 cells were treated in 96 well plates with all drugs both alone and in combination. Cell viability was performed with ATP quantification using CellTiter-Glo. Detection of relative protein expression was performed with multiplexed array. Toxicity studies were done by dosing at similarly therapeutic levels in NOD SCID mice.

Results: Expression of CA-125 in OVCAR3 cells was confirmed via flow cytometry. OVCAR3 cells were treated similarly, but Meso64-TR3 showed significantly higher cell-killing activity than TR3 at the same concentrations ($P < 0.01$). TR3 and Meso64-TR3 combination therapy with SMAC mimetics showed a greater response than both drugs alone. EC$_{50}$ was reduced from 14.5 pM to 7.0 pM with SW III-123 and 4.3 pM with SW IV-134. Relative expression of bax, caspase 3, SMAC, TNFα, HSP27/60.
were all increased in combination therapy (Figure 1A). Meso64-TR3 showed similar activity when combined with carboplatin as it did with SW1V-134 (P = 0.90) and outperformed carboplatin alone (p < 0.001) (Figure 1B). All combinations of drugs given to treatment-naive mice; weight, hemoglobin, platelets, and liver function tests were all statistically similar to controls (Figure 1C).

**Conclusion:** Meso64-TR3 exhibits superior activity in treating ovarian cancer cells compared to nontargeted TR3 agents and amplified when used in combination with SW III-123, and a greater extent with SW IV-134. When compared to carboplatin, the combination of Meso64-TR3 and SW IV-134 was superior to carboplatin alone and noninferior to carboplatin in combination. Therapeutic doses showed minimal toxicity in a mouse model. These targeted agents should be further explored.

2108 - Poster Session
Molecular portraits of clear cell ovarian and endometrial carcinoma with comparison to clear cell renal cell carcinoma


**a**Fox Chase Cancer Center, Philadelphia, PA, USA, **b**Caris Life Sciences, Irving, TX, USA, **c**Cleveland Clinic, Cleveland, OH, USA, **d**University of Tennessee West Cancer Center, Memphis, TN, USA, **e**Wayne State University, Detroit, MI, USA, **f**Florida Hospital Cancer Institute, Orlando, FL, USA, **g**Western Pennsylvania Hospital, Pittsburgh, PA, USA, **h**Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, **i**WVU Healthcare, Morgantown, WV, USA, **j**UC Health Barrett Cancer Center, Cincinnati, OH, USA, **k**Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA

**Objective:** Advanced clear cell gynecologic malignancies remain among the most challenging diseases to manage. In clear cell ovarian carcinoma (OCCC), prior studies have evaluated immunohistochemistry (IHC) and hot-spot sequencing. Here, we evaluate OCCC and endometrial clear cell carcinoma (ECCC) using more comprehensive technologies and compare their molecular profiles to clear cell renal cell carcinoma (ccRCC).

**Method:** A total of 164 OCCC, 75 ECCC, and 234 ccRCC specimens were evaluated by Caris Life Sciences from 2015 to 2018 using next-generation sequencing (NGS), fragment analysis (FA), and in situ hybridization (ISH). Comparisons were done using χ² analysis.

**Results:** The median age was 57.5 years (26–80 years) for OCCC and 67 years (44–83 years) for ECCC. In OCCC, the highest mutations rates were in ARIDIA (87.5%), PIK3CA (46.8%), PPP2RIA (16.7%), ATM (12.8%), and TP53 (11.1%). In ECCC, the
highest rates were in ARID1A (75.0%), TP53 (34.8%), PIK3CA (25.0%), PPP2R1A (8.7%), and PTEN (8.3%). MSI-high was detected in OCCC (6.4%) by NGS, and ECCC (11.5%) by FA. The only significant difference was in TP53 between OCCC and ECCC (11 vs 34.8%, P = 0.019). Compared to ccRCC, OCCC and ECCC were significantly (all P < 0.05) more likely to have mutations in ARID1A (85 vs 5.1%), ATM (9.9 vs 1.1%), ERBB2 (2.9 vs 0%), FBXW7 (11.9 vs 0%), FGFR2 (2.9 vs 0%), KRAS (8.5 vs 0%), MSH6 (3 vs 0%), PIK3CA (39.4 vs 3.3%), PPP2R1A (13.8 vs 0%), and TP53 (19.1 vs 6.3%) and have higher tumor mutation burden (TMB) (7 vs 6.6%). Significant differences (all P < 0.05) between OCCC and ccRCC included ARID1A (87.5 vs 5.1%), ATM (12.8 vs 1.1%), BAP1 (0 vs 12.2%), FBXW7 (7.7 vs 0%), KDM5C (3 vs 29.2%), KRAS (10.6 vs 0%), MSH6 (4.7 vs 0%), PBRM1 (0 vs 43.9%), PIK3CA (46.8 vs 3.3%), POLE (4.7 vs 0%), PPP2R1A (16.7 vs 0%), SETD2 (0 vs 31.1%), and VHL (0 vs 80.3%). Significant differences (all P < 0.05) between ECCC and ccRCC included ARID1A (75 vs 5.1%), CTNNB1 (4.2 vs 0%), ERBB2 (4.2 vs 0%), FBXW7 (4.2 vs 0%), FGFR2 (4.2 vs 0%), KDM5C (0 vs 29.2%), KRAS (4.2 vs 0%), PBRM1 (0 vs 43.9%), PIK3CA (25 vs 3.3%), PPP2R1A (8.7 vs 0%), SETD2 (0 vs 31.1%), STK11 (4.2 vs 0%), TP53 (34.8 vs 6.3%), and VHL (0 vs 80.3%). See Table 1.

**Conclusion:** OCCC and ECCC are similar diseases requiring novel approaches. Prospective clinical trials are needed to examine targeted therapies as well as checkpoint inhibition in these gynecologic disease subtypes.

**Table 1.** Molecular portraits of clear cell ovarian and endometrial carcinoma with comparison to clear cell renal cell carcinoma.

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<th>Pathway</th>
<th>Marker</th>
<th>Method</th>
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<th>ECCC (%)</th>
<th>ccRCC (%)</th>
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Column values represent the % total cases with mutation present by Next Generation Sequencing (NGS) or comprehensive in situ hybridization (ISH).

**2109 - Poster Session**

**Somatic and germline genetic testing in advanced ovarian/peritoneal/fallopian tube cancer and pathologic chemotherapy response score (pCRS) after neoadjuvant chemotherapy**

C.M. Cosgrove, L. Senter, R. Owda, D.E. Cohn, A.A. Suarez and R. Salani. *The Ohio State University, James Cancer Hospital, Columbus, OH, USA, The Ohio State University, Columbus, OH, USA, James Cancer Hospital, Columbus, OH, USA.*
Objective: We sought to evaluate a pathologic chemotherapy response score (pCRS) system in a single-institution cohort from an NCI-designated CCC institution as it relates to somatic and germline genetic mutations/alterations.

Method: Pathologic specimens of women with advanced ovarian/fallopian tube/peritoneal cancer who received neoadjuvant chemotherapy (NACT) and then interval debulking surgery (IDS) from January 2016 to December 2017 were prospectively assigned a pCRS per the AJCC/UICC/CAP protocol (January 2016): 1, no or minimal tumor response; 2, appreciable tumor response amid viable tumor, both readily identifiable and tumor regularly distributed; and 3, complete or near-complete response with no residual tumor or minimal irregularly scattered tumor foci seen as individual cells, groups, or nodules up to 2 mm in maximum size. A pCRS was assigned by board-certified pathologists. Clinicopathologic data were analyzed. Clinical genetic test results were reviewed for each pCRS group.

Results: Forty-three subjects had either germline and/or somatic genetic testing. Nineteen (44.2%) of subjects had germline, somatic, or epigenetic tumor mutations/alterations classified as either deleterious or were suspected to be pathologic: 1 (11.1%) of pCRS1, 15 (57.7%) of pCRS2, and 3 (37.5%) of pCRS3 (P = 0.048). When the mutations were evaluated, most were BRCA1/2 (84.2%) followed by RAD51C/D genes (15.8%). Thirteen of 15 mutations in pCRS2 patients were in BRCA1/2; in fact, 13 of 16 individuals with BRCA4 mutations had a pCRS2. Of the individuals with genetic alterations, 11 of 15 (73.3%) with a pCRS2 recurred as did the one with pCRS1 and 3 of 3 pCRS3 recurred. The subject with a pCRS1 had a mutation in BRCA and relapsed at 427 days.

Conclusion: Germline, somatic, and epigenetic variants are common in advanced ovarian/fallopian tube/peritoneal cancer. The presence of a deleterious genetic alteration was more common in patients who exhibited histologic response to chemotherapy, either pCRS2 or pCRS3. Most women with a deleterious genetic alteration will demonstrate a pCRS2 and have BRCA4 alteration. Women with no or minimal histologic response, pCRS1, rarely had a genetic alteration identified. Despite histologic response to chemotherapy at IDS most women with advanced cancer will recur even when a genetic alteration is present.

2110 - Poster Session

Diamonds in the rough: An analysis of complete pathologic responders in ovarian cancer

C.J. LaFargue, N.D. Fleming, A.M. Nick, A. Chelaru-Raicu, B. Fellman, T. Castellano, A. Ogasawara, M.S. Home, E.A. Blake, A.K. Crim, S.N. West, R.L. Coleman, K. Matsuo, K. Hasegawa, K.N. Moore and A.K. Sood. «The University of Texas MD Anderson Cancer Center, Houston, TX, USA, »Tennessee Oncology, Nashville, TN, USA, »The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, »Saitama Medical University International Medical Center, Hidaka, Japan, »University of Southern California, Los Angeles, CA, USA, »Keck School of Medicine of USC, Los Angeles, CA, USA

Objective: To identify the clinical and demographic features of ovarian cancer patients who attain a pathologic complete response (pCR) at interval tumor reductive surgery (TRS) following neoadjuvant chemotherapy (NACT).

Method: All patients with suspected advanced-stage ovarian cancer who received NACT followed by interval TRS between June 2004 and September 2018 at our institution were identified. To determine clinical differences between those with pCR versus non-pCR, 3 collaborating institutions provided records of all known pCR patients from the past 10 years. PFS and OS were estimated using Kaplan-Meier product limit estimator. Patient characteristics were compared using standard summary statistics.

Results: A total of 476 patients were identified, with 21 having attained a pCR for an overall rate of 4.4%. In addition, 28 patients who had attained a pCR at collaborating institutions were included. There was no difference in median baseline CA-125 or platelet values between the pCR and non-pCR patients (731 vs 932, P = 0.65, and 358,000 vs 400,000, P = 0.18, respectively.) The proportion of patients with BRCA1 or BRCA2 mutations was similar between the pCR and non-pCR groups (27.6% vs 21.1%, P = 0.62, respectively). Regardless of whether pCR was attained, patients who harbored either a BRCA1 or BRCA2 mutation had a significantly better PFS than those who did not (17.9 and 12.7 vs 11.3 months, P = 0.039 and 0.023, respectively). Clear cell histology had a marginally increased risk of recurrence compared to serous (HR = 1.79, P = 0.06). The median follow-up for all patients was 24 months (range 0.3–148 months). Patients who attained a pCR had a significantly better PFS and OS compared to non-pCR patients (22.3 vs 11.6 months, P ≤ 0.001, and 67.2 vs 39.7 months, P = 0.013, respectively), and 53% (26/49) of pCR patients had no recurrence at time of analysis. See Figure 1.

Conclusion: Patients who attain a pathologic complete response after NACT have a significantly longer PFS and OS. These findings could have important implications for future clinical trial design.
Objective: The objective of this study was to assess recurrence and survival rates in patients with stage II endometrial cancer based on type of adjuvant treatment received because there are currently limited data to guide adjuvant treatment.
Method: A retrospective cohort study of women diagnosed with 2009 FIGO stage II uterine cancer of any histology from 1999 to 2018 at a single tertiary care center was performed. Patients were grouped based on adjuvant therapy: observation, chemotherapy, radiation, or a combination of chemotherapy and radiation. Patient demographics, tumor characteristics, recurrence rates (RR), PFS, and OS were compared.

Results: A total of 103 patients were identified. After surgical intervention, 25 (24.2%) underwent observation, 9 (8.7%) received chemotherapy, 55 (53.4%) received radiation, and 14 (13.6%) received combination therapy. Most patients had endometrioid histology ($n = 92, 89.3\%)$ and grade 2 or 3 cancers ($n = 97, 94.2\%)$. Older patients were more likely to be observed, and younger patients more likely to receive some type of adjuvant treatment ($P < 0.01$). Patients who received combination therapy were more likely to have grade 3 tumors ($61.5\%, P = 0.04$). Tumor size also varied between groups, with those who received chemotherapy having the largest (6.7 cm) tumors, followed by observation (5.6 cm), radiation (4.4 cm), and chemotherapy/radiation (3.5 cm, $P = 0.04$). Surgical approach, incidence of staging, depth of invasion, and lymphovascular space invasion (LVSI) were not statistically different between groups. The overall recurrence rate was 23.3%. There was no difference in RR, PFS, or OS between groups. A subanalysis of patients with only endometrioid histology also showed no difference in RR, PFS, or OS based on adjuvant treatment received. On multivariate analysis, the only factor predictive of recurrence in the overall cohort was the presence of LVSI ($P < 0.01$).

Conclusion: Given that stage II endometrial cancer patients have a relatively high recurrence rate, adjuvant treatment for these patients is warranted. More research is needed to determine the best modality and whether patients' age, tumor histology, grade, or size should be factored in in determining type of adjuvant treatment.

2112 - Poster Session
Costs and benefits of tumor testing for BRCA mutations in high-grade serous ovarian cancer as a companion diagnostic for PARP inhibitor treatment


Objective: Women with high-grade serous ovarian carcinoma (HGSC) have a 1 in 5 chance of carrying a BRCA mutation and are eligible for germline testing, but this testing will miss some women with a somatic mutation in their tumor. Testing HGSC tissue for BRCA mutations (tumor testing) could identify those with either a germline or somatic mutation, who could be treated with a PARP inhibitor. The objective was to conduct a cost-effectiveness analysis to compare universal genetic (germline) testing to tumor testing as a companion diagnostic for PARP inhibitor treatment.

Method: A Markov Monte Carlo simulation model compared the costs and benefits of these 2 strategies. Primary outcomes included average life expectancy gain in HGSC patients, including PARP inhibitor maintenance for BRCA mutation carriers (germline or somatic) with platinum-sensitive disease. Tumor testing performance measures were derived from published literature. Costs (USD) were estimated from Medicare claims and wholesale acquisition costs for drugs. Sensitivity analyses accounted for uncertainty around various parameters. Time horizon was 50 years.

Results: Tumor testing identified more BRCA mutations, but was more costly than germline testing. Assuming 10,000 newly diagnosed women with HGSC every year in the United States, the model predicts that tumor testing and germline testing will identify 1,908 and 1,808 women eligible for PARP inhibitor treatment, respectively. Average lifetime costs for tumor testing and germline testing were $43,174 and $41,353, and average life expectancy gains were 3.64 and 3.63 years, respectively, yielding an ICER of $162,740. Tumor testing is cost-effective (ICER < $100,000) if tumor testing and annual PARP inhibitor costs are less than $2,000 and $120,000, respectively.

Conclusion: Tumor testing will identify more women with HGSC eligible for PARP inhibitor treatment than germline testing alone, but tumor testing will be cost-effective only with reduction in current testing and drug costs.

2113 - Poster Session
Tumor size loses prognostic significance for progression free survival in the absence of myometrial invasion in grades 1-2 endometrioid endometrial adenocarcinoma

M.J. Kao, E.V. Adams, E. Sampene, A.N. Al-Niaimi and S.M. McGregor. aUniversity of Wisconsin Hospitals and Clinics, Madison, WI, USA, bUniversity of Wisconsin School of Medicine and Public Health, Madison, WI, USA
**Objective:** Endometrial adenocarcinoma is the most common gynecologic malignancy in Western society. Prognosis and recommendations for adjuvant therapy are based on pathologic findings including tumor size, depth of invasion, lymphovascular space invasion, and extrauterine disease. Size and depth of invasion are regarded as independent factors of prognosis, but the interaction between tumor size and depth of invasion has not been evaluated. The objective of this study was to evaluate tumor size in relation to depth of invasion of grade 1–2 endometrioid tumors as a factor determining PFS.

**Method:** A retrospective analysis of all patients with grade 1–2 endometrioid endometrial adenocarcinoma between 2005 and 2016 at an academic institution was performed. Patient demographic, surgical, and pathologic data were collected, including tumor size, depth of invasion, lymphovascular space invasion, and extrauterine spread. Time and location of first recurrence and long-term overall survival data were also obtained. A Kaplan-Meier survival analysis was performed comparing myoinvasive and nonmyoinvasive tumors with tumor size cutoffs of 2 cm and 5 cm.

**Results:** A total of 802 patients were analyzed. There were 323 (40%) patients without myoinvasion: 155 (48%) <2 cm, 168 (52%) ≥2 cm, 293 (91%) <5 cm, and 30 (9%) ≥5 cm. There were 479 (60%) patients with myometrial invasion: 71 (15%) <2 cm, 408 (85%) ≥2 cm, 367 (77%) <5 cm, and 112 (23%) ≥5 cm. Only 2.3% and 0% of patients with nonmyoinvasive tumors ≥2 cm and ≥5 cm had recurrence in comparison to 12% and 18% for myoinvasive tumors, respectively, which was significant according to the log rank $P$ value for the unadjusted model for both cutoffs in a Kaplan-Meier analysis ($P < 0.0001$, see Figure 1).

**Conclusion:** Large tumor size is an adverse prognostic factor for PFS in the context of myoinvasive disease, but grade 1–2 endometrioid tumors without myoinvasion carry an excellent prognosis regardless of tumor size.
Results: A total of 111 patients were identified. Sixteen (14.4%) were confirmed to have uterine involvement. Stage, histologic subtype, grade, and surgical approach were similar between groups. Patients with extracervical disease were older (47.8 vs 41.5 years, \( P = 0.03 \)) and were more likely to have invasion >1.0 cm (68.8% vs 16.8%, \( P < 0.01 \)), tumor size ≥2 cm (100% vs 41.1%, \( P < 0.01 \)), lymphovascular space invasion (LVSI, 75.0% vs 19.5%, \( P < 0.01 \)), parametrial involvement (18.8% vs 3.2%, \( P = 0.04 \)), and positive lymph nodes (31.3% vs. 7.4%, \( P = 0.01 \)). The incidence of any surgical or postoperative complication between groups was similar; however, when subdivided by type, the uterine involvement group was more likely to have a postoperative gastrointestinal (GI) complication (i.e., ileus, obstruction) (25.0% vs 4.2%, \( P = 0.01 \)). Patients with uterine involvement were also more likely to receive adjuvant treatment (\( P < 0.01 \)). Patients with uterine involvement had a higher RR than those without (37.5% vs 14.7%, \( P = 0.04 \)) and shorter PFS (\( P < 0.01 \)). OS was similar between groups. On multivariate analysis, uterine involvement was not an independent predictor of recurrence.

Conclusion: The presence of extracervical uterine disease in patients with IA2-IB1 cervical cancer undergoing radical hysterectomy is associated with a higher risk of recurrence and shorter PFS. This is likely driven by the correlation with larger, more deeply invasive tumors in these patients. Perioperative complications are comparable between groups.

2115 - Poster Session
Stem cell-like characteristics of patient-derived high-grade serous ovarian cancer xenografts are reversed by miRNA let-7 overexpression
E. Chirsheva\(^a\), N. Hojob\(^b\), L. Sanderman\(^c\), H. Wang\(^a\), L.J. Hong\(^b\), Y.J.M. Ioffe\(^b\) and J. Unternaehrer-Hamma\(^a\), \(^a\)Loma Linda University Medical Center, Loma Linda, CA, USA, \(^b\)Loma Linda University School of Medicine, Loma Linda, CA, USA, \(^c\)California State University, San Bernardino, San Bernardino, CA, USA

Objective: Aggressiveness and recurrence of epithelial ovarian cancer has been attributed to cancer stem cells (CSC) within tumors. Deregulation of miRNAs has been linked to cancer progression and the stem cell state. Current experiments focused on the tumor suppressor miRNA let-7, which in many cancers is associated with decreased survival. We aimed to understand the role of let-7 in the stem cell-like properties (stemness) of ovarian cancer cells derived from patients.

Method: We characterized a panel of high-grade serous ovarian cancer (HGSOC) patient-derived cells. Cell surface expression of CSC markers was analyzed by flow cytometry. Expression at the protein level was detected by Western blot, and at the RNA level by q-RT-PCR. Migration was determined by wound healing assay and chemoresistance by MTT assay. Let-7 overexpression was by transfection of miRNA mimics. Patient-derived xenografts (PDX) were established subcutaneously in NOD-SCID-Gamma (NSG) mice. Six-week-old nude (J:NU) mice underwent ovarian bursa injections of luciferized HGSOC cells. Bioluminescence was quantified by IVIS Lumina III and analyzed by Living Image software.

Results: We characterized cells from several PDX for their epithelial (E) versus mesenchymal (M) and stem cell properties. All PDX cells were classified as E/M hybrids. In contrast to previously characterized cell lines, in PDX the M characteristics did not correlate with stemness. Cells with low let-7 were more stem cell-like and formed ovarian tumors more robustly. Paradoxically, they were less migratory and more sensitive to cisplatin. Increasing let-7 levels disrupted the stem cell phenotype. See Figure 1.

Conclusion: PDX-derived cells all exhibited hybrid E/M phenotypes. Decreased let-7 levels may predict stemness in HGSOC. In PDX derived from HGSOC patients, in contrast to previously described cell lines, stem cell-like characteristics can be dissociated from the invasive/mesenchymal phenotypes.
Fig. 1. Let-7 negatively correlates with pluripotency in EOC: (A) qPCR of let-7a, e, g, i, b, and d, arranged based on let-7 levels. (B) pluripotency markers Oct-4, Nanog, Lin-28a, and HMGA2. Ovarian surface epithelium serves as normal control. Human embryonal carcinoma serves as pluripotency control. Ovcar8, PDX4, 6, 7, 8, and 9 arranged according to pluripotency factor expression levels.

2116 - Poster Session
Distinctive clinic-pathological characteristics and prognosis among different histologic types of cervical cancer
L. Cao, H. Wen, Z. Feng, X. Han and X. Wu, Fudan University Shanghai Cancer Center, Shanghai, China

Objective: This study aimed to investigate the clinical-pathologic characteristics and prognosis among different histologic types in early cervical cancer (FIGO stage IA2–IIA2).

Method: Patients who underwent radical surgery for cervical cancer between March 2006 and February 2014 at our institution were included. The pathological histologic types included squamous cell carcinoma (SCC), adenocarcinoma (AC), and adenosquamous carcinoma (ASC). Differences of pathological risk factors including tumor size, depth of stromal invasion, lymph vascular space invasion (LVSI), peripheral nerve infiltration, parametrial invasion, vaginal margin involvement, pelvic lymph node metastasis, and ovarian metastasis were compared among the three groups. PFS and OS were also analyzed.

Results: A total of 5,181 patients were involved in our study, including 4,510 patients with SCC (87.0%), 488 patients with AC (9.4%), and 183 patients with ASC (3.5%). The median (IQR) age was 46 (40–53) years. FIGO stage distribution was as follows: IA2, 1.2%; IB1, 47.9%; IB2, 7.5%; IIA1, 30.8%; and IIA2, 12.6%. Women with AC were more likely to present with earlier stage disease ($P < 0.001$) and smaller tumor size ($P < 0.001$) compared with the other two types. Compared with SCC, fewer patients with AC had deep stromal invasion (AC 30.4% vs SCC 36.2%, $P < 0.001$) and LVSI (AC 26.7% vs SCC 37.9%, $P < 0.001$). For patients who underwent oophorectomy, ovarian metastasis rate was highest in AC (15/358, 4.2%) compared with 0.7% (23/3180) in SCC and 1.4% in ASC (2/147), respectively ($P < 0.001$). More patients with ASC had peripheral nerve infiltration compared with those with SCC and AC ($P = 0.002$ and $P < 0.001$, respectively). There were no differences in parametrial invasion, pelvic lymph node metastasis, and vaginal margin involvement among the three groups. The median (IQR) follow-up time was 59 (32–82) months. Five-year PFS rates were SCC, 85.1%; AC, 78.2%; and ASC, 72.3%. Five-year OS rates were SCC, 89.7%; AC, 83.1%; and ASC, 79.6%. SCC patients presented longer PFS and better OS compared with AC patients ($P_{PFS} < 0.001$, $P_{OS} < 0.001$) and ASC patients ($P_{PFS} < 0.001$, $P_{OS} < 0.001$) patients.

Conclusion: Patients with AC and ASC had worse survival outcomes than those with SCC. A considerable proportion of AC patients could have ovarian metastasis. ASC patients tended to have peripheral nerve infiltration.
2117 - Poster Session
Comparative assessment of clinical progestin formulations in a murine model of endometrial hyperplasia
C.H. Yang\textsuperscript{a}, C. Unice\textsuperscript{b}, A. Almomen\textsuperscript{c} and M.M. Janát-Amsbury\textsuperscript{a}. \textsuperscript{a}The University of Utah, Salt Lake City, UT, USA, \textsuperscript{b}Utah State University, Logan, UT, USA, \textsuperscript{c}King Saud University, Riyadh, Saudi Arabia

Objective: The clinical management of endometrial hyperplasia (EH) remains a challenge because of the lack of standardized guidelines for nonsurgical therapeutic approaches. The goal of this study is to assess the safety and efficacy of currently available progestin formulations in a murine model of EH.

Method: EH was induced in 44 mice through the subcutaneous implantation of estrogen controlled-release pellets. Mice were randomly assigned into 5 groups, control/no treatment (\(n = 8\)), medroxyporgesterone acetate (MPA, Provera\textsuperscript{®}) (\(n = 9\)), norethindrone (NE, Aygestin\textsuperscript{®}) (\(n = 8\)), megestrol acetate (MA, Megace\textsuperscript{®}) (\(n = 9\)), and depo-medroxyprogesterone (Depo-Provera\textsuperscript{®}) (\(n = 10\)). MPA, NE, and MA groups received a daily oral dose of 4 mg/kg. The Depo group received an equal dose of 4 mg/kg twice per week in form of intramuscular injections. After 4 weeks of treatment, mouse total body weight, organ weights as well as histopathological changes including gland-to-stroma ratio, progesterone receptor (PR) expression, and proliferation marker (Ki67) were evaluated.

Results: All mice in the control group developed atypical EH. MPA and Depo groups had significantly reduced uterine weights (\(P < 0.05\) and \(P < 0.01\)). Treatment efficacy of MA (100%) and Depo (100%) was higher than that of MPA (77.8%) and NE (87.5%). Gland-to-stroma ratio was significantly reduced in MA and Depo groups (\(P < 0.001\)). Evaluating Ki-67 expression, all formulations significantly reduced estrogen-induced endometrial proliferation (\(P < 0.001\)) with the strongest effect observed in the MA group. Immunohistochemical staining revealed that PR expression was downregulated in the MPA and NE groups with additional adverse hepatic effects.

Conclusion: All tested progestin formulations caused regression of EH. Megace and Depo-Provera had the most favorable treatment profiles. Cyclic progestin treatment could be more effective than continuous treatment. This warrants the implementation of progestin treatment guidelines in particular for patients with type I endometrial cancer, who seem to benefit from Megace to slow the progression of tumors.

2118 - Poster Session
Towards early personalized patient management: Molecular classification of endometrial carcinoma applied to endometrial biopsy specimens
R. Ali-Fehm\textsuperscript{a}, S. Sakr\textsuperscript{b}, E. Abdulfatah\textsuperscript{c}, E. Wakeling\textsuperscript{d}, N. Yerrapoth\textsuperscript{d}, I.G. Tsolekian\textsuperscript{d}, D. Ujayli\textsuperscript{e}, J.D. Naaman\textsuperscript{f}, S. Bandyopadhyay\textsuperscript{a} and R.T. Morris\textsuperscript{a,g}. \textsuperscript{a}Wayne State University School of Medicine, Detroit, MI, USA, \textsuperscript{b}Karmanos Cancer Center/Wayne State University, Detroit, MI, USA, \textsuperscript{c}The University of Michigan Hospitals, Ann Arbor, MI, USA, \textsuperscript{d}Wayne State University, Detroit, MI, USA, \textsuperscript{e}Oakland University, Rochester, MI, USA, \textsuperscript{f}Michigan State University, East Lansing, MI, USA, \textsuperscript{g}Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA

Objective: The current risk stratification systems of endometrial cancer (EC) are based on postsurgical pathological information. However, pathologists are unable to reproducibly diagnose histotype and grade, hence the need for more reliable classification systems. The Cancer Genome Atlas (TCGA) recently identified 4 EC subtypes that subsequently proved reproducible using clinically applicable surrogate tests. Using these tests, we sought to determine the level of concordance between endometrial biopsies (Bx) and subsequent hysterectomy specimens (HS) in assessing the molecular classification of EC.

Method: Fifty Bx with corresponding HS for EC patients were collected. In addition, 10 cases of Bx-proven complex atypical hyperplasia (CAH) and found to have EC on resection were included. DNA was isolated from FFPE. MSI analysis was performed with Promega Analysis System. MSI was interpreted as stable, low or high. Immunohistochemistry (IHC) for mismatch repair (MMR) proteins and PS3 was performed. MMR status was interpreted based on current protocol. PS3 was abnormal if there was complete negative or diffuse expression in tumor cells. Sanger sequencing was performed to detect mutations in exons 9 and 13 of POLE gene. Level of concordance for tumor grade, histotype, IHC and molecular profile in both specimens was determined using kappa estimates. Kappa statistic of 0.86 (95% CI) is consistent as “near perfect” level of agreement.
**Results:** Patient ages ranged from 27 to 85 (median 60) years. All patients underwent definite surgical treatment. Bx included 65% endometrioid carcinoma (EEC), 17% CAH, 15% serous carcinoma (SC), 1.5% clear cell, and 1.5% mixed carcinoma. High level of concordance was achieved for MMR loss: MLH1, 1.0, 95% CI 0.0–7.74; PMS2, 0.91, 95% CI 0.61–7.08; MSH2, 1.0, 95% CI 0.0–7.74; and MSH6, 0.83, 95% CI 0.79–6.49; MSI high, 0.91, 0.63–6.86; P53 wild, 1.0, 95% CI 0.0–7.74; and abnormal, 1.0, 95% CI 0.0–7.74. In contrast, grade and histotype showed only moderate levels of agreement. Highest level of discrepancy in morphology was between SC and FIGO grade 3 EEC. POLE gene mutation was detected in 2 patients (3.5% of entire cohort and 14% of FIGO grade 3 EEC). For both cases, mutations were detected only in HS. When comparing CAH with subsequent HS tumor, the profile was identical to that of EC.

**Conclusion:** In our cohort of EC, a high level of concordance was achieved between Bx and HS for IHC and molecular profile, superior to that of grade and histotype, providing earlier and more reliable prognostic information to inform management.

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**2119 - Poster Session**

**Low-risk uterine endometrioid carcinoma: The necessity of intraoperative histopathological assessment and lymphadenectomy**

H.Q. Nguyen, M.A. Elshaikh, I.G. Tsolakian, J.D. Naaman, S. Chaugle, R. Khalil, S. Bandyopadhyay, R.T. Morris and R. Ali-Fehmi. Wayne State University School of Medicine, Detroit, MI, USA, Henry Ford Health System, Detroit, MI, USA, Wayne State University, Detroit, MI, USA, Michigan State University, East Lansing, MI, USA, Henry Ford Hospital, Detroit, MI, USA

**Objective:** Current practice of surgical management of low-risk uterine endometrioid carcinoma (EEC) and based on Mayo criteria FIGO grade 1 or 2, greatest tumor dimension (GTD) ≤ 2 cm, and myometrial invasion ≤50%) is hysterectomy without lymphadenectomy. Lymphadenectomy is considered for patients whose tumor does satisfy all 3 criteria and requires intraoperative histopathological assessment. The use of frozen section diagnosis can significantly prolong the surgery and is not always available in all health care facilities. This study investigates the use of preoperative histologic grade with intraoperative greatest tumor dimension measurement, bypassing the intraoperative assessment of myometrial invasion, to determine the indication of lymphadenectomy.

**Method:** This is a retrospective database collection of patients who underwent hysterectomy with or without comprehensive surgical staging for EEC between 1995 and 2016. All high-risk histologic types, such as clear cell, serous, or carcinosarcoma, are excluded. This investigation compared those with preoperative FIGO grade 1 or 2 and GTD ≤ 2 cm to patients with preoperative FIGO grade 3 or GTD > 2 cm. Lymph node metastasis (LNM) and recurrence were compared in these groups. This study also compared the use of 2 criteria (preoperative FIGO grade 1 or 2 and GTD ≤ 2 cm), bypassing frozen section diagnosis, to the use of Mayo criteria in predicting LNM.

**Results:** This study reviewed 1,325 cases. Overall, LNM occurred in 7.6% of patients. Patients with GTD > 2 cm have higher rate of LNM (10.1%) and recurrence (10.4%) compared to those with GTD ≤ 2 cm (LNM = 2.7%, recurrence = 5%; P = 0.000 and P = 0.001 respectively). When combining preoperative FIGO grade 1-2 with GTD ≤ 2 cm, the rate of LNM is 2.3%, while the rate of LNM when using Mayo criteria is 1.1%. Fisher exact test to compare the rate of LNM in 2 groups of criteria couldn’t find any statistical difference regarding LNM detection (P = 0.126). See **Table 1**.

**Conclusion:** The results indicate that combined preoperative FIGO and GTD can detect LNM as well as Mayo criteria; therefore, the intraoperative histopathological assessment may be not necessary and could be eliminated in selected women with low-risk uterine endometrioid carcinoma.
2120 - Poster Session
Overall survival and adjuvant therapy in women with clear cell carcinoma of the ovary
A. Nizam, B. Bustamante, A. Sakaris, J.S. Whyte, M. Frimer, A.W. Menzin and G.L. Goldberg, Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA

Objective: Clear cell carcinoma of the ovary (CCCO) is a rare variant of epithelial ovarian cancer. Despite the fact that many women with CCCO present with early-stage disease, there is ongoing uncertainty regarding their OS and the potential benefit of adjuvant therapy.

Method: An Institutional Review Board-approved study identified all our patients with CCCO between January 2011 and May 2018. Demographics and outcome measures were abstracted from the medical records and the tumor registry. Cox proportional hazard models, log rank tests, and comparisons of means were used to calculate significance ($P < 0.05$).

Results: Ninety-three women were identified during the study period. The median age at diagnosis was 56 years (range 26–76 years). Fifty-one patients (55%) presented with stage I disease, and 33 (36%) presented with stage III or IV disease. Seventy-two patients (77.4%) received multiagent chemotherapy. The median OS for the entire group was 28 months (range 1–162 months). OS was not significantly influenced by the stage at presentation ($P = 0.98$), but may be trending to significance. OS was not affected by the use of adjuvant chemotherapy ($P > 0.05$) (see Figure 1). There was no significant difference in OS based on age at diagnosis, family history of cancer, or ethnicity.

Conclusion: Our cohort showed no significant difference in OS based on stage at presentation. Adjuvant chemotherapy did not significantly affect OS in our cohort of patients. Data regarding the prognosis and optimal adjuvant treatment of CCCO have yet to be determined. Further multiinstitutional prospective trials are needed to determine the optimal management of this rare disease.

Fig. 1. Predictors of Lymph Node Metastasis
Fig. 1. Overall Survival in Early vs. Late Stage Clear Cell Carcinoma of the Ovary.

2121 - Poster Session
Does adjuvant chemotherapy improve overall survival in women with stage I epithelial ovarian cancer?
A. Nizam, B. Bustamante, L. Scanlon, J.S. Whyte, A. Sakaris, A.W. Menzin, M. Frimer and G.L. Goldberg, Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA

Objective: Roughly one-fourth of women with epithelial ovarian cancer (EOC) present with early-stage disease. Currently there is no consensus regarding the use of adjuvant chemotherapy to improve OS in patients with stage I EOC.

Method: An Institutional Review Board-approved study identified all our patients with stage I EOC between January 2011 and May 2018. Demographics and outcome measures were abstracted from the medical records and the tumor registry. Cox proportional hazard models, log rank tests, and comparisons of means were used to calculate significance (P < 0.05).

Results: One hundred and seventy women were identified during the study period. The median age at diagnosis was 60 years (range 28–92). Eighty-nine (52%) of patients presented with stage IA disease; 15 (9%) presented with stage IB disease; and 66 (39%) presented with stage IC disease. One hundred (59%) patients received adjuvant chemotherapy. The median OS was 48 months (range 0–378). OS did not differ by substage of the disease at presentation (P > 0.05). There was no difference in OS for those women who received adjuvant chemotherapy versus those who underwent clinical observation (P > 0.05). Chemotherapy did not improve OS in those with stage IA or stage IC disease (P = 0.39 and P = 0.1, respectively). See Figure 1.

Conclusion: Our data showed no significant difference in OS in patients receiving adjuvant chemotherapy compared to those who did not receive adjuvant chemotherapy. However, there was a trend toward significance in OS in women with stage IC EOC treated with platinum-based EOC. The optimal number of cycles of chemotherapy is unclear. Further multiinstitutional prospective trials are needed to determine the optimal management of stage 1 EOC.
Investigation of post-immunotherapy response rates utilizing progression free survival ratios in women with gynecologic malignancies

M.E. Buechel¹, K.G. Essel², K. Ding³ and K.N. Moore⁴. ¹The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, ²The University of Oklahoma, Oklahoma City, OK, USA

Objective: The use of immune-therapeutics in gynecologic oncology patients challenges our traditional paradigm of how to assess disease response rates. Historically patients have worse PFS with each subsequent regimen of treatment. In other malignancies, a PFS ratio (PFSr) has been proposed as a marker of response. If the PFSr is <1, there is an improvement in predicted response. We sought to utilize the PFSr to assess disease response. In addition, we hypothesized that use of immunotherapy alters a patient's response to subsequent therapies by altering either the immune profile of the tumor or immune response of the patient. Our objective was to look at the PFSr of pre- and post-immunotherapy treatments in patients with gynecologic malignancies.

Method: A retrospective analysis of patients of all gynecologic oncology patients who were treated with immunotherapy from June 2015 to March 2018 was performed. Demographic, clinical, and pathologic data were collected and analyzed with appropriate statistical methods. The two PFSr’s (pre-immunotherapy and post-immunotherapy) were summarized using PROC ICLIFETEST. The difference between the two PFSr’s was assessed by using PROC PHREG for clustered censored data after reciprocal transformation of the ratios so that they became right-censored.

Results: A total of 56 patients were included in our analysis. Patients carried a diagnosis of ovarian (52%), cervical (29%), and uterine (20%) malignancies with a median age of 52 years. Patients had a median number of 2 previous lines of therapy. Majority of the patients were treated with a cytotoxic regimen prior, and only 52% of patients received any treatment post-immunotherapy. The median PFS for patients pre-immunotherapy was 6.5 months (95% CI 3.6–8.9), on immunotherapy 3.6 months (95% CI 2.8–7.2), and post-immunotherapy 7.4 months (95% CI 4.2–9.4). This gave us a PFSr of 1.28 (95% CI 0.69–2.02) and 0.48 (95% CI 0.26–0.88) for pre- and post-immunotherapy ratios, respectively.

Conclusion: Patients had a higher PFS post-immunotherapy compared to both pre-immunotherapy and immunotherapy PFS. The PFSr difference was not statistically significant likely secondary to our small sample size. However, this warrants further investigation into the utility of the PFSr as an endpoint in early clinical trials. In addition, while a mechanism of the improvement in PFS post-immunotherapy is only speculative, this should be further investigated to help guide our utilization of immunotherapy of patients with gynecologic malignancies.
Are outcomes different for ovarian cancer patients who receive adjuvant chemotherapy in the community? A SEER analysis.

C.C. Wang, L.A. Rauh, F. Camacho and C.N. Landen Jr. University of Virginia, Charlottesville, VA, USA

Objective: To assess whether overall survival (OS) is improved in ovarian cancer patients who receive all their care at high-volume surgical and high-volume chemotherapy centers (HVS/HVC) compared to those who receive postoperative adjuvant chemotherapy at low-volume centers after surgery at high-volume centers (HVS/LVC).

Method: The Surveillance, Epidemiology and End Results Medicare database was used to examine 18- to 85-year-old women with new, primary ovarian cancers diagnosed between 2007 and 2011 treated with both surgery and chemotherapy. Facilities with 20 or more ovarian cancer surgeries (80th percentile) in the year after diagnosis were classified as HVS based on literature thresholds. Chemotherapy volume was based on the number of patients receiving chemotherapy for ovarian cancer at each facility the year after diagnosis. Sample-based cutoff for HVC was set at 6 unique cases (60th percentile) annually. Additional cutoffs were also analyzed. Primary outcome was OS. A Cox proportional hazards model was used to evaluate OS. Kaplan-Meier curves were constructed and median survival was analyzed by log rank. Univariate statistic was used for subgroup analyses.

Results: A total of 1,510 women were identified; 67.6% (n = 1,020) received treatment in HVS/HVC and 5.70% (n = 86) in HVS/LVC; the remainder were from low-volume surgical centers. Of all women, 89.3% were ≥65 years; 87.2% were white; 62.3% had serous histology; 15.4% received neoadjuvant chemotherapy (NACT); and 71.8% had advanced-stage disease. Median survival for HVS/HVC versus HVC/LVC was 47.0 and 39.0 months, respectively (P = 0.017, Figure 1). HVS/LVC was associated with worse OS (HR = 1.809, 95% CI 1.281–2.555) compared to HVS/HVC. HVS/LVC remained inferior when patients with “missing” stage, stage I, and mucinous tumors were excluded. No significant differences across subgroups (serous vs other, primary cytoreduction vs NACT, advanced vs local stage) were found when comparing OS. Within groups, the effect remained for serous (P = 0.002), primary cytoreduction (P = 0.003), and stage ≥IIIA (P = 0.011).

Conclusion: Receiving all ovarian cancer care at high-volume centers was associated with improved OS compared to receiving postoperative chemotherapy at low-volume centers after surgery at high-volume centers, suggesting that efforts should be made to centralize all ovarian cancer care.
**Fig. 1.** Kaplan-Meier curve of the overall survival for high-volume surgery/high-volume chemotherapy centers (HVS/HVC) and high-volume surgery/low-volume chemotherapy centers (HVS/LVC).

2124 - Poster Session

Direct health care cost to provide adjuvant vaginal cuff brachytherapy for endometrial cancer

S.W. Dutta\(^a\), T.C. Wu\(^b\), B. Libby\(^c\), D.J. Lash\(^d\), K.D. Romano\(^e\) and T.N. Showalter\(^e\). \(^{a,b}University of Virginia, Charlottesville, VA, USA, \(^c\)James Cancer Hospital, Columbus, OH, USA

**Objective:** Using time-driven activity-based costing, we calculated the cost to deliver three versus six fractions in order to determine the value of each regimen.

**Method:** Process maps were created to represent each step from initial consult to completion of therapy. The high-dose-rate brachytherapy procedure, which takes place in a dedicated suite, consisted of a computed tomography scan at the first fraction to confirm vaginal cylinder placement and for dose documentation. Subsequent fractions were clinical based. Components of care included personnel, equipment, and consumable supplies. The capacity cost rate was determined for each resource and calculated for each regimen.

**Results:** The total direct costs to deliver three- and six-fraction treatment courses were $1,415 and $2,236, respectively. Personnel cost accounted for 63% of overall expenditures. Computed tomography simulation and planning, required for the first fraction, cost $232 for both regimens. Duties of the procedural nurse (scheduling, patient setup, and turnover) consumed the most time at 35% of all team member minutes, accounting for 155 and 305 minutes for the three- and six-fraction treatments, respectively.

**Conclusion:** Time-driven activity-based cost analysis revealed a 58% increase in delivery costs for six versus three fractions of brachytherapy at our institution. Our center is participating in a multiinstitutional trial comparing the sexual quality differences between the fractionation regimens. This current analysis may influence the interpretation of the trial results when the relative value between the two treatment schedules is considered.
2125 - Poster Session
Cause-specific mortality according to adjuvant therapy of serous and clear cell endometrial cancers: A population-based analysis
M. Xiang, D. English and E. Kidd. Stanford University School of Medicine, Stanford, CA, USA

Objective: Serous and clear cell carcinomas represent a minority of patients in recent clinical trials investigating adjuvant therapy of higher-risk endometrial cancers (PORTEC-3, GOG-249, GOG-258), and national guidelines such as the National Comprehensive Cancer Network permit substantial variations in treatment. To help address this gap in knowledge, we analyzed outcomes of patients in the NCT’s Surveillance, Epidemiology and End Results (SEER) registry-Medicare database, given its large sample size, national representation of real-life practice patterns, and availability of radiation and chemotherapy data.

Method: Patients with FIGO stage I–III serous or clear cell uterine carcinoma diagnosed from 2004 to 2013 who underwent at least total hysterectomy were identified. Receipt of adjuvant external beam radiation (EBRT), brachytherapy (BT), and chemotherapy was determined using the SEER treatment fields and patients’ Medicare claims. The primary outcome was endometrial cancer-specific mortality (CSM) according to adjuvant treatment(s) received, evaluated using Gray’s test (univariable analysis, UVA) and Fine-Gray regression (multivariable analysis, MVA).

Results: A total of 1,796 patients (1,443 serous, 353 clear cell) were identified, of whom 35% received EBRT, 33% BT, and 59% chemotherapy. Median follow-up was 3.9 years in living patients. In stage I–II patients (n = 1,188), BT was significant in both UVA (P = 0.03) and MVA (P = 0.02). In addition, in the subset with serous histology (n = 947), chemotherapy was also significant in UVA (P = 0.002) and nearly significant in MVA (P = 0.07). The 4-year CSM for stage I–II serous cancers was 25% with no BT or chemotherapy, 15% with receipt of one but not both, and 9% with both (P < 0.05 for all pairwise comparisons). In stage III patients (n = 608), only chemotherapy was significant in UVA (P < 0.001) and MVA (P = 0.002). EBRT was not significant except for nearly reaching significance for stage III clear cell cancers in MVA (P = 0.06). Most (81%) patients had removal of at least 1 lymph node, which was associated with lower CSM in stage III (P < 0.001) but not in stage I–II patients in MVA.

Conclusion: For serous and clear cell endometrial carcinoma, stage III patients appeared to benefit from chemotherapy, and stage I–II patients appeared to benefit from BT. Stage I–II patients with serous histology had the best survival outcomes when they received both chemotherapy and BT.

2126 - Poster Session
Minimally invasive surgery rate as a quality metric: Feasibility and validity
R.M. Polan1, E.J. Tanner IIIb and E.L. Barbera. aNorthwestern University Feinberg School of Medicine, Chicago, IL, USA, bJohns Hopkins Hospital, Baltimore, MD, USA

Objective: Minimally invasive surgery (MIS) is a quality metric for endometrial cancer (EC) established by the Society of Gynecologic Oncology. A hospital-level rate of 80% MIS hysterectomy for EC has been proposed. Our study objectives were (1) to determine the frequency with which Commission on Cancer-accredited hospitals met this metric and (2) to compare patient characteristics, patterns of care, and outcomes by hospitals meeting or not meeting this metric.

Method: A retrospective study of women who underwent hysterectomy for EC in 2015 was conducted using the National Cancer Data Base (NCDB). Inclusion criteria were epithelial histology, Charleston comorbidity score of 0, stage I–III disease, and surgery at a hospital caring for ≥20 EC patients per year. Patient characteristics, patterns of care, and outcomes were compared between centers performing ≥80% of hysterectomies by MIS (high MIS) and centers not meeting this quality metric (low MIS). Bivariable tests were used to examine associations.

Results: A total of 510 hospitals treated 20,671 women with EC; 283 (55%) were high-MIS hospitals. Annual hospital volume was similar with a median of 54 patients per hospital for both high- and low-MIS hospitals. In high-MIS hospitals, patients were more likely to be white race (88% vs 83%), have private insurance (53% vs 49%), and have a median household income >$38,000/year (88% vs 83%, all P < 0.001). These patients were more likely to have stage I disease (84% vs 82%, P = 0.002) and endometrioid histology (79% vs 76%, P < 0.001). In high-MIS hospitals, MIS was more often performed robotically (80% vs 71%), and conversion to laparotomy was less common (1.5% vs 3.2%, all P < 0.001). Patients treated at high-MIS hospitals were more likely to have lymph node assessment (76% vs 69%) and a same or next day discharge (77% vs 59%), and less likely to have an unplanned 30-day hospital readmission (1.8% vs 2.9%, all P < 0.001).
**Conclusion:** Achieving an 80% hospital-level rate of MIS for EC is feasible; 55% of identified hospitals met this target in 2015. Patients treated at high-MIS centers had shorter lengths of stay, lower rates of readmission, and higher rates of lymph node assessment and were more likely to undergo a robotic procedure. An MIS rate of 80% for surgical management of EC is feasible and associated with other hospital-level measurements of high-quality care.

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**2127 - Poster Session**
Withdrawn at author's request

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**2128 - Poster Session**
Adverse outcomes among women after concurrent surgery for endometrial cancer and pelvic floor disorders: The cancer of the uterus and treatment of incontinence (CUTI) trial


*Women & Infants Hospital, Brown University, Providence, RI, USA, bUniversity of Alabama at Birmingham, Birmingham, AL, USA, cWomen & Infants Hospital, Brown University, Providence, RI, USA, dUniversity of Alabama Health Services Foundation, Birmingham, AL, USA, eMayo Clinic, Rochester, MN, USA, fHartford Hospital, Hartford, CT, USA, gJohns Hopkins School of Medicine, Baltimore, MD, USA, hUniversity of New Mexico Health Sciences Center, Albuquerque, NM, USA, iBrown University, Providence, RI, USA, jThe University of Texas Southwestern Medical Center, Dallas, TX, USA*

**Objective:** To evaluate postoperative pain and the incidence of adverse events in women undergoing concomitant surgery for endometrial cancer and urogynecologic procedures compared to those undergoing cancer surgery only.

**Method:** This is a secondary analysis from a large multicenter, prospective cohort study comparing outcomes for women undergoing concomitant surgery for endometrial intraepithelial neoplasia (EIN) or clinical stage I/II endometrial cancer and stress urinary incontinence or pelvic organ prolapse compared to cancer surgery alone. Adverse events occurring within 30 days of surgery were collected by structured chart reviews at 2 weeks, 6 weeks, and 6 months after surgery. Adverse events were defined as fevers, infections, transfusions, complications leading to emergency department visits, and hospital readmissions. Postoperative pain scores were measured on postoperative day 1 using the Brief Pain Inventory (BPI). Adverse events and pain scores were compared by surgical group using Fisher’s exact test and the Wilcoxon rank sum test.

**Results:** One hundred and thirteen women (44.8%) underwent concomitant cancer surgery with urogynecologic procedures, and 426 had cancer-only surgery. The two groups were demographically similar with the exception that a higher proportion of women choosing concomitant surgery were Caucasian or Latina ($P = 0.002$). There was no difference in the incidence of emergency visits for complications (6.5% vs 3.5%, $P = 0.17$) or in postoperative fever or infection rates (5.3% vs 3.1%, $P = 0.26$). While blood loss was higher in the concomitant-surgery group (150 cc vs 65 cc, $P < 0.0001$), there was no difference in transfusion rates (0.9% vs 1.2%, $P = 1.0$). Readmission rates were higher in the concomitant-surgery group than the cancer surgery-only group (9.7% vs 3.8%, $P = 0.026$); however, only two readmissions were deemed likely to be related to the urogynecology procedure (pyelonephritis and E. coli bacteremia). There was no difference in 24-hour average postoperative pain scores assessed by the BPI (3.8 vs 3.7, $P = 0.4$).

**Conclusion:** Concomitant endometrial cancer and urogynecologic surgery was associated with low adverse event rates and no increase in postoperative pain. Providers should consider offering concomitant surgery to patients with endometrial cancer and urinary incontinence after a discussion of potential risks and benefits.

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**2129 - Poster Session**
Counseling and documentation for modifiable cervical cancer risk factors: Quality improvement leading to increased reimbursement


*University of Cincinnati Academic Health Center, Cincinnati, OH, USA, bUniversity of Cincinnati Cancer Institute, University of Cincinnati, Cincinnati, OH, USA*

**Objective:** This quality improvement (QI) study aimed to correct deficiencies in documentation of cervical dysplasia risk factors and implement new note templates to improve counseling for modifiable risk factors, as well as reimbursement rates.
Method: Baseline data were collected at cervical dysplasia procedure visits from April 13 to August 10, 2018 (n = 187). After June 28, 2018, a new note template was introduced with documentation of various risk factors including smoking and HPV vaccination status and counseling. Data were analyzed with two-tailed Student t test. Reimbursement of tobacco cessation counseling was defined as $9.43 by current procedural terminology (CPT) code 99406 with modifier 25. Reimbursement of HPV vaccination was defined as $10.00 by CPT code 90649.

Results: Study populations before and after intervention were not significantly different. The rate of documentation of all targeted risk factors significantly increased. Before QI, 89% of opportunities to counsel on smoking cessation were missed, compared to 6% after implementation (Table 1). This correlates to missed revenue of over $3,800 annually. Before QI, 12% of dysplasia encounters included documentation of HPV vaccination status, versus 98% after implementation. Of these, 37.5% received counseling before QI, and 78.5% received counseling after QI. Similar percentages of patients were eligible for vaccination, 12.7% before QI and 16.5% after QI. This correlates to $76 annually in clinic revenue.

Conclusion: The intervention significantly improved documentation of risk factors and rate of smoking cessation counseling. This also increased an area for reimbursement through smoking cessation counseling. While HPV vaccination is not a large source of income, the template prompts providers to offer vaccination and to counsel on the importance of vaccination for the young people in our patients’ lives.

Table 1. Documentation of cervical dysplasia risk factors and counseling provided to patients before and after implementation of QI note template.

<table>
<thead>
<tr>
<th>Risk factor documentation</th>
<th>Pre-QI %</th>
<th>Post-QI %</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraception</td>
<td>70.6</td>
<td>96.5</td>
<td>&lt;0.001</td>
</tr>
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<td>STI history</td>
<td>52.9</td>
<td>97.65</td>
<td>&lt;0.001</td>
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<td>Smoking</td>
<td>67.7</td>
<td>97.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HPV vaccination</td>
<td>11.8</td>
<td>97.65</td>
<td>&lt;0.001</td>
</tr>
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<td>HIV</td>
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<td>89.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking cessation</td>
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<td>&lt;0.001</td>
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<tr>
<td>HPV vaccination</td>
<td>37.50</td>
<td>78.57</td>
<td>0.058</td>
</tr>
</tbody>
</table>

2130 - Poster Session
Definition of a unified risk classification system for adjuvant therapy in stage I endometrial cancer

Objective: Randomized trials describe differing sets of high-intermediate risk (HIR) criteria. We used the National Cancer Data Base (NCDB) to compare the impact of radiation therapy (RT) in stage I endometrial cancer patients meeting different criteria and define a unified classification of unfavorable risk.

Method: Patients with stage I endometrial cancer from 2010 to 2015 were identified in the NCDB and stratified into two cohorts: (1) meeting only GOG-99 criteria for HIR, but not PORTEC-1 criteria, and (2) meeting only PORTEC-1 criteria. High-risk stage I patients with both FIGO stage IB and grade 3 disease were excluded. In each cohort, propensity score-matched survival analyses were performed. Based on these analyses, we proposed a new classification of unfavorable risk. We then analyzed the association of adjuvant RT with survival, stratified by this classification.

Results: We identified 117,237 patients with stage I endometrial cancer, of whom 11,207 patients met GOG-99 criteria only and 5,920 patients met PORTEC-1 criteria only. After propensity score matching, adjuvant RT improved survival (HR = 0.73, 95% CI 0.60–0.89, P = 0.002) in the GOG-99 only cohort. However, there was no benefit of adjuvant RT (HR = 0.89, 95% CI 0.69–1.14, P = 0.355) in the PORTEC-1 only cohort. We therefore defined unfavorable risk stage I endometrial cancer as ≥2 risk factors among lymphovascular invasion, age ≥70 years, grade 2-3 disease, and FIGO stage IB. Adjuvant RT improved survival in unfavorable risk stage I patients (HR = 0.72, 95% CI 0.68–0.80, P < 0.001), but not in other stage I patients (HR = 1.02, 95% CI 0.91–1.15, P = 0.710; P interaction <0.001), shown in Figure 1.
**Conclusion:** We describe a unifying definition of unfavorable risk in stage I endometrial cancer, which may help stratify patients for adjuvant therapy.

![Figure 1](image1.png)

**2201 - Poster Session**

**Uterine cancer normogram to predict lymph node metastasis: Comparison to the Mayo algorithm and an external validation of a European model in an American population**

*M.F. Benoit*¹ and K.K. Ward². ¹Group Health Seattle, Seattle, WA, USA, ²McKesson Specialty Health/The US Oncology Network, The Woodlands, TX, USA

**Objective:** We sought to compare two preoperative/intraoperative uterine cancer normograms for prediction of lymph node metastasis. We used the Mayo criteria and a French algorithm provided by Koskas et al. for likelihood.

**Method:** A total of 490 uterine cancer patients were included in the review. Data were abstracted to include age, ethnicity, stage, tumor size, grade, histology, depth of invasion, cervical involvement, lymphovascular space invasion (LVSI), and MSI. Patient comorbid conditions were analyzed to include BMI, diabetes, and hypertension. Those patients with stage 1, 2, and 3C disease were included in final analysis.

**Results:** Patients were reviewed from January 2012 to July 2018. The average age was 63.68 years. The average BMI was 34.68 kg/m²; 225 (48.9%) patients had hypertension; 72 (15.6%) were hypothyroid; and 119 (25.9%) were diabetic. Patients had TH bilateral salpingo-oophorectomy (BSO) and lymph node dissection (LND), and those with type II tumors had additional staging biopsies and omental biopsy. Of 406 patients, 91.4% were lymph node negative, and 7.9% (38) were lymph node positive. Eighty (17.4%) patients had a type II tumor. The percentage of each group who were coded as high risk and recommended to have LND were 382 (83%) per three-point Mayo criteria, 246 (53.47%) per Mayo criteria to not include tumor size, 196 (42.6%) per Mayo criteria by tumor size alone, and 192 (41.7%) per the French algorithm. The receiver operating curve (ROC) for the French normogram was 0.78 when 4% was used as the cutoff for lymph node metastasis, with a sensitivity of 78% and specificity of 60%. When a 5% cutoff was used, the ROC was 0.71. For every percentage point that the French score rose, the chance of being lymph node positive increased by 0.8% (P < 0.001). The three-point Mayo criteria odds ratio was 7.4, and the ROC was 0.57. Twenty-eight of 99 (28.2%) patients who were tested for MSI were positive. See Figure 1.

**Conclusions:** The French normogram provided a better prediction algorithm for risk assessment of lymph node metastasis. Our results are comparable with those previously published by Koskas et al. providing an external validation of this
normogram previously used in only European and Korean populations. These pre- and intraoperative variables can be incorporated into real-time risk assessment for lymph node metastasis and operative decision making. Mayo criteria not using tumor size could spare an additional 40% of patients an unnecessary LND compared to standard three-point Mayo criteria with better predictive value.

**Fig. 1. Uterine Cancer Normogram ROC1**

### 2202 - Poster Session
**Comparative effectiveness of robotic versus laparoscopic surgery for the treatment of endometrial cancer**

E.L. Barber\(^a\), A. Pyrzak\(^b\), E.J. Tanner III\(^b\), J.F. Boggess\(^c\) and E.C. Rossi\(^c\). \(^a\)Northwestern University Feinberg School of Medicine, Chicago, IL, USA, \(^b\)Johns Hopkins Hospital, Baltimore, MD, USA, \(^c\)University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

**Objective:** To determine the comparative effectiveness of robotic-assisted versus traditional laparoscopic hysterectomy for the treatment of endometrial cancer.

**Method:** We used the National Cancer Data Base to identify women with stage I–III epithelial histology endometrial cancer undergoing surgical management from 2010 to 2015. The primary exposure was type of minimally invasive hysterectomy, either robotic or traditional laparoscopy (LSC), and analysis was by intention to treat. A balanced cohort was created using propensity score matching (PSM) to address confounding. \(\chi^2\) tests, \(t\) tests, modified Poisson, and linear regression were used to examine associations.

**Results:** We identified 93,276 women who underwent hysterectomy for endometrial cancer. From 2010 to 2015, robotic approach increased (35.1% to 59.4%, 4.5% per year); laparotomy decreased (46.8% to 20.2%, 5.0% per year); and LSC increased (18.1% to 20.4%, 0.5% per year) (all \(P < 0.001\)) (Figure 1). Compared to patients undergoing LSC, those undergoing robotic surgery were more likely to be white race (88.3% vs 85.6%), have endometrioid histology (86.9% vs 85.1%) and private insurance (52.6% vs 51.0%), whereas patients undergoing LSC were more likely to be in the highest income quartile (39.3% vs 35.4%), have a Charlson comorbidity score of 0 (74.5% vs 73.6%), and have grade 1 tumors (45.6% vs 44.1%) (all \(P < 0.001\)). Mean age (62 years) and prevalence of stage I disease did not differ. Planned robotic hysterectomy was associated with higher likelihood of any nodal evaluation (70.4% vs 55.9%, RR = 1.26, 95% CI 1.23–1.29), whereas planned LSC was associated with higher rates of conversion to laparotomy (8.0% vs 1.9%, RR = 4.1, 95% CI 3.8–4.5; PSM, RR = 4.0, 95% CI 3.6–4.5) and a small increase in 90-day mortality (0.75% vs 0.47%, RR = 1.59, 95% CI 1.25–2.01; PSM, RR = 1.51, 95% CI 1.12–2.03).
Conclusion: Robotic hysterectomy for endometrial cancer increased dramatically from 2010 to 2015, and this increase coincided with a marked decrease in laparotomy. Traditional laparoscopy did not decrease, but increased at one-ninth the rate of robotics. Planned robotic hysterectomy was associated with a fourfold lower risk of conversion to laparotomy and increased likelihood of nodal assessment compared to planned laparoscopy. A small benefit in 90-day mortality was found for robotic over laparoscopic hysterectomy.

Fig. 1. Surgical Approach for Endometrial Cancer Over Time

2203 - Poster Session
Neuroendocrine carcinoma of the endometrium: Disease course, treatment and survival
K. Schlechtweg, L. Chen, C.M. St. Clair, F. Khoury Collado, J.Y. Hou, A. Melamed, A.I. Tergas and J.D. Wright. aColumbia University, New York, NY, USA, bColumbia University College of Physicians and Surgeons, New York, NY, USA, cNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, dBrigham and Women’s Hospital/Massachusetts General Hospital, Boston, MA, USA

Objective: Neuroendocrine carcinoma of the endometrium (NECE) accounts for only 0.8% of all endometrial carcinoma. The limited literature consists of case reports and small case series, with the largest including 25 patients. We performed a population-based study to describe disease course, treatment, and survival in women with NECE compared to endometrioid endometrial cancer (EC).

Method: The National Cancer Data Base was used to identify women with NECE and women with poorly differentiated EC from 2004 to 2015. The cohort was limited to women with histologic confirmation and who received hysterectomy without neoadjuvant therapy. Kaplan-Meier survival curves were developed to compare survival between groups using a log-rank test. Cox proportional hazard regression models were fit to analyze associations between survival and histology while adjusting for clinical and demographic differences.

Results: A total of 28,291 women with EC and 364 women with NECE were identified. More women with neuroendocrine tumors were non-white and presented with later stage disease ($P < 0.05$ for both). Stage III–IV tumors were diagnosed in 56%
of women with NECE versus 26% of women with EC ($P < 0.001$). Women with NECE were more likely to receive chemotherapy (60% vs 30%, $P < 0.001$), but were less likely to receive radiation (28% vs 48%, $P < 0.001$). In a multivariable model, women with NECE were more than twice as likely to die than those with EC tumors (HR = 2.29, 95% CI 1.85–2.84). Similar trends were noted in analyses limited to stage I (HR = 1.61, 95% CI 1.02–2.57) and stage III (HR = 2.63, 95% CI 1.91–3.61) neoplasms. In a Kaplan-Meier analysis, median survival was 17 months (95% CI 12–23) for women with NECE and 144 months (95% CI 140–148) for those with EC ($P < 0.001$). Five-year survival was 38% (95% CI 32.7–43.8%) in those with NECE vs 69% (95% CI 68.2–69.4%) in those with EC ($P < 0.001$). See Figure 1.

**Conclusion:** Neuroendocrine carcinoma of the endometrium is a rare uterine carcinoma. Compared to patients with poorly differentiated EC, patients with NECE present with later stage disease and have decreased survival.
2204 - Poster Session

Trends in use and outcomes of less radical surgery for early-stage cervical cancer
T.Y. Sia1, L. Chen1, A. Melamedb, J.Y. Houc, C. St. Clairc, A.I. Tergasc, F. Khoury Colladoc and J.D. Wrightc.

1Columbia University College of Physicians and Surgeons, New York, NY, USA, bMassachusetts General Hospital, Boston, MA, USA, cNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA

Objective: Given the morbidity of radical hysterectomy and the excellent prognosis of women with early-stage cervical cancer, less radical surgery has been proposed as a treatment strategy for these women. We analyzed the use and outcomes of simple hysterectomy (SH) compared to radical hysterectomy (RH) for women with stage IA2 and small, stage IB1 cervical cancers.

Method: The National Cancer Data Base was used to examine women with stage IA2 and ≤2 cm IB1 squamous, adenocarcinoma, and adenosquamous cervical cancers diagnosed from 2004 to 2015 and treated with definitive hysterectomy. Women were classified based on the type of surgery as simple hysterectomy or radical (radical or modified radical) hysterectomy. Treatment trends over time were analyzed. Propensity score analysis using inverse probability of treatment weighting was performed to examine survival.

Results: A total of 1,530 women with stage IA2 and 3,931 women with stage IB1 cancers ≤2 cm in diameter were identified. Rates of SH increased from 38% to a peak of 53% between 2004 and 2014 for stage IA2 cancers (P = 0.01), and from 30% in 2004 to a peak of 44% in 2013 for stage IB1 cancers (P < 0.001). In multivariate models, women treated at academic centers were less likely to undergo SH (P < 0.05). After propensity score weighting, there was no association between SH and mortality when compared to RH for stage IA2 cancers (3.5% vs 4.9%, P = 0.20, HR = 0.70, 95% CI 0.41–1.20). Among patients with stage IB1 cancers, however, treatment with SH was associated with increased overall mortality when compared to RH (7.6% vs 4.9%, P = 0.003). Patients with stage IB1 cervical cancers ≤2 cm treated with SH were at 55% increased risk of death (HR = 1.55, 95% CI 1.18–2.03. See Figure 1.

Conclusion: Use of simple hysterectomy is increasing for women with small, early-stage cervical cancers. Patients with stage IB1 cervical cancer treated with SH were at increased risk of death compared to patients treated with RH.

Figure 1: Survival Curves After Propensity Score Weighting

(A) Stage IA2
(B) Stage IB1

Number at risk
Number at risk

2205 - Poster Session

Survival trends in gynecologic malignancies display modest progress and persistent challenges: An investigation of future opportunities
A.M. Jackson, Y. Casablanca, C. Tian, N.W. Bateman, T.P. Conrads and K.M. Darcy. Gynecologic Cancer Center of Excellence, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Objective: To determine population-based trends in cancer-related mortality (CRM) versus noncancer mortality (NCM) over three decades for women with ovarian (OC), uterine cancer (UC), or cervical cancer (CC) and further analyze CRM by demographic variables, extent of disease, and histology.
Method: Women diagnosed with a primary OC, UC, or CC between 1980 and 2009 in the 9-region Surveillance, Epidemiology, and End Results program (SEER) were eligible. Competing risks of CRM and NCM were evaluated using Fine and Gray’s subdistribution hazards modeling. HR and 95% CI per 10-year increase in the period were estimated.

Results: There were 30,720 OC patients, 73,462 UC patients, and 28,589 CC patients eligible for analysis. In women diagnosed between 1980 and 2009, mortality rates per 100,000 dropped for OC and CC and remained stable for UC (Figure 1A). CRM and NCM in OC fell by 14% (95% CI 0.84–0.88, \( P < 0.0001 \)) and 17% (95% CI 0.78–0.88, \( P < 0.0001 \)), respectively, during this time period (Figure 1B). Subgroup analysis showed reductions in adjusted CRM in postmenopausal women, in all racial groups except non-Hispanic black patients, and in all histologic subtypes except low-grade serous and mucinous cancers (Figure 1C). CRM and NCM dropped by 7% (95% CI 0.90–0.96, \( P < 0.0001 \)) and 9% (95% CI 0.87–0.96, \( P < 0.0001 \)), respectively, in CC during this time period (Figure 1B). Subgroup analysis indicated reductions in adjusted CRM for those aged <65 years, non-Hispanic white women, and patients with local or regional disease and in all histologic subtypes (Figure 1D). Both CRM and NRM decreased by 8% for UC (95% CI 0.90–0.95, \( P < 0.0001 \) and 95% CI 0.89–0.95, \( P < 0.0001 \), respectively) (Figure 1B). Reductions in adjusted CRM were seen in postmenopausal women, all races except Asian and Pacific Islanders, in local and regional disease, and in endometrioid and serous cancers (Figure 1E).

Conclusion: Improvements in both CRM and NCM are seen in gynecologic cancer since 1980, most notably in OC. Reductions in mortality rate are seen in OC and CC, but not in UC. Subgroup analysis identifies opportunities for focused investigation and research in order to decrease mortality in gynecologic malignancies.
(AC/ASC). (D) Adjusted hazard ratio per period of time from 1980-2009 for cancer-related deaths in uterine cancer by age at diagnosis, race/ethnicity, stage, and histology include endometrial endometrioid (EEC), uterine serous (USC), uterine clear cell (UCC), uterine carcinoma (UCS), and leiomyosarcoma (LMS). (E)

2206 - Poster Session
Comparison of short and long interval flush maintenance for implanted catheters in gynecologic malignancies
I.C. Cooka and H.M. Cottrillb. aUniversity of Kentucky Medical Center, Lexington, KY, USA, bBaptist Health Lexington, Lexington, KY, USA

Objective: To determine whether the time interval between heparin flushes performed for maintenance of implanted venous access catheters influences complication rates that necessitate removal of the device.

Method: All patients with gynecologic malignancies who had implanted venous access catheters placed between 2010 and 2017 were reviewed. Those who completed chemotherapy and had catheter maintenance for greater than 3 months were included for analysis. Groups were divided based on their maintenance interval: short interval (SI) at 4 to 6 weeks, which is according to manufacturer’s specifications, or long interval (LI) at 10 to 12 weeks, which was historically performed with patient’s 3-month surveillance visit. Complications were defined as events during the flush maintenance period that required removal of the port. Patient demographics and risk factors for inflammation, clotting, and infection were also collected for analysis. As a secondary outcome, cost analysis was performed. SPSS was used to analyze data via Fisher’s exact test and χ² analysis. Significance was defined as P < 0.05.

Results: Data were collected on 259 patient charts from 2010 to 2017, of which 185 met inclusion criteria. Two complications requiring removal were seen during the study period: infection and port malfunction. Complication rates were not statistically different between the SI group (n = 90), 1.11%, and the LI group (n = 95), 2.10% (P = 0.525). The groups were also noted to be evenly matched with no significant difference in patient characteristics or demographics. Currently, $168 is billed for each implanted catheter flush encounter at the study facility. Patients traveled an average of 78.64 miles round trip to reach the facility. Considering only travel costs (gas, vehicle wear and tear) and billing, the LI scheduling could reduce a patient’s expense by 50 to 66% and save as much as $59 to $119 each month in addition to the individual’s copay.

Conclusions: Our findings support the hypothesis that complication rates are not increased when using a long-interval flush maintenance schedule. In addition, the potential savings for the patient are not insignificant and warrant consideration.

2207 - Poster Session
Clinical utility of the risk of malignancy indices for preoperative differentiation between ovarian cancer and borderline ovarian tumor
J. Park. Dong-A University Hospital, Busan, Korea, Republic of (South)

Objective: This study aimed to determine an appropriate risk of malignancy index (RMI) cutoff value by comparative analysis of the four malignancy risk indices (RMI 1, RMI 2, RMI 3, and RMI 4) for distinguishing between ovarian cancer (OC) and borderline ovarian tumor (BOT).

Method: We retrospectively enrolled 339 patients: 115 women with BOTs and 224 with OCs. Preoperative serum CA-125 level, menopausal status, tumor sizes, and ultrasound findings were used to calculate the RMI 1, RMI 2, RMI 3, and RMI 4 scores for each patient, and the results were compared.

Results: There were no significant differences in the area under the ROC curve (AUC) for RMI 1, RMI 2, RMI 3, and RMI 4 (0.792, 0.791, 0.785, and 0.785, respectively). However, the statistical significance in the diagnostic capability of RMI compared to other factors (CA-125, menopause, tumor size, and ultrasound) was proven. See Table 1.

Conclusion: This study is the first to investigate the performances of the four malignancy indices in invasive OCs and BOTs. Although there was no significant difference in the compared RMI scores, the RMI s were very effective at predicting an accurate preoperative diagnosis in patients with all invasive OC and BOT histotypes.

Table 1.
Specialized hereditary breast and ovarian cancer syndrome clinics: Are we achieving our desired outcomes?

B.F. Lees, M. Rastogi, K.M. Woo, M.A. Elezaby and L.M. Barroilhet. University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

Objective: To improve early detection and survival in women with Hereditary Breast and Ovarian Cancer (HBOC) syndromes, national organizations have advocated the development of specialized clinics. We evaluated clinical quality outcomes related to ovarian cancer screening and risk-reduction guidelines at our institutional high-risk Prevention Assessment and Tailored Health Screening (PATHS) clinic, compared to national guidelines.

Method: This is an Institutional Review Board-approved, retrospective review of quality outcomes data for suspected and/or proven HBOC genetic mutation carriers seen at the University of Wisconsin from January 1, 2007, to December 31, 2014. Genetic testing dates, results, and indications; appointment and surgical dates; and screening compliance data were collected. Data were analyzed by indication and by year, the latter using linear regression coefficients.

Results: Of 398 patients with suspected HBOC, 310 (78%) underwent genetic testing, and 78% (243/310) had an identified genetic mutation. BRCA1 (56%, 135/243) and BRCA2 (40%, 97/243) mutations were the most commonly diagnosed mutations. Positive genetic mutation rate was highest among patients with known familial mutations (96%, 74/77); 58.5% (140/239) had a diagnosis of cancer prior to genetic testing, with no significant change over time (P = 0.88). The mean time from genetic diagnosis to specialist appointment decreased over time, at an average rate of 3.35 months per year (95%CI 1.86–4.84, P < 0.001). The mean age of genetic diagnosis remained stable, 37.5 years (range 19–51 years). The mean age of risk-reducing oophorectomy in BRCA women remained outside of the recommended age window (Figure 1). Physician and patient compliance with ovarian cancer screening measures were 78% and 61%, respectively.

Conclusion: Our institutional data demonstrated improvement in timely access to specialist care over the study period and showed that patients are undergoing appropriate genetic testing. Compliance with ovarian cancer screening guidelines is an area for improvement. More than half of patients being referred to genetic testing carry a diagnosis of cancer and are being tested at ages that limit the ability to perform prophylactic measures to maximize benefit. Monitoring quality outcomes for
specialized high-risk clinics assesses adherence to national guidelines and identifies areas for improvement.

![Chart showing age at prophylactic oophorectomy](image)

Fig. 1.

**2209 - Poster Session**

**Impact of a structured screening program on guideline adherence for women at high risk of ovarian cancer**

X.M. Guo, M. Cowan, A. Pyrzak, K. Hope, L. Shulman and E.L. Barber. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA*

**Objective:** To examine the impact of a structured ovarian cancer screening program on adherence to National Comprehensive Cancer Network (NCCN) guidelines for risk-reducing salpingo-oophorectomy (RRSO) in patients with *BRCA1/2* mutations.

**Method:** All patients with *BRCA1/2* mutations who were screened in the Northwestern University Ovarian Cancer Early Detection and Protection Program (NOCEDPP) from 2002 to 2016 were identified. Patients were excluded if they had both ovaries removed prior to initiation of screening or if their visits were not recorded in the NOCEDPP database. The primary endpoint was age at ovarian removal. Data were also collected on those who chose ongoing screening or withdrew from the program. Associated clinicodemographic data were abstracted, including metrics for participation in the screening program. Univariate analysis was used to determine significance.

**Results:** A total of 177 patients were identified (*BRCA1*, *n* = 115; *BRCA2*, *n* = 62). Median age at first visit was 34 years. Patients remained in the program a median of 18 months (IQR 4–57.25 months), having a median of 7 visits (IQR 3–12 visits). There were 77 RRSOs and 5 oophorectomies after a positive screen (i.e., adnexal mass, elevated CA-125). Forty (48.8%) were performed by the upper limit of the NCCN-recommended age for their respective mutation (*BRCA1* = 40 years; *BRCA2* = 45 years). There was 1 malignancy found after a positive screen, and 3 STICs in RRSOs (3.9%). Of the patients who have not undergone surgery, 49 patients are continuing screening and are not yet at the NCCN-recommended age for RRSO, while 4 chose to continue screening later in to their lives, and 42 (23.7%) patients were lost to follow-up. Patients were more likely to have RRSO by guideline-recommended age if, compared to the medians, they received genetic testing earlier (89% vs 37%, *P* <
0.01), were in the screening program longer (69% vs 38%, \( P < 0.01 \)), and had more visits (66% vs 32%, \( P < 0.01 \)), or if they carried a BRCA2 mutation compared to a BRCA1 mutation (69% vs 39%, \( P < 0.01 \)).

**Conclusion:** Adherence to NCCN guidelines for recommended age of RRSO in BRCA patients was low at less than 50% for those participating in the NOCEDPP. However, early testing and active participation in a structured ovarian cancer screening program increased the likelihood of having RRSO by recommended age. Furthermore, patients embraced the program, and less than 25% were lost to follow-up.

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2210 - Poster Session

**Alvimopan for routine use in gynecologic oncology surgical cases to prevent postoperative ileus: A cost-effectiveness analysis**

*C. Wojciehoski, A. Kailasam, M. Morgan, K.J. Hansen, A. Ayers and J.P. Shepherd. Trinity Health of New England, Hartford, CT, USA*

**Objective:** To quantify costs with alvimopan, a peripheral µ-opioid receptor antagonist, for preventing postoperative ileus after hysterectomy for gynecologic oncology indications.

**Method:** We created separate decision analysis models using TreeAge Pro for endometrial, ovarian, and cervical cancer. Alvimopan strategies included no alvimopan, alvimopan only if ileus, alvimopan only if bowel injury, routine alvimopan postoperative day 1, and routine preoperative alvimopan. Bowel injury, ileus, and dyspepsia were modeled with impact on length of stay (LOS). Modeled costs included alvimopan (per dose), surgery (by preoperative diagnosis with and without bowel involvement), and postoperative ileus.

**Results:** Routine alvimopan, either POD1 or preoperative had the highest costs. It also had greatest LOS and ileus reductions (Table 1). Alvimopan only if ileus had minimal LOS effect, reiterating solely prophylactic effect. Despite alvimopan drug costs >$2,000, overall cost increases were lower because of reductions in LOS and ileus. Sensitivity analyses showed alvimopan saved money at ≤$75/dose in ovarian cancer (baseline $165/dose). Thresholds were lower for cervical (≤$47) and endometrial cancer (≤$6).

**Conclusion:** Routine alvimopan reduced ileus by 72%–75%. Higher baseline ileus or bowel involvement, greater absolute ileus, and LOS reductions were seen in ovarian cancer. Costs are ~$1,000, but would save money at ≤$75/dose. Further research and health policy discussions may determine whether ileus and LOS reductions justify current costs.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ovarian</th>
<th>Cervical</th>
<th>Endometrial</th>
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<td><strong>Costs</strong></td>
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<td></td>
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<tr>
<td>No Alvimopan</td>
<td>$32,718.52</td>
<td>$20,398.76</td>
<td>$11,776.86</td>
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<tr>
<td>Alvimopan if Ileus</td>
<td>$33,453.37</td>
<td>$20,886.37</td>
<td>$11,808.93</td>
</tr>
<tr>
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<td>$33,597.23</td>
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<tr>
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<td>$33,762.81</td>
<td>$21,649.82</td>
<td>$12,101.17</td>
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<tr>
<td>Routine Preop Alvimopan</td>
<td>$33,813.33</td>
<td>$21,825.71</td>
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<table>
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<th>Ileus Rate</th>
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<td>29.7%</td>
<td>19.7%</td>
<td>3.30%</td>
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<td>Alvimopan if Ileus</td>
<td>29.7%</td>
<td>19.7%</td>
<td>3.30%</td>
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<tr>
<td>Alvimopan if Bowel Injury</td>
<td>25.5%</td>
<td>19.7%</td>
<td>3.17%</td>
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<tr>
<td>Routine POD1 Alvimopan</td>
<td>13.2%</td>
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<td>8.29%</td>
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<th>Length of stay by alvimopan strategy (days)</th>
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<tr>
<td>No Alvimopan</td>
<td>7.48</td>
<td>6.89</td>
<td>2.18</td>
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<tr>
<td>Alvimopan if Ileus</td>
<td>7.48</td>
<td>6.89</td>
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<td>Alvimopan if Bowel Injury</td>
<td>7.27</td>
<td>6.88</td>
<td>2.17</td>
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</table>
**Objective:** We evaluated the efficacy of various strategies utilized for the control of postoperative pain after minimally invasive hysterectomy. The primary enhanced recovery after surgery (ERAS) protocol of interest utilized premedication (acetaminophen, celecoxib, and pregabalin), then intraoperative subcutaneous liposomal bupivacaine, followed by scheduled oral acetaminophen and ibuprofen postoperatively. Patients also had tramadol and oxycodone as needed for moderate or severe breakthrough pain, respectively.

**Method:** We conducted a retrospective cohort study that included all patients who underwent minimally invasive hysterectomy (total laparoscopic hysterectomy, and laparoscopic-assisted vaginal hysterectomy) for both benign and oncologic indications over a 2-year period. We then compared ERAS protocols with and without premedication, liposomal bupivacaine with standard of care, and On-Q® with standard of care to the standard of care with no local, which served as the control. Patient medical records were evaluated for demographics, surgical characteristics, opioid type and dose, pain scores, length of stay, and complications. Opioids were converted to oral morphine dose equivalents.

**Results:** A total of 954 patients were included within the six protocols. Median opioid usage was the lowest in the ERAS group with premedication and highest in the control group (22.5 mg vs 55.0 mg, \( P < 0.001 \)). Patients in the ERAS group with premedication, when compared to control, were three times more likely to decline opioids (\( P < 0.001 \)). When compared to the control, median pain scores in the ERAS groups were 20%–25% lower. See Figure 1.

**Conclusion:** ERAS protocol with premedication was associated with significant reductions in postoperative opioid use and median pain scores when compared to traditional methods.

![Median Opioid Use By Protocol](image)

**Fig. 1.**
2212 - Poster Session
Performance and outcome of pelvic exenteration for gynecologic malignancies
K. Matsuoa, R.S. Mandelbaumb, C.L. Adamsa, L.D. Romanb and J.D. Wrightb. aUniversity of Southern California, Los Angeles, CA, USA, bNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA

Objective: To examine performance and outcome of pelvic exenteration conducted for gynecologic malignancies.

Method: This is a population-based retrospective study examining the Nationwide Inpatient Sample between 2001 and 2015. Women with cervical, uterine, vaginal, and vulvar malignancies who underwent pelvic exenteration were examined. Comorbidity, perioperative complications, total charges, length of stay, and mortality were assessed.

Results: There were 2,647 cases examined. Cervical cancer was the most common malignancy (45.1%) followed by vaginal cancer (27.6%). Median age was 56 years (IQR 47–66 years), and 58.5% of women had a Charlson Comorbidity Index ≥3, which significantly increased from 57.6% in 2001–2003 to 66.4% in 2013–2015 (P < 0.001). Obese women undergoing exenteration have increased significantly from 2.6% in 2001–2003 to 23.4% in 2013–2015 (P < 0.001). The perioperative complication rate was 66.8%, including 35.5% with multiple complications. The number of women with multiple perioperative complications increased from 25.2% in 2001–2003 to 49.5% in 2013–2015 (P < 0.001). Median length of stay was 14 (IQR 9–21) days, and the number of women hospitalized ≥28 days significantly increased from 14.6% in 2001–2003 to 19.6% in 2013–2015 (P = 0.014). The median total charges were $119,274 (IQR $75,535–$203,744) and increased from $73,051 to $155,410 between 2001 and 2015 (net difference +$82,359, P < 0.001). The mortality rate during the index admission was 1.9% and remained stable over the years of study (P = 0.38).

Conclusion: Women undergoing pelvic exenteration for gynecologic malignancies became more obese and comorbid during the study period. Pelvic exenteration for women with gynecologic malignancies is associated with high morbidity and mortality as well as substantial treatment-related costs.

2213 - Poster Session
Implementation of enhanced recovery after surgery in gynecologic oncology surgery at a major teaching community hospital improves quality, decreases hospital stay and cost
N.I. Gwacham and L. Cinicolo. Saint Barnabas Medical Center, Livingston, NJ, USA

Objective: This report aims to provide an analysis of the effect of an enhanced recovery after surgery (ERAS) program on patient outcomes, cost, and overall quality during its implementation on a gynecologic oncology service at a major teaching community hospital

Method: A retrospective review of gynecologic oncology patients undergoing elective hysterectomy after the implementation of the ERAS program (January 2016 to December 2017) was performed. Patient demographics, postoperative outcomes, and inherent cost were compared to a historical patient cohort (January 2015 to December 2015). Statistical analysis was performed using the t test.

Results: The inaugural participants (n = 180) in the ERAS program (January 2016 to December 2016) were compared to an historical patient cohort (n = 138). Both cohorts were also then compared to the most recent year of patients (second cohort) in the program (January 2017 to December 2017, n = 286). There was no difference in BMI, race, or malignancy; however, there was a significantly increased complexity of patients, as determined by case mix index, between the inaugural patients and the second cohort (1.38 vs 1.53, P = 0.003). Rate of blood transfusions was not significantly decreased; however, there was a general trend toward fewer transfusions since ERAS implementation (4.95% vs 4.10% vs 2.91%). Length of stay in the second cohort of patients was significantly shorter compared to the historical group of patients (1.15 vs 1.58, P = 0.02). Rates of intestinal obstruction were decreased between the historical group and second cohort (2.12% vs 0.94%, P = 0.07); however, this was not statistically significant. Infection rates were also lower between the historical group and the inaugural patients (2.65% vs 0.38%, P = 0.29), but this was not statistically significant. There was also a significant decrease in direct cost ($5,851 vs $4,729, P = 0.04) between the inaugural patients and the second cohort. There was no difference in 30-day readmissions or rates of urinary tract infection and ileus between the groups. In general, there was a trend toward improvement in all categories with each subsequent year in the ERAS program.
Conclusion: The implementation of the ERAS program in gynecologic oncology surgery at a major teaching community hospital decreases cost and length of stay, despite increasing patient complexity.

2214 - Poster Session
A cost-utility analysis of sentinel lymph node mapping versus complete lymphadenectomy in the management of early-stage cervical carcinoma
R.S. Suidan, C.C.L. Sun, S.B. Cantor, M. Frumovitz, S.H. Giordano and L.A. Meyer. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: To evaluate the cost utility of sentinel lymph node mapping (SLN) versus complete pelvic lymphadenectomy (LND) in the management of early-stage cervical carcinoma.

Method: A decision analysis model compared two LND strategies in women undergoing open radical hysterectomy for early-stage cervical carcinoma: (1) complete pelvic LND in all patients, and (2) SLN based on the National Comprehensive Cancer Network algorithm. In the SLN algorithm, 15% of patients map unilaterally, requiring a contralateral side-specific LND, and 5% do not map, requiring a bilateral LND. Costs and outcomes were obtained from published literature and Medicare reimbursement rates (Table 1).

Results: In the base case scenario (open surgery), complete LND had a cost of $26,186 and an effectiveness of 4.17 QALYs, while SLN had a cost of $24,632 and an effectiveness of 4.33 QALYs. With a difference of $1,554 and 0.16 QALYs, SLN was both less costly and more effective than complete LND, dominating it and making it the most cost-effective strategy. No ICER could be determined. In a sensitivity analysis assuming all patients underwent minimally invasive surgery rather
than open surgery, SLN was still the most cost-effective strategy. These findings were robust to multiple other one- and two-way sensitivity analyses varying the risks and utility of lymphedema, the rate of successful SLN mapping, survival estimates, and costs (Table 1). For the estimated 5,000 women undergoing surgery for early-stage cervical carcinoma each year in the United States, the annual cost of complete LND and SLN is $131 million and $123 million, respectively.

**Conclusion:** Compared to complete LND, SLN had lower costs and higher quality-adjusted survival, making it the most cost-effective strategy in the management of early-stage cervical carcinoma.

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**2215 - Poster Session**  
The role of PET/CT in surveillance after chemoradiation for cervical cancer  
*University of California, San Francisco, San Francisco, CA, USA*,  
*UCSF Helen Diller Comprehensive Cancer Center, San Francisco, CA, USA*

**Objective:** To determine how PET or PET/CT scans contribute to the detection of recurrence in patients receiving chemoradiation for cervical cancer.

**Method:** We performed a retrospective review of 286 patients with cervical cancer treated with primary chemoradiation at a single institution from 2003 to 2014.

**Results:** Most patients had FIGO stage IIB-IVA disease (68.5%), negative nodes (63.6%), and no distant metastases (84.9%). The majority received a pretreatment PET (61.2%). Post-treatment PET, defined as a PET <5 months after therapy completion, was performed in 43.0%. Surveillance PET, defined as a PET >5 months after therapy completion, was performed in 37.8%. Surveillance PET was performed in asymptomatic patients without suspicion for recurrence (63.7%), for restaging in the context of recurrence previously detected by another modality (22.5%), for follow-up of ambiguous imaging findings (7.8%), or for new symptoms (5.9%). The rate of recurrence was 38.5%, with a median time to recurrence of 12.1 months (IQR 7.1–27.4 months). Distant recurrences were most common (54.5%), followed by locoregional (31.8%) and unknown (13.6%). Twenty-eight percent of recurrences were detected by surveillance PET in asymptomatic patients without prior clinical or radiographic suspicion for recurrence. While asymptomatic patients undergoing PET were more likely to have earlier stage disease and fewer distant recurrences, multivariate regression controlling for these factors demonstrated that patients with recurrent asymptomatic disease detected on PET had improved overall survival compared to patients with recurrence detected by other modalities, with a median survival of 43.5 months versus 22.8 months ($P < 0.005$). Lead-time bias was excluded as an explanation for these findings by demonstrating that asymptomatic recurrences in the surveillance PET cohort occurred a median of 2.6 months later than other recurrences. See Figure 1.

**Conclusions:** Post-treatment surveillance PET scans performed in asymptomatic patients were associated with a 20.7-month improvement in median survival. Evaluating the optimal timing and cost-effectiveness of PET will determine the role this modality should play in surveillance of patients undergoing chemoradiation for treatment of their cervical cancer.

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**2216 - Poster Session**  
Second curettage for treatment of low-risk gestational trophoblastic neoplasia: A cost-effectiveness analysis  
*Oregon Health & Science University, Portland, OR, USA*
Objective: Low-risk nonmetastatic gestational trophoblastic neoplasia (GTN) is typically treated with methotrexate (MTX) or actinomycin D with second curettage emerging as an alternative treatment modality. We sought to estimate the cost-effectiveness of second curettage for the treatment of low-risk GTN.

Method: A decision-analytic model was created using TreeAge software to compare costs and outcomes for women with WHO staged low-risk GTN undergoing treatment with 5-day MTX, biweekly pulsed actinomycin D, or second curettage. Probabilities were derived from the literature. Outcomes of interest included side effects from chemotherapy, need for additional chemotherapeutic agents, hemorrhage, uterine perforation, and cure rates. Utilities were applied to discounted life expectancy at a rate of 3% to generate combined quality-adjusted life-years (QALYs). The cost-effectiveness threshold was set at a willingness-to-pay of $100,000 per QALY. Sensitivity analyses were then performed in order to assess the robustness of our assumptions.

Results: Second curettage was a cost-effective strategy, and 49 additional patients achieved a cure compared to both chemotherapy regimens when applied to a theoretic cohort of 1,000 women. Of the three studied treatment arms (5-day MTX, biweekly pulsed actinomycin D, and second curettage), second curettage was a cost-effective strategy with an incremental cost-effectiveness ratio (ICER) of $9,603 compared to MTX (Table 1). Though cost-effective, second curettage was associated with an additional 83 hemorrhages and 17 uterine perforations (Table 1). Sensitivity analysis on the cure rate of second curettage was performed, and it would remain cost-effective with cure rates of 25.9% or greater (compared to the base cure rate of 40% reported by Osborne et al. 2016) (Figure 1).

Conclusion: Our study found that second curettage is a cost-effective method of treatment for women with low-risk GTN. This suggests there may be a larger role for second curettage in the treatment of low-risk GTN.

Fig. 1.

2217 - Poster Session
Model for prediction of delayed chemotherapy following cytoreductive surgery in patients with epithelial ovarian cancer
E.M. Newlin\textsuperscript{a}, E.V. Connor\textsuperscript{b}, X. Han\textsuperscript{b} and H. Mahdi\textsuperscript{a}. \textsuperscript{a}Cleveland Clinic, Cleveland, OH, USA, \textsuperscript{b}The Cleveland Clinic Foundation, Cleveland, OH, USA

Objective: Develop a model to predict risk of delayed chemotherapy after cytoreductive surgery for epithelial ovarian cancer.

Method: A retrospective chart review was conducted for patients with a diagnosis of epithelial ovarian cancer (EOC) who underwent surgical management of EOC at 3 hospitals in an academic health system from January 1, 2010, to December 31, 2015. Clinical and demographic data were collected from the electronic record. Delayed chemotherapy (defined as >6 weeks after surgery) was the primary outcome. Binomial logistic regression models were employed to study the effects of potential risk factors. The study variables significant at $P < 0.1$ in univariate logistic regression analyses were selected into the stepdown method, which is based on the concordance index (C-index). A subset of the risk factors was selected to achieve a relative parsimonious model with the maximum C-index as the final multivariate logistic regression model, which was internally validated. C-index was used to describe discriminant power, and a calibration plot was then generated. See Figure 1.
**Results:** Out of 334 reviewed patients, data from 288 patients were included after excluding those with missing time to chemotherapy \((n = 35)\) or patients with stage 1A/1B disease \((n = 12)\). Of all patients, 30.6\% \((n = 88)\) had delayed chemotherapy >6 weeks after surgery or never received chemotherapy. The patients in the delayed chemotherapy group had higher overall mortality at time of data collection \((P = 0.0015)\). The following predictors were included in the final model (\(P\) values from multivariate analysis): age \((P = 0.05)\), platelets \((P = 0.04)\), BMI \((P = 0.002)\), stage \((P = 0.11)\), presence of a postoperative complication \((P = 0.008)\), surgical re-exploration \((P = 0.19)\), and intraoperative blood transfusion \((P = 0.16)\). Our final model had a C-index 0.724. After internal validation, bootstrap method was used 1,000 times to get the average C-index as 0.686.

**Conclusion:** Our prediction model identified patients at risk of delayed chemotherapy. These delays in chemotherapy could have an impact on overall patient survival. Patients known to be at a higher risk of delay may benefit from closer outpatient follow-up or tailored recovery plans to expedite time to adjuvant treatment.

Fig. 1.

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**2218 - Poster Session**

Withdrawn at author's request

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**2219 - Poster Session**

**Sequencing of therapy in women with stage III endometrial carcinoma receiving adjuvant combination chemotherapy and radiation**

A.H. Latham\(^a\), L. Chen\(^b\), J.Y. Hou\(^c\), F. Khoury Collado\(^d\), C. St. Clair\(^e\), A.I. Tergas\(^e\) and J.D. Wright\(^e\). \(^a\)New York-Presbyterian/Columbia University Medical Center, New York, NY, USA, \(^b\)Columbia University College of Physicians and Surgeons, New York, NY, USA, \(^c\)Columbia University, New York, NY, USA

**Objective:** While women with stage III endometrial cancer are often treated with chemotherapy (CT) and external beam radiation (RT), the optimal sequence of these modalities is unknown. We examined the association between the sequence of CT and RT on survival for women with stage III endometrioid endometrial cancer.

**Method:** The National Cancer Data Base was used to identify women with stage IIIC endometrial carcinoma who underwent hysterectomy and were treated with adjuvant CT and RT from 2004 to 2015. Patients were stratified based on the sequence of therapy: RT then CT, CT then RT, or concurrent therapy. The association between treatment sequence and mortality was examined after propensity score analysis using inverse probability of treatment weighting to balance the clinical and demographic characteristics between the cohorts.
Results: A total of 6,981 patients were identified including 5,116 (73%) who received CT then RT, 696 (10%) who received RT then CT, and 1,169 (17%) who received concurrent therapy. The use of CT prior to RT increased from 40% in 2004 to 76% in 2015, while use of RT before CT decreased from 34% to 4% and concurrent therapy decreased from 26% to 20% across the same period ($P < 0.001$). Compared to CT before RT, there was no difference in survival with RT then CT (HR = 1.00, 95% CI 0.86–1.17), while concurrent therapy was associated with a 47% increased risk of mortality (HR = 1.47, 95% CI 1.29–1.66). In a sensitivity analysis combining the groups that received RT first (RT first then CT or concurrent RT–CT), mortality was 25% higher (HR = 1.25, 95% CI 1.13–1.39) compared to a strategy of CT followed by RT.

Conclusion: Among women with stage III endometrial cancer treated with combination CT and RT, a strategy employing CT first is associated with the lowest mortality.

2220 - Poster Session
Use of vaginal chlorhexidine antisepsis prior to hysterectomy to reduce surgical site infection
M.A. Schwartz, R. Schoenbrun, P. Hua, S.A. Tomita, T. Orfanelli, J. Overbey, C. Ascher-Walsh, S.V. Blank and H.C. Loudon. Icahn School of Medicine at Mount Sinai, New York, NY, USA

Objective: Chlorhexidine exhibits a greater reduction in bacterial counts compared with povidone iodine when used as preoperative skin antisepsis. Decreasing bacterial counts in the vagina reduces the risk of surgical site infection (SSI). The American College of Obstetricians and Gynecologists supports 4% chlorhexidine vaginal preparation (CVP) as safe and superior to povidone iodine (PI). The primary objective was to evaluate SSI rates before and after implementation of CVP for antisepsis in patients undergoing hysterectomy.

Method: All patients undergoing hysterectomy (open, laparoscopic, robotic, or vaginal) received a perioperative bundle to reduce SSI from from July 1, 2017, to June 30, 2018, at a single academic institution and were reviewed. Before January 1, 2018, preoperative vaginal antisepsis was achieved with PI, and after this date, 4% CVP was used. Patient demographics and surgical variables were extracted from medical charts, and SSI diagnoses were obtained from inpatient records. Data pre- and post-use of CVP were compared using t tests, Mann-Whitney U tests, and Fisher exact tests as appropriate. Univariate and multivariate logistic regression analyses were used to assess the association between SSI rate and CVP, race, mode of hysterectomy, and BMI.

Results: A total of 822 patients with a median age of 54 years (range 29–95) were included; 50.2% ($n = 413$) of patients underwent hysterectomy after the implementation of standardized use of preoperative CVP. Demographic and surgical variables were similar between groups, with the exception of race ($P = 0.002$). Overall, SSI rates pre- and post-standardized use of CVP were 3.4% ($n = 14/409$) and 2.2% ($n = 9/413$), respectively. Incidence of SSI was not significantly associated with use of CVP ($P = 0.28$). In multivariable analysis (Table 1), vaginal preparation method ($P = 0.31$), BMI ($P = 0.48$), and race ($P = 0.48$) were not significantly associated with SSI incidence. Mode of hysterectomy was significantly associated with SSI ($P = 0.007$). Among patients with malignancy undergoing hysterectomy ($n = 262$), the incidence of SSI was 8.2% ($n = 10/122$) with PI and 3.6% ($n = 5/140$) with CVP. Despite this trend, there was no significant association found between vaginal preparation and SSI for patients with cancer ($P = 0.11$).

Conclusion: Use of CVP rather than PI vaginal antisepsis was not associated with a decrease in SSI in patients undergoing hysterectomy. For patients with malignancy, there was a nonsignificant trend towards improvement in SSI incidence with the use of CVP.
Table 1: Multivariable and Univariable Analysis for Logistic Regression.

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<th>Variable</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
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<td>p-value</td>
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<td>25-29.9</td>
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<tr>
<td>≥30</td>
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</table>

2221 - Poster Session
Recurrence patterns among women with early-stage cervical cancer following minimally invasive versus abdominal radical hysterectomy
A. Freeman\textsuperscript{a,b}, E. Garcia\textsuperscript{a}, R. Guerra\textsuperscript{a}, W. Pierson\textsuperscript{b}, J.S. Chapman\textsuperscript{a,b} and L.M. Chen\textsuperscript{a,b}. \textsuperscript{a}University of California, San Francisco, San Francisco, CA, USA, \textsuperscript{b}UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

Objective: To compare disease recurrence patterns in women undergoing minimally invasive surgery (MIS) versus abdominal radical hysterectomy for early-stage cervical cancer.

Method: Women undergoing MIS (robotic-assisted or laparoscopic) and abdominal radical hysterectomy by gynecologic oncologists were identified from a single institution from 2006 through 2016. Robotic surgery for gynecologic oncology at our institution began in 2008. Demographic and clinicopathologic data were collected, including mode of preoperative imaging. Primary outcome was recurrence site.

Results: A total of 53 MIS cases (53 robotic and 0 laparoscopic) and 55 abdominal radical hysterecmy cases were identified during the study period. Patients in the MIS group were more likely to obtain preoperative positron emission tomography (PET) than the open surgery cohort (65% vs 38%, \( P = 0.0067 \)). More than 90% of patients in both groups underwent advanced preoperative imaging. Forty percent of patients were recommended for adjuvant radiation, with or without chemosensitization. Recurrences (3.6%) in the open surgery cohort were local and locoregional and occurred at 19 and 22 months, respectively. One of the five patients in the MIS group (9.6%) had a distant (port site) recurrence, and the other four were local or locoregional, occurring between 7 and 10 months post-surgery. All patients with recurrences in the MIS group received adjuvant radiation except for 1 patient with stage IA1 squamous cell carcinoma.

Conclusion: In this single institution retrospective analysis, there was no statistical difference (\( P = 0.26 \)) in recurrence patterns among women with early-stage cervical cancer undergoing MIS compared to laparotomy. MIS patients recurred earlier and with more distant recurrences, although our sample size is too small to make any definite conclusions. Preoperative imaging to identify Sedlis criteria may help improve outcomes among women with early-stage cervical cancer undergoing surgery.
**2222 - Poster Session**

Unfitness and cancer: State-of-the-art activity tracking devices reveal the unexpectedly sedentary lives of our cancer patients


*Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA, **University at Buffalo, Buffalo, NY, USA, *Roswell Park Cancer Institute, Buffalo, NY, USA

**Objective**: Increased physical activity (PA) improves the immune system and anticancer responses, while inactivity is associated with higher mortality in ovarian cancer. PA is a modifiable risk factor; however, studies of PA in cancer patients rely on patient-reported questionnaires without objective measures. In this pilot study, our objective was to obtain real-time data using a Fitbit activity-tracking device to measure PA and sleep in patients with ovarian and endometrial cancer and compare these data to patients’ self-reported PA, sleep, and quality of life.

**Method**: Patients with endometrial or ovarian cancer and ECOG 0–1 were recruited at time of diagnosis or recurrence before initiation of subsequent therapy. Enrollees were given a Fitbit Charge2 device for a 9-month study period and advised to wear the device at least 5 days per week. Demographic variables, anthropomorphic measurements, activity data, and sleep patterns were obtained. Quality-of-life (QOL) assessments using EORTC questionnaires, Pittsburgh Sleep Quality Index, and Godin Leisure-Time Exercise Questionnaires (GLTEQ) were conducted every 3 months and correlated to Fitbit data.

**Results**: There were 27 evaluable patients with a mean age of 58.7 ± 10.3 years. Mean BMI was 31.9 ± 8.6 kg/m². Patient compliance with device use was 85.2%, and activity was classified using American College of Sports Medicine criteria. Biometric data from Fitbit devices demonstrated a median daily step count of 1,309.8 (range 6.3–26,408.3) with 5.61 hours of sleep per night (range 2.1–7.7 hours). Average self-reported PA was at least moderate for 76.2% of patients with an average GLTEQ score of 28.1 ± 5.23, in sharp contrast to Fitbit data demonstrating sedentary activity in most patients (85.2%, n = 23). Poor quality of sleep was reported by 55.6%; however, only 7.4% of patients averaged a recommended 7+ hours of sleep. Self-reported PA and sleep showed little correlation with objective real-time tracking and QOL parameters.

**Conclusion**: Objectively recorded PA and sleep time show most of our patients live a sedentary lifestyle with inadequate sleep, and overreport PA and sleep time. Use of widely available activity tracking devices is feasible in our older patient population to objectively measure modifiable risk factors that may have an impact on patient survival.

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**2223 - Poster Session**

Trends in reflex testing among Ashkenazi Jewish patients: Is BRCA1/2 founder mutation testing enough?


*Weill Cornell Medical College, New York, NY, USA, **New York-Presbyterian Hospital/Weill Cornell Medical College, New York, NY, USA, *New York-Presbyterian Hospital, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA

**Objective**: Following the 2013 Supreme Court ruling invalidating exclusive license rights to isolated human genes and genetic testing, and subsequent rapid integration of multigene panel testing, we sought to evaluate changes in genetic assessment modalities among Ashkenazi Jewish (AJ) patients from June 2013 to December 2016.

**Method**: Medical records for all AJ patients undergoing genetic assessment at a single institution between June 2013 and December 2016 were reviewed. Testing modalities were characterized as multigene panel testing, targeted testing (*BRCA1/2* founder, or other non-*BRCA1/2* cancer-associated genes), or reflex multigene panel testing. Reflex testing was defined as an initial targeted testing strategy followed by more comprehensive screening if the initial test yielded a negative result.

**Results**: A total of 732 AJ patients underwent genetic assessment, and 101 patients were found to have a pathogenic mutation including 78 (77%) *BRCA1/2* founder allele mutations, 3 (3%) non-founder *BRCA1/2* mutations, and 20 (20%) mutations in non-*BRCA1/2* cancer-associated genes. The uptake of multigene panel testing increased over time (2013, 3%; 2014, 9%; 2015, 28%; 2016, 43%; P < 0.001). The uptake of *BRCA1/2* founder mutation testing decreased over time (2013, 83%; 2014, 76%; 2015, 48%; 2016, 31%; P < 0.001). The rate of targeted testing for non-*BRCA1/2* mutations remained stable. Reflex testing use increased between 2013 and 2014 (44% versus 56%) but then decreased in 2015 and 2016 (48% and 2%, respectively) (Figure 1).
**Conclusion:** Because of the high frequency of founder mutations among AJ patients, many consensus guidelines still recommend only BRCA1/2 founder mutation testing for this population. With the advent of next-generation sequencing and loss of BRCA1/2 patents, large multigene panels have become accessible and cost- and time-efficient. Among our AJ patient population, reflex testing initially increased after the Supreme Court ruling but then decreased, likely because of increased use of multigene panel testing as an initial testing strategy. Presence of non-BRCA1/2 founder mutations among AJ patients coupled with these trends highlight the need to revisit genetic testing guidelines that emphasize founder mutation testing alone in AJ patients.

**Table 1: Uptake of Various Genetic Assessment Modalities**

![Graph showing uptake of genetic assessment modalities over years]

<table>
<thead>
<tr>
<th>Year</th>
<th>Multigene panel testing</th>
<th>BRCA founder mutation testing</th>
<th>Targetted testing (non BRCA1/2 genes)</th>
<th>Reflex testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>200</td>
<td>180</td>
<td>150</td>
<td>120</td>
</tr>
<tr>
<td>2014</td>
<td>180</td>
<td>160</td>
<td>130</td>
<td>110</td>
</tr>
<tr>
<td>2015</td>
<td>160</td>
<td>140</td>
<td>110</td>
<td>90</td>
</tr>
<tr>
<td>2016</td>
<td>140</td>
<td>120</td>
<td>90</td>
<td>70</td>
</tr>
</tbody>
</table>

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2224 - Poster Session

**Treatment and survival in elderly women with gynecologic cancer not inferior with Medicare versus private insurance: A National Cancer Database investigation**


*Inova Fairfax Hospital, Falls Church, VA, USA, Gynecologic Cancer Center of Excellence, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, Inova Schar Cancer Institute, Inova Center for Personalized Health, Falls Church, VA, USA, John P Murtha Cancer Center, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, Department of Obstetrics and Gynecology, Inova Fairfax Hospital, Falls Church, VA, USA*

**Objective:** Medicare eligibility in the United States begins at 65 years of age, but some individuals retain private insurance and decline the Medicare provision. This study determined whether Medicare versus private insurance affects treatment and/or survival in women diagnosed at ≥65 years with uterine, ovarian, or cervical cancer.

**Method:** Propensity score analysis using inverse probability treatment weighting (IPTW) was applied to women with Medicare (alone or with supplemental insurance) versus private insurance only in the National Cancer Data Base to balance the population by demographics, comorbidity, histology, and stage. Patients were diagnosed at ≥65 years with a first primary stage I-IV uterine, ovarian, or cervical cancer between 2004 and 2014. Treatment proportions and survival differences were compared.
Results: There were 171,599 eligible women including 148,239 with Medicare versus 23,360 with private insurance. Older age at diagnosis, comorbidity score ≥ 1+, aggressive histology, and advanced stage were more common in uterine, ovarian, and cervical cancer patients with Medicare versus private insurance. Surgical treatment was less common in uterine (91.3% vs 93.8%), ovarian (69.5% vs 75.9%), and cervical (32.8% vs 38.3%) cancer patients with Medicare versus private insurance, respectively. Radiation did not vary, but chemotherapy was less common in uterine (20.4% vs 22.2%), ovarian (68.8% vs 72.3%) and cervical (50.4% vs 54.1%) cancer patients with Medicare versus private insurance, respectively. Survival was worse for uterine (HR = 1.26, 95% CI = 1.22–1.30), ovarian (HR = 1.19, 95% CI 1.15–1.23), and cervical (HR = 1.25, 95% CI 1.16–1.34) cancer patients with Medicare versus private insurance, respectively. IPTW balanced for differences in age at diagnosis, comorbidity score, histology, and stage between Medicare and private insurance. Balancing also corrected for the disparity in the proportion treated with surgery or chemotherapy, and in the survival of women with Medicare compared with private insurance (Figure 1).

Conclusion: Treatment and survival for women ≥ 65 years with uterine, ovarian, or cervical cancer were not inferior with Medicare compared with private insurance after balancing.

Fig. 1. Survival distributions and risk of death expressed with hazard ratio (HR) and 95% confidence interval (CI) in uterine cancer (A, D), ovarian cancer (B, E) or cervical cancer (C, F) patients diagnosed ≥ 65 years old with Medicare compared with private insurance.

2225 - Poster Session
Distance to referral center and race/ethnicity among women choosing preoperative urogynecology referral: Cancer of the uterus and treatment of incontinence (CUTI) study

Objective: To determine whether distance to referral center or race/ethnicity have an impact on acceptance of urogynecology referral and concomitant stress urinary incontinence (SUI) surgery in women with endometrial cancer and SUI symptoms.

Method: A multicenter, prospective cohort study was conducted across 8 U.S. sites. Eligible women had endometrial intraepithelial neoplasia (EIN) or clinical stage I/II endometrial cancer with plan for hysterectomy, and screened positive for
SUI symptoms. All eligible women were offered a preoperative referral to a urogynecologist. Acceptance of referral was assessed by distance to referral center and race/ethnicity with χ² or Fisher exact tests.

**Results:** Of the 556 women enrolled, 17 were ineligible or withdrew and 4 were missing baseline data, leaving 535 women in the analysis. Of these, 249 (46.54%) accepted preoperative urogynecology referral. Acceptance of referral was lower for women who lived 50–99.9 miles (45/125, 36.0%, P = 0.002) or 100–149.9 miles (14/52, 26.9%, P = 0.003) from referral center, compared to women <50 miles (155/285, 54.4%) from referral center. Of Caucasian women, 217/450 (48.2%) accepted referral, compared to 14/18 (77.8%) of Hispanic women (P = 0.0004) and 10/55 (18.2%) of African American women (P = 0.0008).

**Conclusion:** Race/ethnicity and distance to referral center appeared to have an impact on acceptance of urogynecology referral for concomitant SUI and cancer surgery. Larger population studies evaluating the impact of race/ethnicity and proximity to center are warranted to further clarify the role of health disparities in treatment choice.

**2226 - Poster Session**

**Body mass index and intention for health behavior change before and after treatment of endometrial cancer**

R. Harrison, H. Zhao, W. He, C.C.L. Sun, R.S. Suidan, S. Armbruster, J.A. Rauh-Hain, K.H. Lu, S.H. Giordano and L.A. Meyer. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Objective:** Obesity is a risk factor for both endometrial cancer (EC) and other chronic diseases. A diagnosis of EC may be an impetus for health behavioral change to mitigate future obesity-related health risks. We describe BMI and intention to make health behavior changes before and after EC diagnosis.

**Method:** We identified incident EC cases from 2009 to 2015 in the Truven Health Marketscan database and linked these with BMI and intent-to-change data from a health risk assessment database. Hysterectomy was designated as the index date. Cases were excluded if they were treated without surgery or pre- and post-treatment BMI data were unavailable; see **Table 1** for cohort selection. Summary statistics and two sample Wilcoxon test were performed.

**Results:** There were 637 cases identified. Mean pre-treatment BMI was 35.5 kg/m² (median = 35, IQR 27–42.3). Mean post-treatment BMI was 35.6 kg/m² (median = 34, IQR 28–42). Median BMI change observed in the entire cohort was 0 kg/m² (IQR −1 to 2). The median follow-up was 599 days (IQR 360–1,091). In 62.5% of cases, weight gain (n = 297, 46.6%) or no change in weight (n = 101, 15.9%) was observed. In 37.5% of cases, weight loss was seen (n = 239, 37.5%). Among the 297 cases observed to gain weight after treatment, the mean pre-treatment BMI was 34 kg/m² and mean BMI increase was 3 kg/m² (median = 2, IQR 1–3). Among the 239 cases who lost weight after treatment, the mean pre-treatment BMI was 39 kg/m² and mean BMI decrease was −3 kg/m² (median = −2, IQR −4 to −1). Median pre-treatment BMI of patients who lost weight following treatment was higher than those who gained weight (38 kg/m² vs 33 kg/m², P < .0001). Among women with available intent-to-change survey data, there were no differences in intention to lose weight, change diet, or exercise responses before or after the diagnosis of EC. Furthermore, there was no association between responses regarding attempting weight loss, diet, or exercise and a decrease in BMI.

**Conclusion:** An EC diagnosis does not seem to be an impetus for meaningful weight loss. Many women in our cohort gained weight. In our study, an EC diagnosis was not associated with different responses to weight-related health behavior surveys nor were these responses associated with BMI changes. The systematic delivery of evidence-based interventions for meaningful weight loss should be a priority for EC patients in the survivorship setting.
Table 1. Cohort Selection

<table>
<thead>
<tr>
<th>Inclusion / Exclusion Criteria</th>
<th>Included / Remaining</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1:</strong> Individuals with ≥1 inpatient or ≥2 outpatient insurance claims ≥30 days apart associated with EC diagnosis, 2009-2015</td>
<td>4457</td>
<td>-</td>
</tr>
<tr>
<td><strong>Step 2:</strong> Underwent hysterectomy</td>
<td>3273</td>
<td>1184</td>
</tr>
<tr>
<td><strong>Step 3:</strong> Prevalent cases excluded in 3-Year wash-out time window (2006-2008) for the following reasons: (1) having EC diagnosis (2) receiving hysterectomy (3) having a diagnosis of prior history of EC</td>
<td>3239</td>
<td>34</td>
</tr>
<tr>
<td><strong>Step 4:</strong> BMI data available for analysis</td>
<td>637</td>
<td>2602</td>
</tr>
<tr>
<td><strong>Final Cohort</strong></td>
<td>637</td>
<td>-</td>
</tr>
</tbody>
</table>

1 Available pre- and posttreatment BMI data was required for analysis; posttreatment BMI data was required to be ≥6 months from index date.

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**2227 - Poster Session**

**Chemotherapy adversely impacts sleep quality in patients with gynecologic and breast malignancies**


*Women & Infants Hospital, Brown University, Providence, RI, USA, bUniversity of Vermont College of Medicine, Burlington, VT, USA, cWomen & Infants Hospital, Brown University, Providence, RI, USA*

**Objective:** To determine the effect of chemotherapy on sleep quality and quality of life among women with ovarian, endometrial, and breast cancer undergoing chemotherapy.

**Method:** A prospective cohort study was performed at a single academic institution among women with a diagnosis of ovarian, endometrial, or breast cancer who were chemotherapy naïve and scheduled to receive cytotoxic treatment. Eligible patients completed the Pittsburgh Sleep Quality Index (PSQI), a validated questionnaire that measures sleep quality over the preceding month via seven different domains prior to initiating treatment, mid-treatment, and at the end of treatment. Composite PSQI scores were then tabulated. To evaluate quality of life (QOL), participants completed the Functional Assessment of Cancer Therapy (FACT)-G questionnaire along with a disease-specific subscale at the same time points.

**Results:** Ninety-seven women enrolled in the study: 27 ovarian, 23 endometrial, and 47 breast cancer (BRCA) patients. BRCA patients were younger than their gynecologic cancer (GynCa) counterparts (median age 50 vs 62 years, \( P < 0.0001 \)). Sixty-four percent of ovarian, 39% of endometrial, and 6% of BRCA patients had stage III or IV disease. Poor sleep quality (PSQI > 5) was common at all time points, but was most prevalent at mid-treatment (73% vs 59% at baseline, \( P = 0.0038 \)), before improving slightly at the end of treatment (61%). Of the GynCa patients, 53% reported poor sleep quality at baseline, as did 64% of BRCA patients. There was no difference seen between cancer types. QOL was also negatively affected at mid-treatment and the end of treatment, with FACT-G scores of 76 and 81, respectively (\( P < 0.0001 \) compared to baseline), although to what extent sleep disturbance contributed to this deterioration cannot be determined (Table 1).

**Conclusion:** A majority of gynecologic and breast cancer patients have poor sleep quality prior to starting chemotherapy, which worsens with treatment; baseline sleep impairment may be due to anxiety and/or cancer-related symptoms, especially in patients with more advanced-stage disease. More attention should be paid to developing and studying interventions designed to improve sleep quality before, during, and after chemotherapy, which could improve tolerance of treatment and quality of life for patients.
**Table 1.**

<table>
<thead>
<tr>
<th></th>
<th>Slope for FACT-G</th>
<th>p-value comparing slopes by cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>Total</td>
<td>Gyn cancer</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>(n = 88)</td>
<td>(n = 41)</td>
</tr>
<tr>
<td><strong>Mid</strong></td>
<td>-2.67</td>
<td>-2.30</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>(n = 79)</td>
<td>(n = 39)</td>
</tr>
<tr>
<td><strong>End</strong></td>
<td>-2.87</td>
<td>-2.71</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>(n = 72)</td>
<td>(n = 37)</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td>0.77</td>
<td>0.63</td>
</tr>
</tbody>
</table>

**2228 - Poster Session**

**Trends in surgical complexity in ovarian cancer surgery in the era of increasing neoadjuvant chemotherapy: A National Cancer Database study**

W. Horner\(^a\), V. Pleasant\(^b\), K. Peng\(^a\), M. Brackmann\(^a\), J.A. Ebot\(^a\), R. Gutfreund\(^a\), R.K. Reynolds\(^b\) and S. Uppal\(^a\). \(^a\)The University of Michigan Hospitals, Ann Arbor, MI, USA, \(^b\)University of Michigan, Ann Arbor, MI, USA

**Objective:** Utilization of neoadjuvant chemotherapy (NACT) in the treatment of advanced ovarian cancer has been increasing. However, the impact of this change on the complexity of cytoreductive surgeries for ovarian cancer is unknown.

**Method:** Using the National Cancer Data Base (NCDB), we performed a retrospective cohort study of women diagnosed between 2004 and 2015 with stage III or IV epithelial ovarian cancer who underwent either primary cytoreductive surgery (PDS) followed by adjuvant chemotherapy or NACT followed by interval debulking surgery. Based on the methodology of NCDB, cases were assigned a surgical complexity category as (1) inadequate, (2) low, (3) moderate, or (4) high complexity (details in Figure 1). The primary outcome was the trend in surgical complexity over time. We also evaluated temporal trends in treatment modality, perioperative mortality, and survival.

**Results:** A total of 52,582 (76.3%) underwent PDS, and 16,307 (23.7%) underwent NACT. Overall, the utilization of NACT increased from 11% in 2004 to 38% in 2015 (P < 0.001). This increase was consistent in all quartiles of hospital case volume. Patients undergoing high-complexity surgeries, during the same time frame, increased from 27% to 33% (PDS cohort) and from 17% to 25% (NACT cohort) (P < 0.001). The maximum increase in high-complexity surgery was seen at the high-volume centers. Overall 30-day mortality decreased from 3.4% in 2004 to 1.4% in 2015, and 90-day mortality decreased from 7.6% to 4%. During the same time, 5-year survival increased from 32% to 40%.

**Conclusion:** Increase in the utilization of NACT has decreased 30- and 90-day mortality substantially. Moreover, the overall complexity of ovarian cancer surgery has increased in both PDS and NACT cohorts. These results should be reassuring for fellowship training programs and applicants for gynecologic oncology fellowship amid concerns that the increasing NACT proportion would negatively affect the high-complexity surgery case volumes.
Patterns of perioperative use and persistent use of opioids after gynecologic surgery

J.D. Wright, Y. Huang, A.I. Tergas, F. Khoury Collado, C.M. St. Clair, J.Y. Hou, A. Melamed, and D. Hershman. *Columbia University College of Physicians and Surgeons, New York, NY, USA, bNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, cMassachusetts General Hospital, Boston, MA, USA*

**Objective:** While there is increasing awareness of the risk of opioid dependence among patients who receive prescription opioid drugs, little is known about prescribing patterns after gynecologic surgery. We examined the patterns of perioperative opioid use after major and minor gynecologic surgery and explored the incidence and risk factors for persistent opioid use among these women.

**Method:** The MarketScan database was used to identify opioid-naive women age 18–64 years who underwent gynecologic surgery from 2010 to 2016. The following procedures were examined: abdominal, minimally invasive, and vaginal hysterectomy, myomectomy, oophorectomy, dilation and curettage, tubal ligation, and endometrial ablation. Primary, perioperative opioid use was defined as filling an opioid prescription from 30 days before to 2 weeks after the surgical procedure. The oral morphine milligram equivalent (OME) of each opioid prescription was calculated. Prolonged opioid use was defined as receipt of an opioid prescription between 90 and 180 days after the primary procedure.

**Results:** A total of 729,625 women who underwent gynecologic surgery were identified. A prescription for perioperative opioids was filled in 438,039 (60.4%) patients. Initial opioid use was highest after minimally invasive (79.5%) and abdominal (79.3%) hysterectomy and lowest after dilation and curettage (36.7%). The median OME dispensed was 200 (IQR 135–300). Prolonged opioid use was identified in 29,643 (6.8%) patients. Prolonged opioid use was highest after open (7.5%) and laparoscopic (7.4%) oophorectomy and D&C (7.2%) and lowest after myomectomy (4.8%). In a multivariate model, prolonged opioid use was more common in younger women, Medicaid recipients, those with a history of depression, anxiety, or substance abuse, and those with greater medical comorbid condition ($P < 0.05$ for all).
**Conclusion:** Persistent opioid use is common after major and minor gynecologic surgery. Underlying mood disorders and substance abuse are strong risk factors for persistent opioid use.

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**2230 - Poster Session**

*A decision analysis of treatment strategies for pelvic lymph node positive stage IB1 cervical cancer*

*T. Zigras², N. Roumeliotis², H.S. Brar², H. Wijeysundera³ and S.E. Ferguson². ²University of Toronto, Toronto, ON, Canada, ³University of Toronto - Faculty of Medicine, Toronto, ON, Canada, ⁴University of British Columbia, Vancouver, BC, Canada*

**Objective:** To evaluate the cost-effectiveness of treatment strategies for women with stage IB1 cervical cancer with positive pelvic lymph nodes.

**Method:** A Markov model was constructed to evaluate 4 treatment strategies: (1) aborted radical hysterectomy with primary chemoradiation (PCRT), (2) radical hysterectomy followed by adjuvant chemoradiation (RHYST), (3) paraaortic lymphadenectomy to assess metastasis, aborted radical hysterectomy with primary chemoradiation and extended field radiation if paraaortic lymph nodes involved (PCRT plus PA), and (4) paraaortic lymphadenectomy, radical hysterectomy followed by adjuvant chemoradiation and extended field radiation if paraaortic lymph nodes positive (RHYST plus PA). All relevant literature was identified to extract probability data. Outcome evaluated was cost-effectiveness in which quality-adjusted life years (QALYs) was the effectiveness measure. Only direct medical costs were included. The base case was assumed to be a 47-year-old woman with stage IB1 cervical cancer with positive pelvic lymph nodes identified at the time of surgery, following which the model ran for a lifetime.

**Results:** The cost of PCRT was $83,039 and yielded a QALY of 16.2 years, and the cost of RHYST was $106,639 with a QALY of 17.7 years. Similarly, completing paraaortic dissection in addition yielded a slightly increased cost of $83,498 and a QALY of 16.31 years in the PCRT plus PA strategy and $107,046 and QALY of 17.78 years in the RHYST plus PA strategy. At a willingness-to-pay of $50,000, the RHYST plus PA strategy dominated, followed by the PCRT plus PA.

**Conclusion:** RHYST plus PA was the dominant strategy for stage IB1 cervical cancer with positive pelvic lymph nodes. Clinicians must consider the impact of toxicities and long-term complications on quality of life when selecting a treatment strategy.

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**2231 - Poster Session**

*A cost-effectiveness analysis of sentinel lymph node detection in vulvar cancer by preoperative lymphoscintigraphy versus intraoperative detection alone*

*B.N. Brzezinska², J.P. Shepherd³, K. Rath⁴ and A. Clements⁵. ²Riverside Methodist Hospital, Columbus, OH, USA, ³Trinity Health of New England, Hartford, CT, USA, ⁴Ohio Health Gynecologic Cancer Surgeons, Columbus, OH, USA*

**Objective:** To determine the cost-effectiveness of preoperative lymphoscintigraphy (LSG) for detection of inguinofemoral (IF) sentinel lymph nodes (SLN).

**Method:** We compared two strategies. One strategy used preoperative LSG prior to IF SLN excision, while the other strategy omitted preoperative LSG. The two potential outcomes in the model were death or survival. We included initial costs associated with the procedures of injected solutions, radiation oncology preparation, time in the operating room, and cost of lymphoscintigraphy. Costs were determined by CPT code and other published estimates. Cost analysis was then performed using Treeage software, and incremental cost-effectiveness ratios (ICERs) were calculated. The measure of effectiveness was incremental survival benefit. ICER thresholds for considering LSG to be cost-effective were the value of a statistical life (VSL), ranging from $6.8 million to $8.7 million per cancer death prevented.

**Results:** Using a baseline probability of 0.93 for finding an SLN with LSG, our model estimated LSG costs were $2,783.84 with 84.7% survival. Our model then estimated the cost and survival without LSG by varying the SLN detection rate. In our model, survival was equivalent when probability of SLN detection without LSG was 0.93 (equal detection compared to LSG), but costs were lower without LSG. If detection without LSG was >0.93, not performing LSG was the dominant strategy with both higher survival and lower costs. Conversely, costs were equal when the probability of finding an SLN without LSG was 0.6 (incremental benefit of LSG = 0.33). For any SLN detection without LSG below 0.6, performing LSG was the dominant strategy, with both lower costs and higher survival. Formal cost-effectiveness analysis was then performed using ICERs for SLN detection probabilities without LSG from 0.60 to 0.93. In this range, costs were higher with LSG, but survival was also
improved. Figure 1 shows that as long as the incremental detection with LSG was at least 1.05% higher with LSG for VSL of $8.7 million or at least 1.47% higher with LSG for VSL of $6.8 million, LSG was cost-effective with ICERs below the VSL.

Conclusion: In our model, LSG is cost-effective as long as it increases detection of SLN by at least 1.05–1.47%. Comparative trials are needed to confirm that these extremely modest detection improvements are realized with this technique compared to standard SLN dissection.

2232 - Poster Session
Effect of implementing hospital level minimum-volume standards for ovarian cancer

Objectives: Survival is improved for women with ovarian cancer treated at high-volume hospitals. Given this association, minimum hospital volume standards have been proposed for some procedures. We modeled the impact of implementing minimum hospital volume standards for ovarian cancer.

Method: The National Cancer Data Base was used to identify hospitals treating women with ovarian cancer from 2005 to 2015. We estimated the number of newly diagnosed ovarian cancer patients treated by each hospital during the prior year. Multivariate models were utilized to estimate the ratio of observed-to-expected (O/E) 60-day and 1-, 2-, and 5-year mortality based on each hospital’s volume during the prior year. The mean O/E ratio of hospitals was plotted based on prior-year volume. The number of hospitals that would be restricted if minimum-volume standards were implemented was modeled.

Results: A total of 150,116 patients treated at 1,321 hospitals were identified. Increasing hospital volume was associated with decreased 60-day ($P = 0.004$), 1-year ($P < 0.001$), 2-year ($P < 0.001$), and 5-year ($P = 0.008$) mortality. In 2015, using a minimum volume cutpoint of 1 case in the prior year would eliminate 144 (13.6%) hospitals (treated 2.6% of all patients), while a cutpoint of 2 would eliminate 269 (25.5%) hospitals (treated 5.2% of all patients). The mean O/E ratios for hospitals with a prior-year volume of 1 was 1.14 for 60-day mortality, 1.06 for 1-year mortality, 1.12 for 2-year mortality, and 1.08 for 5-year mortality. Among hospitals with a prior-year volume of 1, 49.2% had an O/E ratio for 2-year mortality of >1 (indicating worse-than-expected performance), while 50.8% had an O/E ratio of <1 (indicating better-than-expected performance). The mean O/E ratios for hospitals with a prior-year volume of 2 were 1.11 for 60-day mortality, 1.09 for 1-year mortality, 1.08 for 2-year mortality, and 1.07 for 5-year mortality. Among hospitals with a prior-year volume of 2 or less, 48.9% had an O/E ratio for 2-year mortality of ≥1, while 51.1% had an O/E ratio of <1.

Conclusion: Low-volume hospitals have significantly higher-than-predicted mortality than high-volume hospitals for ovarian cancer. Implementation of minimum hospital volume standards would restrict a significant number of hospitals including many centers with better-than-predicted outcomes.

2233 - Poster Session
What are endometrial cancer patients dying from? A population-based study
[B.F. Lees, J.M. Hampton, A. Trentham-Dietz, P.A. Newcomb and R.J. Spencer. University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, University of Wisconsin, Madison, WI, USA; Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Objective: To identify the most common causes of death and potentially modifiable risk factors in endometrial cancer patients.

Method: A total of 745 women diagnosed with endometrial cancer were enrolled in a prospective population-based study from 1991 to 1994. Subjects completed structured interviews about 1 year after diagnosis that included menstrual/reproductive factors, lifestyle factors, and personal and family history of cancer. Study files were linked with the National Death Index to identify dates and causes of death through 2016. Proportional hazards regression was used to estimate HR and 95% CI for death from all causes, endometrial cancer, or circulatory disease adjusting for age and stage at diagnosis. HR were also examined according to BMI, smoking, and diabetes.
Results: Of the 745 women, 450 (60%) were deceased after a median of 19.9 years of follow-up (range 1.1–26.0 years). The two most common causes of death were circulatory disease (n = 145, 32%) and any cancer (n = 135, 30%). Endometrial cancer was the underlying cause of death for only 10% of women (n = 46). Endometrial cancer survival varied by stage at diagnosis with distant disease having lower overall survival (median 16.9 years) compared to localized disease (median 21.3 years). Obesity (BMI ≥30 vs normal 18.5–24.9 kg/m²) and diabetes at time of cancer diagnosis increased the risk of all-cause mortality (HR = 1.77, 95% CI 1.36–2.31; HR = 1.74, 95% CI 1.34–2.27) and circulatory-disease specific mortality (HR = 2.01, 95% CI 1.25–3.24; HR = 2.65, 95% CI 1.74–4.03). Risk of endometrial cancer mortality associated with obesity (HR = 1.84, 95% CI 0.83–4.05) and diabetes (HR = 0.61, 95% CI 0.22–1.75) was limited by small sample sizes. Smoking at the time of diagnosis was associated with increased risk of death from all causes (HR = 1.59, 95% CI 1.16–2.17), but not endometrial cancer (HR = 0.62, 95% CI 0.18–2.18).

Conclusion: Results from this long-term prospective study show that endometrial cancer patients are 3 times more likely to die from circulatory disease than endometrial cancer. Obesity, smoking, and diabetes increase the risk of death and are potentially modifiable. Oncology practices should incorporate counseling regarding these factors into survivorship care as risk of death from endometrial cancer is relatively low in this population.

2234 - Poster Session
Implementation of a sentinel lymph node mapping algorithm for endometrial cancer: Surgical outcomes and hospital charges
K.I. Stewart, J. Eska, G. Chisholm, A. Abraham, N.D. Fleming, M. Frumovitz, L.A. Meyer, S.N. Westin, T.A. Aloia and P.T. Soliman. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: At the completion of validating our sentinel lymph node (SLN) mapping procedure in endometrial cancer through a prospective trial (2013–2016), our institution implemented an SLN mapping algorithm. The purpose of this study was to compare operative times, surgical outcomes, resource utilization, and hospital charges before and after the implementation of a SLN algorithm.

Method: All patients with biopsy-proven, clinical stage I endometrial cancer who underwent surgery were identified pre-(2012) and post-(2017) implementation of the SLN algorithm. Patients were excluded if other procedures were performed at the time of surgery or if SLN mapping was performed in the pre-algorithm group. Clinical data were summarized and compared between groups. Total hospital charges, including both hospital and professional charges, incurred on the day of surgery were extracted from the hospital financial system for each patient, and all charges were adjusted to 2017 U.S. dollars.

Results: A total of 203 patients were included: 70 patients in 2012 and 133 patients in 2017. There was no difference in median age (P = 0.21), BMI (P = 0.45), and stage (P = 0.43). In 2012, 39/70 (54.9%) underwent lymphadenectomy based on frozen section. In 2017, 120/133 (90.2%) underwent SLN mapping alone and 18/133 (13.5%) underwent SLN mapping followed by lymphadenectomy. The use of minimally invasive surgery was similar (87.1% vs 90.2%, P = 0.33). Median estimated blood loss was not significantly different between groups (145 vs 209, P = 0.88). There was a significant decrease in both operative time (210 vs 171 minutes, P = 0.0051) and utilization of intraoperative frozen section (61.4% vs 15%, P < 0.0001) with implementation of the SLN algorithm. No significant differences were noted in intraoperative (P = 0.10) or 30-day postoperative complication rates (P = 0.85). Median total hospital charges decreased by $1,841 in 2017 compared to 2012 (P = 0.89).

Conclusion: Implementation of an SLN algorithm resulted in a decrease in both operative time and the utilization of intraoperative frozen section. There was no difference in total hospital charges and no change in surgical morbidity.

2235 - Poster Session
Low rates of cascade genetic testing among families with hereditary gynecologic cancer: An opportunity for improvement in cancer prevention

Objective: Testing relatives of patients at risk for hereditary breast and ovarian cancer (HBOC) or Lynch syndrome (LS) represents a substantial opportunity for cancer prevention, but rates of cascade testing are not well described. We aim to define rates of cascade genetic testing in families with HBOC or LS and assess instruments designed to increase these rates.
**Method:** We identified patients at a single academic institution who underwent genetic counseling and testing with results classifying them with HBOC or LS between 2011 and 2016. We surveyed these patients to assess rates of result disclosure and subsequent testing among family members, and to clarify perceptions of available resources. Medical records and pedigrees from genetic counseling appointments were used to determine cancer status and numbers of total and first-degree relatives of each participant.

**Results:** Of the 104 patients consented, 54 (52%) completed the survey at an average time point of 37 (±20) months after receiving genetic testing results. Participants were 95% Caucasian (5% African American) with a mean age of 54 years (±14). Most (83%) admitted to having good (54%) or very good (29%) strength of communication with family, and 86% felt very (43%) or extremely (43%) comfortable sharing health information. Twenty-eight (52%) had a diagnosis of cancer: 46% ovarian, 43% uterine, and 11% colon representing all stages, grades, and recurrence status. Of all respondents, 39% of any relative and 84% of first-degree relatives were informed of genetic testing results, with 11% of any relative and 37% of first-degree relatives actually undergoing genetic testing themselves. The rate of any relative tested was lower among patients with cancer than without (8% vs 14%, \( P = 0.038 \)). There was no significant preference among educational materials (website, video, brochure, counseling letter) aimed to improve level of understanding or assistance in disclosing results to family.

**Conclusion:** Disclosure rates are high among patients with HBOC or LS who undergo genetic counseling, but cascade testing rates are much lower, indicating barriers other than family communication, especially among those with a cancer diagnosis. Further studies are necessary to clarify barriers and improve rates of cascade genetic testing for high-risk family members.

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**2238 - Poster Session**

**Quality of life in women with BRCA mutations**

B. Powell\(^a\), A. Alabaster\(^b\), M.A. Armstrong\(^b\), N. Stoller\(^c\), T.R. Raine-Bennett\(^b\) and A. Le\(^d\), \(^a\)Kaiser Permanente Northern California, San Francisco, CA, USA, \(^b\)Kaiser Permanente Northern California Division of Research, Oakland, CA, USA, \(^c\)Kaiser Permanente Northern California, Oakland, CA, USA, \(^d\)Kaiser Permanente San Francisco, San Francisco, CA, USA

**Objective:** To measure the impact of prophylactic salpingo-oophorectomy on quality of life and menopausal symptoms in women with BRCA mutations.

**Method:** Women, age 40 years and older, with BRCA mutations identified in a large California health care system were invited to participate and complete a questionnaire including validated measures of quality of life. Responses on the Impact of Events Scale, PD-8 depression scale, sexual activity questionnaire, and cancer worry scale were compared between those with intact ovaries and those who had undergone pre- or postmenopausal oophorectomy. Categorical variables were compared using a \( \chi^2 \) test. Continuous variables were compared using a Kruskal-Wallis test.

**Results:** Of the 240 women in the final cohort, 21 women had intact ovaries (median age 53 years), and 219 had undergone oophorectomy (median age 57). Comparing those with intact ovaries to those with oophorectomy, the median score on menopausal symptoms was 14 versus 23 (\( P = 0.02 \)); the depression score 2 versus 3 (\( P = 0.26 \)); and cancer worry score 5 versus 4 (\( P < 0.0001 \)), respectively. There was no difference in the number who were sexually active (52.4% vs 49.5%, \( P = 0.8 \)), nor significant difference in sexual pleasure or discomfort. Comparing women who underwent oophorectomy before menopause (\( n = 114 \), median age 51 years) versus after menopause (\( n = 105 \), median age 63 years), scores for premenopausal group on the menopausal symptoms checklist were higher (26 versus 19, \( P = 0.04 \)) and depression (4 vs 2, \( P = 0.0006 \)), and similar for cancer worry. More women with premenopausal oophorectomy were sexually active (56.3% vs 42.0%, \( P = 0.04 \)) but had similar sexual pleasure and discomfort scores.

**Conclusion:** As expected, women with BRCA mutations and intact ovaries had fewer menopausal symptoms than those who had undergone oophorectomy but also reported more cancer worry. Women who were premenopausal at oophorectomy were more sexually active but had more menopausal symptoms and depression than those who underwent oophorectomy after menopause. Health providers should be attentive to the quality of life changes that women with BRCA mutations may experience as a result of oophorectomy.

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**2239 - Poster Session**

**Risk of cardiovascular disease in women with BRCA1 and BRCA2 mutations**

B. Powell\(^a\), A. Alabaster\(^c\), M.A. Armstrong\(^c\), N. Stoller\(^d\) and T.R. Raine-Bennett\(^c\), \(^a\)Kaiser Permanente Northern California Gynecologic Oncology Program, San Francisco, CA, USA, \(^b\)Kaiser Permanente San Francisco Medical Center, San Francisco, CA, USA

**Objective:** To measure the impact of prophylactic salpingo-oophorectomy on quality of life and menopausal symptoms in women with BRCA mutations.

**Method:** Women, age 40 years and older, with BRCA mutations identified in a large California health care system were invited to participate and complete a questionnaire including validated measures of quality of life. Responses on the Impact of Events Scale, PD-8 depression scale, sexual activity questionnaire, and cancer worry scale were compared between those with intact ovaries and those who had undergone pre- or postmenopausal oophorectomy. Categorical variables were compared using a \( \chi^2 \) test. Continuous variables were compared using a Kruskal-Wallis test.

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**Conclusion:** As expected, women with BRCA mutations and intact ovaries had fewer menopausal symptoms than those who had undergone oophorectomy but also reported more cancer worry. Women who were premenopausal at oophorectomy were more sexually active but had more menopausal symptoms and depression than those who underwent oophorectomy after menopause. Health providers should be attentive to the quality of life changes that women with BRCA mutations may experience as a result of oophorectomy.
USA, \textit{\textsuperscript{c}Kaiser Permanente Northern California Division of Research, Oakland, CA, USA, \textsuperscript{d}Kaiser Permanente Northern California, Oakland, CA, USA}

\textbf{Objective}: To estimate the prevalence of cardiovascular disease risk factors and endpoints in women with \textit{BRCA} mutations.

\textbf{Method}: Women, age 40 years and older, with \textit{BRCA} mutations identified in a large California health care system completed a questionnaire and underwent a lipid and fasting glucose panel. Bivariate analysis of clinical and demographic factors was performed. The Atherosclerotic Cardiovascular Disease (ASCVD) calculator was used to predict 10-year risk of a cardiovascular event.

\textbf{Results}: Of the 233 women, 19 women had intact ovaries (median age 56.0 years), and 214 had undergone risk-reducing salpingo-oophorectomy (RRSO). There were no significant findings for women with intact ovaries. Among the 108 women with RRSO younger than 50 years (median age 51.0 years), compared to the 106 women who had RRSO at or over age 50 years (median age 63.5 years), 6.5\% versus 10.4\% reported diabetes ($P = 0.30$); 23.2\% versus 28.3\% had elevated fasting blood glucose ($P = 0.39$); 21.3\% versus 34.0\% reported hypertension ($P = 0.04$) with median systolic blood pressure of 118 mm Hg versus 125.5 mm Hg ($P < 0.009$); 25\% versus 32\% reported hyperlipidemia ($P = 0.40$); and 42\% versus 49\% had any abnormal lipid test ($P = 0.28$). More women who underwent RRSO younger than 50 years had lower ASCVD risk scores than older women (1\% vs 5\%, $P < 0.001$). An elevated 10-year ASCVD risk of more than 10\% (high risk) was seen in 6.1\% versus 24.8\%, respectively ($P = 0.0001$). See Table 1.

\textbf{Conclusion}: Women who underwent RRSO at age 50 years and over had higher ASCVD 10-year risk than women who underwent RRSO at younger ages, most likely owing to older age at study entry. The ASCVD risks for women with \textit{BRCA} mutation who had RRSO did not suggest increased risk associated with being a \textit{BRCA} mutation carrier or cancer treatments. The ASCVD risk for mutation carriers in our cohort undergoing RRSO under, at, and over age 50 years is consistent with the ASCVD risk observed in women in the U.S. population.
Objective: Pelvic exenteration (EXT) is often the only potentially curative option for women with recurrent malignancies, but concerns about long-term effects of this ultra-radical procedure exist. This prospective study aimed to evaluate quality of life (QOL) in patients after EXT.
Method: This prospective, Institutional Review Board-approved study opened in January 2006. Patients with recurrent gynecologic cancers scheduled for EXT were eligible. Enrolled patients were interviewed pre-EXT, at 3, 6, and 12 months post-EXT, and annually until year 5, using 17 QOL measures. This study focused on 2 measures: the European Organization for Research and Treatment of Cancer QOL Core Questionnaire (QLQ-C30), and the Female Sexual Function Index (FSFI).

Results: Forty-five patients were enrolled. Median age was 58 years (range 28–80 years). Primary cancer sites were cervix, 16 (36%); uterine corpus, 11 (24%); vagina, 9 (20%); vulva, 8 (18%); and ovary, 1 (2%). Type of EXT was total, 24 (53%); anterior, 19 (42%); and posterior, 2 (4%). Twenty-six (61%) had a continent urinary diversion, while 19 patients (42%) had vaginal reconstruction. Median overall survival was 87.7 months (range 10.5–130.5 months) with 18 patients (40%) dying of disease during follow-up (median follow-up 56.3 months). The number of completed questionnaires decreased to 31% (n = 14) at year 5. There was no significant change from baseline at any of the time points for the QLQ-C30 total score. However, of the 15 QLQ-C30 domains, 3 had significant variation. Physical functioning decreased from baseline at 3–24 months (P < 0.001), while emotional functioning and sleep improved at 3 months (P = 0.006 and P = 0.017, respectively) and persisted for 5 years. There was no significant change from baseline at any time point for the FSFI; however, 91% of patients had clinically significant sexual dysfunction (SD) at baseline, and this high rate persisted for 5 years. Patients with vaginal reconstruction had better FSFI total scores at 36 months, compared to those without.

Conclusion: Emotional functioning and sleep improved significantly and permanently after 3 months, while total QLQ-C30 scores did not differ even 5 years post-EXT. Almost all patients had SD at baseline, although patients with vaginal reconstruction had improved FSFI total scores at 36 months. These data highlight the impact of EXT on QOL and can aid in preoperative counseling and operative planning.
Objective: Adjuvant hysterectomy following primary chemoradiation for bulky early-stage cervical cancer has been shown to decrease local relapse rate. With the increase of minimally invasive surgery (MIS) in gynecologic oncology, studies are needed to characterize its role in completion hysterectomy. The objective of this study is to compare complications and recurrence rates between MIS and open adjuvant hysterectomy following chemoradiation for FIGO stage IB2 and IIA2 cervical cancer.

Method: Following Institutional Review Board approval, patients were identified at a single, safety net institution who had undergone adjuvant hysterectomy following chemoradiation for FIGO stage IB2 and IIA2 cervical cancer from August 2006 to December 2017. Medical records were retrospectively reviewed to extract demographic data, cancer treatment, surgical details, complications, and follow-up. Descriptive statistics were used, and proportions were compared with the X² test.

Results: Fifty-four patients met inclusion criteria for the study. Twelve patients (22.2%) had 23 total complications attributable to the hysterectomy with a median follow-up time of 56.2 months (range 0.1–143.4 months). There were 25 (46.3%) open versus 29 (53.7%) MIS hysterectomies performed. The majority, 49 (90.7%), of the adjuvant hysterectomies were extrafascial with only 5 (9.3%) radical or modified radical hysterectomies. There was an overall complication rate of 42.6% for ≥ grade 2 complications (Table 1). The number of patients with complications in the MIS group was 8 (27.6%) compared to 4 (16%) in the open surgery group (OR = 2.0, 95% CI 0.5–7.7, P = 0.312). There were 9 vaginal cuff defects, dehiscences, and fistulas in the MIS group compared to 3 in the open group, resulting in a complication rate for these late grade 3 complications of 31.0% and 12.0%, respectively (OR = 3.3, 95% CI 0.8–13.9, P = 0.104). There were 3 recurrences in each group yielding a recurrence rate of 12.0% for patients undergoing open surgery and 10.3% for patients undergoing MIS (P = 0.844).

Conclusion: While not statistically significant, the rate of vaginal cuff dehiscence in women undergoing MIS was sizeably higher, as was the likelihood of requiring operative intervention. This suggests that an MIS approach might not be ideal in women who have received external radiation and brachytherapy.

Table 1. Complications for open versus MIS adjuvant hysterectomy.

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Total complications</th>
<th>Open surgery (n=25)</th>
<th>MIS (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Port site hematoma</td>
<td>1 (4.3%)</td>
<td>0 (0%)</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Wound seroma</td>
<td>1 (4.3%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Acute blood loss anemia requiring transfusion</td>
<td>4 (17.4%)</td>
<td>2 (8%)</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>Ureteral injury</td>
<td>1 (4.7%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>UTI</td>
<td>2 (8.7%)</td>
<td>1 (4%)</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2 (8.7%)</td>
<td>0 (0%)</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>Vaginal cuff necrosis/defect</td>
<td>6 (26.0%)</td>
<td>2 (8%)</td>
<td>4 (13.8%)</td>
</tr>
<tr>
<td>Vaginal cuff dehiscence requiring repair in OR</td>
<td>3 (13.0%)</td>
<td>0 (0%)</td>
<td>3 (10.3%)</td>
</tr>
<tr>
<td>Fistula (2 vesicovaginal, 1 rectovaginal)</td>
<td>3 (13.0%)</td>
<td>1 (4%)</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>No. patients with any complication</td>
<td>12 (22.2%)</td>
<td>4 (16.0%)</td>
<td>8 (27.6%)</td>
</tr>
<tr>
<td>Total number of complications</td>
<td>23 (42.6%)</td>
<td>8 (32.0%)</td>
<td>15 (51.7%)</td>
</tr>
</tbody>
</table>

2243 - Poster Session
The budget impact of introducing pembrolizumab to the formulary in the United States for previously treated PD-L1 positive advanced cervical cancer
Objective: To assess the potential budget impact of adding pembrolizumab to the formulary of a U.S. health plan for the treatment of PD-L1 positive advanced cervical cancer with disease progression on or after platinum-containing chemotherapy in a setting for the United States.

Method: The budget impact was estimated using a model that incorporated the use of a PD-L1 immunohistochemistry test and the subsequent treatment with pembrolizumab. The model calculates the difference between the current expenditure in the budget and the anticipated costs when pembrolizumab was added to the formulary. Patient estimates were based on published data sources for the prevalence, incidence, and survival rates in this patient population. Current expenditure was estimated from real-world treatment utilization data in this population. Costs incorporated in the model included systemic anticancer drug acquisition costs, drug administration cost, drug-monitoring cost, and adverse event costs and were calculated over a 5-year time horizon.

Results: The model estimated that there were 1,236 patients eligible for treatment with pembrolizumab, based on the approved U.S. label. The budget impact showed that the introduction of pembrolizumab was anticipated to be cost saving in each year evaluated in the model except for year 2 in both the second- and third-line treatment settings. An incremental cost of $71 and $221 per patient per year in second-line and third-line patients, respectively, was estimated. When the budget impact was mapped over 5-year study period, pembrolizumab was projected to be associated with a cumulative cost saving of $2,169,436 and $600,518 for the second-line and third-line patient populations, respectively.

Conclusion: Pembrolizumab was projected to offer a cost-saving treatment for patients who have previously failed cervical cancer therapy over a 5-year period.

2244 - Poster Session
Does chemotherapy or radiation benefit surgical stage I uterine carcinosarcoma patients? An analysis of 3,447 patients.

S. Chow, J.K. Chan, D.S. Kapp, A.K. Mann, W.S. Liou and C.I. Liao. aKaiser Permanente Santa Clara, Santa Clara, CA, USA, bCalifornia Pacific Medical Center, San Francisco, CA, USA, cStanford University School of Medicine, Stanford, CA, USA, dPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, eKaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

Objective: To determine the role of chemotherapy and radiation on the outcomes of surgically staged I uterine carcinosarcoma patients.

Method: Data were obtained from the National Cancer Data Base (NCDB) from 2004 to 2014. χ² test, Cox regression, and Kaplan-Meier analyses were used.

Results: Of 3,447 patients, the mean age was 66 (range 19–90) years. A total of 2,581 (74.9%), 696 (20.2%), 84 (2.4%), and 86 (2.5%) were white, black, Asian, and other/unknown, respectively. In the overall group, 100% of patients underwent lymph node dissection, and 20.3% had omentectomy with their surgical staging. According to the American Joint Committee on Cancer 7th edition for surgical staging, 2,179 (63.2%) were stage IA; 1,018 (29.5%) were stage IB; and 250 (7.3%) were undefined stage I. A total of 1,213 (35.2%) underwent no adjuvant treatment; 698 (20.2%) chemotherapy only (CT); 616 (17.9%) radiation only (RT); and 920 (26.7%) both chemotherapy and radiation (CT+RT) after surgery, respectively. In stage IA patients, the 5-year OS was 68.1%. The OS for no treatment was 60.7% versus 71.2% for CT (P = 0.002), 64.6% for RT (P = 0.247), and 79.6% for CT+RT (P < 0.001). For stage IB, the OS was 56.5%. The OS for no treatment was 43.2% compared to 64.1% for CT (P = 0.015) and 51.3% for RT (P = 0.115), and CT+RT was 68.9% (P < 0.001). On subset analysis of endometrium involvement only, the OS for no treatment was 76.2%; furthermore, CT, RT, and CT+RT were not associated with an improved outcome with OS at 69.6% (P = 0.447), 73.4% (P = 0.577), and 72.9% (P = 0.821), respectively. On multivariate analysis, older age (HR = 1.03, 95% CI 1.03–1.04, P < 0.001), black race (HR = 1.58, 95% CI 1.32–1.90, P < 0.001), higher substage (HR = 1.48, 95% CI 1.27–1.72, P < 0.001), and lymphovascular invasion (HR = 1.38, 95% CI 1.14–1.68, P = 0.001) were independent predictors of worse survival. Adjuvant CT (HR = 0.64, 95% CI 0.52–0.79, P < 0.001) and CT+RT (HR = 0.52, 95% CI 0.42–0.64, P < 0.001) were predictors for improved survival.

Conclusion: Our data suggest that adjuvant chemotherapy and radiation is associated with an overall survival benefit in stage I uterine carcinosarcoma. However, in the subset of those without myoinvasion, adjuvant therapy did not have any benefit.
A cost-effectiveness analysis of universal genetic testing for common hereditary cancer mutations in women compared with family history-based testing

A.B. Drummey, J. Brown, L. Drury, L. Amacker-North, K. Warsinske, K. Tyrie and R.W. Naumann. Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA

Objective: Identifying patients who would benefit from hereditary cancer genetic testing by family history alone can miss a significant portion of both BRCA and Lynch mutation carriers. The purpose of this study is to determine whether population-based testing with a common hereditary cancer panel in all women regardless of family history is a cost-effective cancer prevention strategy.

Method: A Markov decision-analytic model was constructed to estimate life expectancy with universal testing versus family history-based testing. The model was run from age 20 to 85 years. Testing was performed at age 35 years. The option of risk-reducing surgery was factored in for ovarian, breast, and uterine cancer. The model considered estimates of cancer development and death based on current screening guidelines for known and unknown BRCA and Lynch mutation carriers as well as noncompliance with recommendations for genetic testing and risk-reducing surgery. In addition, known rates of tubal ligation, hysterectomy, and bilateral salpingo-oophorectomy for nonmalignant conditions were taken into account in both groups. The model calculated the development of and mortality from breast, ovarian, colon, and uterine cancer.

Results: The improvement in overall life expectancy with universal genetic screening compared with testing based on family history is 7.10 life-years per 100,000 persons screened, assuming a pathogenic BRCA mutation rate of 0.67% and Lynch syndrome-related mutation rate of 0.23%. Universal genetic screening would save 52.8 deaths from cancer per 100,000 women screened (8.6 breast, 3.7 colon, 25.6 ovary, and 14.8 uterine). Testing would reduce the overall number of deaths from ovarian cancer by 3%. Based on the real-world cost of the common hereditary cancer panel of $250 per screen, the calculated benefit would be $35,162 per life-year saved by universal genetic testing. When considering quality-of-life utility adjustments for cancer, the undiscounted benefit of universal testing was $20,725 per quality-adjusted life-year.

Conclusion: Universal genetic testing appears to be an effective cancer prevention strategy. At current costs, universal genetic testing appears to be within the range of acceptable cost-effectiveness under real-world conditions. The benefit of screening is mainly due to the prevention of deaths from gynecologic cancers.

Maintaining adherence rates for genetic testing in an era with fewer in-office counselors


Objective: National guidelines promote universal genetic testing for all women with epithelial ovarian cancer (EOC) to allow for targeted therapies and hereditary cancer prevention. Traditional in-person genetic counselors may help reach this guideline but are in limited supply. We aimed to assess whether barriers to universal testing differed before and after a dedicated genetic counselor was available in our practice.

Method: We identified women with EOC presenting for new patient visits at a large academic institution between January 2015 and March 2018. A genetic counselor was present during the study period up to April 2017; after this, point-of-care genetic testing was initiated by gynecologic oncologists. Testing and counseling status, demographics, and health maintenance compliance were determined from the medical record. Continuous variables were compared using t tests or Mann-Whitney U test, and categorical variables were compared using the χ² or Fisher exact test as appropriate.

Results: Among the 225 patients identified with adequate follow-up data, 168 (75%) underwent genetic testing, and 135 (60%) underwent genetic counseling. Most patients were Caucasian (92%) with a diagnosis of high-grade serous carcinoma (87%) and advanced stage (89%). After departure of an embedded genetic counselor, the test rate was similar at 75% to 74% (P = 0.93), but the rate of genetic counseling decreased from 63% to 26% (P < 0.01). Patients who did not receive testing were more likely to be older (71 ± 11.9 years vs 67 ± 10.6 years, P = 0.05) and noncompliant (NC) with other health screening (28%
Conclusion: While genetic testing rates remained unchanged, the responsibility of genetic counseling is falling on gynecologic oncologists in an era when genetic counselors are in limited supply. Point-of-care testing is an adequate service delivery model to maintain high rates of testing despite less traditional genetic counseling. Awareness of barriers such as insurance status and noncompliance with other health screening may aid in adherence to national guidelines. Future studies should investigate efficient strategies to aid gynecologic oncologists with genetic counseling.

2247 - Poster Session
Maintenance therapy utilization in platinum-sensitive recurrent epithelial ovarian cancer: A 'real-world' analysis

H.A. Moss, L.J. Havrilesky, N.D. Kauff, and A.A. Secord. *Duke University Medical Center, Durham, NC, USA, ¹Duke University School of Medicine, Durham, NC, USA, ²Duke Cancer Institute, Durham, NC, USA

Objective: To evaluate maintenance therapy use for women with platinum-sensitive recurrent ovarian cancer (PSROC) and to model survival outcomes using real-world claims data.

Method: A retrospective study including patients with PSROC receiving platinum-based chemotherapy between March 2017 and August 2018 was conducted using the Flatiron Health Database. This longitudinal, demographically and geographically diverse database derived from electronic health records contains data covering more than 2 million oncology patients. Patients were excluded if chemotherapy regimens included less than 4 or more than 8 cycles. Information regarding somatic or germline BRCA mutations and homologous recombination deficiency (HRD) was obtained. A decision analysis was performed comparing achievable PFS in months between two scenarios: (1) real-world maintenance therapy utilization, and (2) ideal utilization of maintenance therapies.

Results: A total of 825 patients with recurrent OC were identified; 248 were treated with platinum-based therapy at recurrence, and 113 completed 4–8 cycles of chemotherapy. Seventy-nine patients (69.9%) had BRCA testing, and 4 patients (3.54%) had HRD testing. Nineteen (16.8%) had germline or somatic BRCA mutations (tBRCA); 60 (53.1%) had an intact wildtype BRCA gene; and 34 (30.1%) were unknown. Following chemotherapy, of patients with tBRCA mutations, 36.8% received a PARP inhibitor (PARPi); 15.8% received bevacizumab (B); and 57.4% were observed. Of patients with wtBRCA, 30% received a PARPi; 21.7% received B; and 48.3% were observed. Maintenance therapy (MT) was more common in younger patients and in those with prior optimal cytoreductive surgery (*P* < 0.05). BRCA or HRD status was not significantly associated with MT. Ideal MT use would have resulted in a 2-month PFS improvement in the entire PSROC cohort. Among patients with BRCA mutations or HRD-positive tumors, ideal use of maintenance therapy would have increased PFS by 8 months.

Conclusion: While many patients with PSROC are receiving maintenance therapy, treatment choice does not seem to be determined by BRCA or HRD status. The majority of patients with BRCA mutations are not receiving maintenance PARPi. The real-world data highlight the need to educate providers regarding the importance of genetic testing in selection of maintenance therapy for optimization of clinical outcomes.

2248 - Poster Session
Adjuvant chemotherapy and radiation improve survival of surgical stage I uterine clear cell carcinoma patients

S. Chowa, J.K. Chana, L. Delicia, D.S. Kappp, A.K. Mannaa and C.I. Liaoa. ¹Kaiser Permanente Santa Clara, Santa Clara, CA, USA, ²California Pacific Medical Center, San Francisco, CA, USA, ³California Pacific & Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA, ⁴Stanford University School of Medicine, Stanford, CA, USA, ⁵Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, ⁶Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

Objective: To determine the role of chemotherapy and radiation in the survival of patients with stage I uterine clear cell carcinoma.

Method: Data from 2004 to 2014 were extracted from the National Cancer Data Base (NCDB). Clinical-pathologic features and survival were analyzed using χ² test, Cox regression, and Kaplan-Meier methods.
Results: Of 1,266 women diagnosed with stage I uterine clear cell carcinoma, the mean age of diagnosis was 67 (range 31 to 90) years. Whites, blacks, Asians, and other/unknown accounted for 1,000 (79%), 197 (15.6%), 47 (3.7%), and 22 (1.7%), respectively. A total of 1,001 (79%) were stage IA; 177 (14%) were stage IB; and 88 (6.9%) were undefined stage I. Overall, 585 (46.2%) received no adjuvant treatment; 268 (21.2%) received only adjuvant radiation (RT); 191 (15.1%) received only adjuvant chemotherapy (CT); and 222 (17.5%) received both chemotherapy and radiation therapy (CT+RT). In stage IA disease, the 5-year OS was 81.0%. CT, RT, and CT+RT were associated with an improved 5-year OS compared to no further treatment with corresponding 5-year OS of 87.3% with CT (P = 0.053), 82.7% with RT (P = 0.103), and 89.3% with CT+RT (P = 0.002) compared to 76.4% with no adjuvant treatment. For stage IB, 5-year OS was 70.4%. The 5-year OS for no treatment was 61.2% versus 75.0% for CT (P = 0.371), 79.4% for RT (P = 0.046), and 69.0% for CT+RT (P = 0.408). On subset analysis of those with disease limited to the endometrium only, the 5-year OS for no treatment was 78.1%. CT, RT, and CT+RT were not associated with an improved outcome with 5-year OS at 88.9% (P = 0.319), 888% (P = 0.135), and 100% (P = 0.126), respectively. On multivariate analysis, older age (HR = 1.06, 95% CI 1.03–1.08, P < 0.001), Blacks (HR = 1.66, 95% CI 1.07–2.59, P = 0.024), higher substage (HR = 1.58, 95% CI 1.03–2.41, P = 0.034), Charlson/Deyo score 3 or more (HR = 6.48, 95% CI 1.84–22.92, P = 0.004), and positive washings (HR = 2.43, 95% CI 1.16–5.13, P = 0.019) predicted worse survival. Adjuvant CT (HR = 0.41, 95% CI 0.19–0.88, P = 0.023) and CT+RT (HR = 0.37, 95% CI 0.16–0.84, P = 0.017).

Conclusion: Adjuvant chemotherapy and radiation were associated with improved survival in stage I uterine clear cell carcinoma.

2249 - Poster Session
High-intermediate risk endometrial adenocarcinoma: A subset of early stage endometrial cancer patients who benefit from adjuvant therapy
B.M. Roane,a M.Z. Kamala, T. Rushtonb, D.A. Barringtona, G. McGwinb and R.C. Arenda. aUniversity of Alabama at Birmingham, Birmingham, AL, USA, bUniversity of Alabama at Birmingham, Birmingham, AL, USA

Objective: There is a group of early-stage endometrial cancer patients classified as high intermediate risk (HIR) because of their increased risk of recurrence and lower OS. The use of adjuvant therapy in these patients is debated as it does not improve OS despite reduced local recurrence. Our goal was to define a subset of HIR patients with poorer prognosis and analyze benefits in the use of adjuvant therapy in these patients.

Method: A total of 286 HIR endometrial cancer patients were identified. Patients included had stage I or stage II endometrioid adenocarcinoma and met criteria based on age, grade, and depth of invasion defined in GOG 99. Within this group, high-intermediate risk (HH-IR) patients were defined based on selected criteria from PORTEC-3: stage II or stage I with grade 3 tumors and LVI and/or deep invasion. Comparisons were made between HIR patients, HH-IR patients who received adjuvant therapy, and those who did not. χ² test was used for comparisons between groups. Overall survival was compared using log rank test.

Results: Seventy-nine patients met criteria for the HH-IR group. Average age for all patients was 71.6 years with an average BMI of 31.5. Out of the 79 patients in the HH-IR group, 39 received adjuvant therapy, while only 12% of HIR patients received adjuvant therapy. There was no difference in recurrence rate of HIR patients based on adjuvant therapy use (40% vs 38%), but there was a significantly higher rate of recurrence in HH-IR patients compared to HIR patients (39% vs 12%, P < 0.001). However, mean OS of HH-IR patients receiving adjuvant therapy was improved compared to those who did not (67 vs 43 months, P < 0.001) and was similar to the OS in HIR patients (mean of 64 months). The distribution of sites of recurrence was highest at the vaginal cuff for HH-IR patients who did not receive adjuvant therapy (63%) and outside the pelvis in those patients who did undergo adjuvant treatment (60%).

Conclusion: Adjuvant therapy use in HIR endometrial cancer patients does not improve OS, despite reduction in local recurrence. Here we identify HH-IR patients with a higher risk of recurrence, but improved OS with the use of adjuvant therapy. Future investigation in this group, including molecular testing, will identify the patients who would benefit the most from adjuvant therapy.

2250 - Poster Session
Validation of the laparoscopic hysterectomy readmission score among gynecologic oncology patients undergoing robotic-assisted hysterectomy
M.D.S. Lightfoota, M.H. Vetterm, P. Paetowb, K. Forsythe and F.J. Backesa. aThe Ohio State University, James Cancer Hospital,
Objective: Same-day discharge (SDD) following minimally invasive hysterectomy has been increasingly adopted in gynecologic oncology. It offers increased patient comfort and satisfaction, decreased cost, and decreased hospital-related complications. The Laparoscopic Hysterectomy Readmission Score (LHRS) was developed based on data from the National Surgery Quality Improvement Program. Our objective was to validate the LHRS in adequately identifying patients at risk of readmission within our patient population.

Method: This was a single-institution retrospective study of patients who underwent robotic hysterectomy by a gynecologic oncologist between February and July 2018. The LHRS proposes 1 point each for diabetes, chronic obstructive pulmonary disease, disseminated cancer, chronic steroid use, bleeding disorder, and length of surgery of 2 hours or longer and 2 points for any postoperative complication prior to discharge. An LHRS was calculated for each patient. Statistical analyses were done using Fisher exact and two-sample t tests.

Results: A total of 197 patients were included; 49 (25%) patients had SDD, and 138 (70%) were discharged on postoperative day (POD) 1. The overall readmission rate within 30 days of discharge was 3.1% (n = 6); 1 patient with SDD compared to 5 patients discharged on POD 1 (2% and 7%, respectively, \(P = 1.00\)). Of all patients, 32% had an LHRS of 0; 45%, 1; 14%, 2; 6%, 3; and 3%, 4 or greater. Readmission rates by LHRS were score 0, \(n = 1/64, 2\%\); score 1, \(n = 1/88, 1\%\); score 2, \(n = 0/28\); score 3, \(n = 2/11, 18\%\); and score 4, \(n = 2/5, 40\%\). Table 1 shows the SDD and readmission rates by LHRS. For patients with LHRS scores of 0–2, the risk of readmission was 1% versus 24% for patients with LHRS scores of 3–4 (\(P = 0.0001\)). The single patient who underwent SDD and was readmitted had an LHRS score of 3; the patients who were discharged on POD 1 and readmitted had scores of 0, 1, 3, 4, and 4.

Conclusion: Overall, the rate of readmission following minimally invasive hysterectomy was low. An LHRS of 3 or greater was significantly associated with a higher rate of readmission, indicating that a threshold of an LHRS of 3 could be used to identify patients for whom SDD may not be advisable. The LHRS provides valuable information for preoperative counseling and discharge planning for providers, patients, and hospital systems.

Table 1. Same day discharge and 30-day readmission rates by laparoscopic hysterectomy readmission score (LHRS).

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2251 - Poster Session
Surveillance testing and cancer outcomes among endometrial cancer patients with Lynch syndrome

Objective: The purpose of this study is to assess the uptake of surveillance testing and new cancer detection among women with Lynch syndrome (LS) that was identified after a new diagnosis of endometrial cancer (EC).

Method: This is a retrospective study of women with EC and genetic diagnosis of LS from an integrated California health care system. Of 2,254 women with endometrial cancer in the study period, 28 patients were identified with LS. All participants were referred to genetics after EC diagnosis because of abnormal IHC or a history suggestive of LS and received surveillance...
recommendations based on National Comprehensive Cancer Network guidelines. Descriptive statistics were used to analyze frequency of colonoscopy, urine cytology, esophagogastroduodenoscopy (EGD), prophylactic surgery, and new cancer diagnoses.

**Results:** Of the 28 women with LS identified at the time of EC diagnosis, 23 (82%) were younger than 60 years and 5 (18%) were 60 years and older. The median follow-up was 21 months. Among the 23 women younger than 60 years, 19 (83%) had at least 1 surveillance test; 18 (78%) had a colonoscopy; 8 (35%) had a colon biopsy; and 13 (57%) had an EGD. One (4%) woman had urine cytology that was abnormal and developed bladder cancer 1 year after her EC diagnosis. There was 1 woman (4%) who was diagnosed with breast cancer 2 months after her EC diagnosis. Among the 5 women 60 years and older, 5 (100%) had a colonoscopy, 3 (60%) had a colon biopsy, 23 (60%) had an EGD, and 0 (0%) had urine cytology. There were no abnormal tests or cancers detected in this age group. None of the women in our cohort elected for prophylactic surgery with a colectomy, and only 1 woman (4%) elected for ovarian conservation without an interval oophorectomy after an incidental findings of EC at time of hysterectomy. The remaining 27 women had oophorectomy at time of their initial surgery. See Table 1.

**Conclusion:** There were high rates of compliance with NCCN guideline concordant surveillance testing among women with LS subsequent to a diagnosis of EC, although there were no abnormal biopsies or new GI malignancies identified. Urine cytology screening was not routinely performed, yet 1 patient did develop bladder cancer and had testing only after becoming symptomatic. This may highlight the need for more routine urine cytology screening for LS patients who are at increased risk of urothelial malignancies.

**Table 1.** Surveillance testing, prophylactic surgery, and cancer outcomes among endometrial cancer patients with Lynch Syndrome.

<table>
<thead>
<tr>
<th>Lynch Syndrome Patients, n=28</th>
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<tr>
<td></td>
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<tr>
<td><strong>Total patients with surveillance testing</strong></td>
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<tr>
<td>Colonoscopy</td>
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<td>Colon Biopsy</td>
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<tr>
<td>EGD</td>
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<tr>
<td>Abnormal surveillance test</td>
</tr>
<tr>
<td>Prophylactic surgery (colectomy, oophorectomy)</td>
</tr>
<tr>
<td>Cancer detected</td>
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2252 - Poster Session

**Lynch syndrome in women with endometrial cancer: Comparison of universal and age-based strategies in a California healthcare system**

C.V. Salyer*, S.E. Lentz*, M. Dontsi, M.A. Armstrong*, E. Hoodfar*, M. Alvarado*, E. Landers*, M. Avila*, N.T. Nguyen* and B. Powell*. *Kaiser Permanente, Oakland, CA, USA, †Kaiser Permanente Medical Group, Southern California, Los Angeles, CA, USA, ‡Kaiser Permanente Northern California Division of Research, Oakland, CA, USA, †Kaiser Permanente, San Francisco, CA, USA, ‡Kaiser Permanente Southern California, Pasadena, CA, USA, †Cedars-Sinai Medical Center, Los Angeles, CA, USA, ‡Kaiser
Objective: The objective of this study was to compare risk factors and detection rates for Lynch syndrome (LS) between two regions of the same California health care system with different screening strategies.

Method: This is a retrospective study of all endometrial cancer (EC) cases from two regions of an integrated health care system with different IHC protocols. There were 1,557 cases from northern California (NC) where IHC testing for women younger than 60 years is recommended but nonautomated, and for women 60 years and older with clinical risk factors. There were 697 cases from southern California (SC) where IHC is universal and automated for all EC cases. Demographics, history of LS cancers, and tumor characteristics were compared, and logistic regression was used to identify risk factors for abnormal IHC and genetic testing.

Results: Among women younger than 60 years in NC, 186 (34%) had IHC testing: 52 (10%) were abnormal, and 17 (3%) were abnormal after methylation testing. Among women 60 years and older in NC, 95 (11%) had IHC testing: 23 (3%) were abnormal, and 2 (<1%) were abnormal after methylation. Among women younger than 60 years in SC, 242 (87%) had IHC testing: 54 (19%) were abnormal, and 17 (6%) were abnormal after methylation. In women 60 years and older in SC, 242 (87%) had IHC testing: 96 (26%) were abnormal, and 8 (2%) were abnormal after methylation. In a multivariate analysis, risk factors for abnormal IHC in NC were family history of LS cancers (OR = 3.5, 95% CI 1.1–11.3), diabetes (OR = 1.9, 95% CI 1.1–3.4), tumor grade >1 (OR = 2.3, 95% CI 1.2–4.1), and endometrioid histology (OR = 3.3, 95% CI 1.2–8.9). In SC, risk factors for abnormal IHC were age 60 years and older (OR = 1.6, 95% CI 1.1–2.9), personal history of LS cancer (OR = 1.8, 95% CI 1.1–2.9), family history of LS cancers (OR = 1.8, 95% CI 1.1–2.9), tumor grade >1 (OR = 1.9, 95% CI 1.2–2.8), and endometrioid histology (OR = 2.1, 95% CI 1.0–4.1). Lynch syndrome was diagnosed in a total of 28 women, 23 younger than 60 years and 5 age 60 years and older, including 16 women (3%) in NC and 7 (3%) in SC younger than 60 years (P = 0.72), and 3 women (<1%) in NC and 2 (1%) in SC 60 years and older (P = 0.63). Factors associated with LS diagnosis were younger age (age 60 years and older, OR = 0.110, 95% CI 0.0–0.23) and lower BMI (BMI ≥30, OR = 0.381, 95% CI 0.2–0.8). See Figure 1.

Conclusion: Although universal IHC screening of EC would be expected to identify more cases of LS than age-based IHC screening, no difference was found in the detection of LS in EC when comparing these strategies implemented in northern or southern California regions of the same health care system.
Objective: Opioid overprescribing is a contributing factor to the opioid epidemic. Little is known about what guides prescriber decisions regarding discharge prescription opioids. We sought to describe the opioid-prescribing practices of gynecologic oncologists for patients undergoing exploratory laparotomy.
**Method:** A retrospective cohort study of women undergoing exploratory laparotomy surgery at an academic center in 2016 was conducted. Total oral morphine equivalents (OMEs) prescribed at discharge were calculated. Clinical, demographic, and surgical factors, including enrollment on an enhanced recovery after surgery (ERAS) pathway, were evaluated for association with a discharge prescription of more than the median versus median OME using Poisson regression. Correlation between objective measure of pain (inpatient opioid use) and a subjective measure of pain (pain scores in the 24 hours prior to discharge) was evaluated using the Spearman correlation coefficient.

**Results:** A total of 177 women were included. Median OME prescribed was 450 (IQR 266–480), most commonly as 60 tablets of 5 mg oxycodone. Forty-two percent \((n = 74)\) of patients received a prescription for <450 OME, 27% \((n = 47)\) for 450 OME, and 31% \((n = 55)\) for >450 OME. Receipt of a prescription >450 versus 450 was not associated with age, BMI, race, history of chronic pain, cancer diagnosis, surgical complexity score, enrollment on ERAS, or surgeon. Patients were more likely to receive more than the median if they received an epidural \((1.79, 95\% \text{ CI } 1.10–2.93)\), a prescription for dilaudid versus oxycodone \((RR = 4.61, 95\% \text{ CI } 2.85–7.48)\) or tramadol at discharge \((2.08, 95\% \text{ CI } 1.57–2.78)\). Inpatient opioid use in the first 72 hours was not correlated with OME prescribed at discharge \((\rho = 0.012)\). Although ERAS patients had lower inpatient opioid requirements in the first 72 hours \((65.6 \text{ vs } 249.1 \text{ OME, } P < 0.0001)\), median OME prescribed was not different \((450 \text{ vs } 450, P = 0.52)\). Patient pain scores prior to discharge were not correlated with OME prescribed \((\text{Spearman correlation coefficient } = 0.08, 0.07, \text{ and } 0.04 \text{ respectively})\).

**Conclusion:** Very few clinical, surgical, or patient factors are associated with OME prescribed. Neither objective nor subjective measures of patient pain correlated with opioids prescribed, suggesting prescribing patterns are not guided by these factors. While ERAS reduced inpatient opioid use, without inclusion of algorithms to guide discharge prescribing, this did not translate to reduced opioid prescribing.

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**2254 - Poster Session**

**Characteristics associated with BRCA mutation carriers not undergoing risk-reducing salpingo-oophorectomy**

M.C. Oestreich, A. Wilhite, M. Olson and B.K. Erickson. University of Minnesota, Minneapolis, MN, USA

**Objective:** The objective of this study was to understand clinical differences between patients who undergo risk-reducing salpingo-oophorectomy (RRSO) by the National Comprehensive Cancer Network (NCCN)-recommended age and those who do not. Rates and methods of follow-up for patients who deferred surgery will also be determined.

**Method:** Institutional Review Board approval was obtained for this multisite retrospective cohort study. Inclusion criteria were women 40 years and older with a deleterious BRCA mutation between 2011 and 2017. Women were excluded if they had VUS mutations, ovarian cancer at diagnosis, incomplete records, or previous salpingo-oophorectomy. Patients were identified using ICD 9/10 codes and a regional genetic counseling database. Clinical and demographic data were collected. χ² analysis was used to compare groups.

**Results:** Of the charts reviewed, 95 (72%) patients had undergone surgery, and 37 (28%) had not. Patients who had not undergone RRSO were more likely to have no personal history of breast cancer \((68\% \text{ vs } 39\%, P = 0.003)\) and to have deferred bilateral mastectomy \((57\% \text{ vs } 20\%, P = 0.0005)\) compared to those who had surgery. Reasons for deferring surgery included desire to preserve fertility \((14\%)\), avoid menopause \((5\%)\), obtain time away from work or child care \((5\%)\), or finish breast cancer treatment \((5\%)\). No documented reason for declining surgery occurred in the remainder of patients. Of those who deferred surgery, 40% were followed by medical oncologists, 38% by primary care physicians, 16% by obstetricians/gynecologists, 3% by genetic counselors, and 3% by gynecologic oncologists. Only 41% of patients deferring RRSO ever had a consult with a gynecologic oncologist. Of those who deferred surgery, 42% were being followed every 6 months with both ultrasonography and CA-125, 40% with either CA-125 or ultrasonography, and 18% with no testing. One patient in the no-RRSO cohort \((3\%)\) was diagnosed with stage 1C ovarian cancer while undergoing serial screening with ultrasonography and CA-125.

**Conclusion:** With genetic screening becoming more prevalent, more women will be faced with the difficult decision of when to have risk-reducing surgery. This study demonstrates that despite clear guidelines, a significant number of women older than 40 with a deleterious BRCA mutation delay or decline risk-reducing surgery. There is significant room for improvement in standardization of follow-up and screening. Moreover, efforts should be made to ensure that these patients have access to surgical consultation with a gynecologic oncologist.
2255 - Poster Session

Quality of care for women with uterine cancer at US safety net hospitals

C.R. Gamblea,b, Y. Huangc, J.D. Wrighta,c,d, A.I. Tergasa, J.Y. Houa, F. Khoury Colladoa,e and C.M. St. Claira.

aNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, bWeill Cornell Medical College, New York, NY, USA, cColumbia University College of Physicians and Surgeons, New York, NY, USA, dColumbia University, New York, NY, USA, eNYP/Columbia University Medical Center, New York, NY, USA

Objective: Safety net hospitals (SNHs) play a critical role within the U.S. health care system by providing care to vulnerable patients. We sought to determine the quality of care and outcomes of patients with uterine cancer who received treatment at SNHs.

Method: The National Cancer Data Base was used to identify hospitals treating patients with uterine cancer from 2004 to 2015. Hospitals were stratified into quartiles representing the volume of uninsured/Medicaid patients. The highest quartile hospitals were defined as SNHs. Among hysterectomy patients, we examined readmission, minimally invasive surgery for stage I disease (MIS), lymph node assessment for high-risk histologies (LND), adjuvant therapy for high-risk stage I–II disease, and chemotherapy for stage III–IV disease (CT). Thirty- and 90-day mortality and 5-year OS were calculated. Marginal log Poisson regression and Cox proportional hazard models were developed for multivariate analysis accounting for hospital clustering and confounders.

Results: In the years examined, 443,680 uterine cancer patients were treated at 1,339 hospitals. The median percentage of women who were uninsured/Medicaid at SNHs was 15.8%. Among 324,918 patients who underwent hysterectomy, patients at SNHs were more likely to be black/Hispanic and low income and to have >2 comorbid conditions, aggressive histologies, and advanced disease. They less frequently underwent MIS (63.1% vs 75.8%, aRR = 0.87, 95% CI 0.81–0.93) or LND (78.3% vs 83.0%, aRR = 0.97, 95% CI 0.93–0.99), but more frequently received adjuvant therapy (67.5% vs 64.7%, aRR = 1.08, 95% CI 1.01–1.16) and CT (74.5% vs 73.5%, aRR = 1.06, 95% CI 1.02–1.10). After adjusting for patient demographics, comorbid conditions, cancer characteristics, and treatment, there was no difference between SNHs and non-SNHs in readmission rate (aRR = 1.19, 95% CI 0.92–1.53), 30-day mortality (aRR = 1.05, 95% CI 0.89–1.24), 90-day mortality (aRR = 1.01, 95% CI 0.90–1.15), and long-term overall mortality at any stage. See Figure 1.

Conclusion: SNHs care for socially disadvantaged, medically complex patients with aggressive disease. These patients are less likely to receive MIS and LND, more likely to receive adjuvant treatment, and have similar all-cause mortality rates.

Fig. 1.
**Objective:** The objective of this study was to design and validate a model to predict risk of venous thromboembolism in patients undergoing primary treatment for ovarian cancer.

**Method:** A retrospective cohort was performed from January 2013 to September 2017. Patients with advanced disease were triaged by laparoscopy to determine resectability at tumor-reductive surgery. Patients who were medically inoperable or had metastatic disease received neoadjuvant chemotherapy (NACT). Patients who underwent primary debulking surgery (PDS) or interval surgery received postoperative thromboprophylaxis with enoxaparin for 28 days. VTE was evaluated from the first cycle of NACT or after PDS until the end of adjuvant chemotherapy (carboplatin, paclitaxel, and/or bevacizumab). Clinical and demographic data were correlated with occurrence of VTE. Prognostic factors were compared by using χ² tests or Fisher exact test ($P < 0.05$). A model was created to score the predicted probabilities of VTE. We split our data into training (~70%) and validation (~30%) sets in order to build and validate the prediction model. We used bootstrap cross-validation methods to assess the calibration of our final model.

**Results:** A total of 699 patients were included; 452 patients underwent NACT, and 231 underwent PDS. Seventy-nine percent had serous histology. A total of 53 (8.0%, 95% CI 6.0–10.3) patients developed VTE, 46 and 7 in the NACT and PDS groups, respectively. The proportion of patients with VTE was higher in the NACT group (11.0%, 95% CI 8.2–14.4, $P < 0.001$) versus the PDS group (3.1%, 95% CI 1.2–6.2). A nomogram was created to score the probabilities of VTE and included the type of treatment (NACT vs PDS) and levels of partial thromboplastin time (from 15 to 55 seconds). Sensitivity was 77.4%; specificity was 66.2%; positive predictive value (PPV) was 19.0%; negative predictive value (NPV) was 96.6%; and overall accuracy was 67.3%. In the validation dataset, we had a sensitivity of 64.3%, specificity of 71.5%, PPV of 18.0%, and NPV of 95.4% and overall accuracy of 70.9%.

**Conclusion:** The occurrence of VTE was higher in patients undergoing NACT compared to PDS. This study is the first to demonstrate a simple score risk assessment model to predict VTE in ovarian cancer patients undergoing primary treatment. This model could be useful for identifying candidates for thromboprophylaxis.

**Objective:** We sought to assess the impact of frailty in patients with high-grade ovarian cancer, fallopian tube, or primary peritoneal cancer undergoing neoadjuvant chemotherapy (NACT) or primary debulking surgery (PDS) on surgical and survival outcomes.

**Method:** A retrospective cohort was performed from April 2013 to September 2017. Patients with advanced disease were triaged by laparoscopy to determine primary resectability. Patients with medically inoperable or metastatic disease received NACT. The modified frailty index score (mFI) was calculated based on obstructive pulmonary disease or recent pneumonia, congestive heart failure, myocardial infarction, coronary artery disease, diabetes, hypertension, peripheral vascular disease, cerebrovascular disease (CVA), CVA with neurologic deficit, and ECOG status 3 or 4, with each item receiving a score of 1 if present. The mFI was compared in subgroups: patients who received NACT only, NACT and laparoscopy (NACT-lap), and PDS. mFI was compared using t test, rank sum test, ANOVA, or Kruskal-Wallis test, and adjustments were made for multiple comparisons ($P < 0.05$). PFS was estimated using the Kaplan-Meier method.

**Results:** A total of 560 patients were included; 161 patients underwent PDS, 255 patients NACT only, and 104 patients NACT-lap. Median age was 65 years, and median BMI was 27.0 kg/m². Fifty eight percent of patients had an mFI of 0, 29% mFI of 1, and 13% mFI of ≥2. There was a significant difference in mFI by subgroups of treatment and surgery status. Mean mFI for NACT only, NACT-lap, and PDS was 0.74, 0.54, and 0.43, respectively ($P = 0.012$). The mean mFI for those having debulking surgery (primary or interval) versus no surgery was 0.49 versus 1.04 ($P < 0.001$). There was no association with R0 status and mFI ($P = 0.727$). mFI was significantly associated with PFS. A higher score was associated with a worse PFS (HR = 1.37, 95% CI...
A worse PFS was also correlated with an mFI = 1 versus mFI = 0 (HR = 1.37, 95% CI 1.07–1.74, \( P = 0.013 \)), and an mFI ≥2 versus mFI = 1 (HR = 1.65, 95% CI 1.25–2.18, \( P < 0.001 \)).

**Conclusion:** The mFI can be used as a prognostic. These findings have implications to screen vulnerable ovarian cancer patients and help in clinical decision making.

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**2258 - Poster Session**

**Hospital surgical volume impacts the likelihood of NCCN-recommended surgery for patients with early-stage cervical cancer**

E.M. Avikia, J.D. Wrightb, L. Chenc and M.M. Leitao Jr.a. aMemorial Sloan Kettering Cancer Center, New York, NY, USA, bNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, cColumbia University College of Physicians and Surgeons, New York, NY, USA

**Objective:** Little is known about the impact of volume on outcomes for patients diagnosed with early-stage cervical cancer. We examined whether process and outcome measures varied for patients with early-stage cervical cancer based on hospital surgical volume.

**Method:** We used the National Cancer Data Base to examine women with stages IA2–IB1 cervical cancer from 2011 to 2013. We included only patients with squamous cell, adenocarcinoma, or adenosquamous histology. Annual hospital procedural volume was calculated using the number of hysterectomies performed in the preceding year. Higher volume was defined as hospitals in the top two quartiles of volume and lower volume as those in the bottom two quartiles of volume. Patient demographics, type of hysterectomy (radical, RH, vs simple, SH), mode of hysterectomy (minimally invasive, MIS, vs open), lymph node assessment (LND), and survival outcomes were compared using volume as a continuous variable and by quartiles of volume. Cox proportional hazards model was performed to determine the impact of volume on mortality. Sensitivity analysis was performed to explore the impact of volume on mortality in patients undergoing RH.

**Results:** We identified 3,469 patients. Breakdown of hysterectomy by type included 2,243 (64.7%) RH and 1,226 (35.3%) SH, as well as 1,999 (57.6%) MIS and 1,470 (42.4%) open procedures. Among those who underwent RH, 1,022 (45.5%) were open and 1,221 (54.4%) were MIS. On univariate analysis, SH was more likely to be performed at lower volume compared to higher volume centers (40.4% vs 31.1%, \( P < 0.001 \)). Similarly, RH was more likely to be performed at higher volume centers (68.9% vs 59.6%, \( P < 0.001 \)). Rates of LND were significantly higher at higher volume centers (96.1% vs 87.3%, \( P < 0.001 \)). There was no significant difference in the rates of MIS versus open procedure by center volume (\( P = 0.35 \)). On Cox proportional hazards model, there was no difference in mortality across volume quartiles or by increments of volume (Table 1). In addition, there was no difference in mortality for patients undergoing MIS. Subset analysis of only MIS RH showed a notable trend toward decreased mortality with increasing surgical volume; however, this outcome did not reach statistical significance.

**Conclusion:** Higher volume centers were associated with higher rates of NCCN-recommended surgery for early-stage cervical cancer.

**Table 1.** Cox proportional hazards model with sensitivity analysis of patients undergoing only radical hysterectomy and only MIS radical hysterectomy.
‡ Un-estimable, *p-value <0.05; Insurance Type, Grad, and Race were also included in the model and not significant.

2259 - Poster Session
Impact of enhanced recovery after surgery on the incidence of acute kidney injury

Objective: In enhanced recovery after surgery (ERAS) protocols, a focus on euvoeemia and reduction of opioid medications leads to lower volume administration of intravenous fluids (IVF) and greater use of nonsteroidal antiinflammatory drugs (NSAIDs), interventions that may lead to an increase in postoperative acute kidney injury (AKI). The aim of this study was to compare incidence of AKI after gynecologic surgery in patients who underwent ERAS versus those with traditional management.

Method: Patients who underwent laparotomy for gynecologic malignancy at a single institution were sampled for data abstraction in 3 time periods between June 20, 2011, and June 20, 2018, and compared to a historical control cohort prior to ERAS implementation. Patients with stage V chronic kidney disease were excluded. AKI was determined using the Kidney Disease: Improving Global Outcomes (KDIGO) and National Surgical Quality Improvement Program (NSQIP) definitions. Typical IVF administration in the first ERAS time period was compared with the historical cohort.
Results: At least 1 preoperative and 1 postoperative serum creatinine (sCr) was available in 510 patients (376 ERAS and 134 historical controls). The median baseline sCr was 0.8 mg/dL (IQR 0.69–0.90, range 0.4–1.8). Using KDIGO criteria, there were no differences in rates of AKI (15.2% ERAS vs 18.7% historical controls, P = 0.34). There was also no difference using the NSQIP definition (0.53% ERAS vs 1.5% historical controls, P = 0.28). Median perioperative IVF administration in the ERAS cohort was significantly reduced compared to the historical cohort (median 5,233, IQR 3,955–7,120, vs median 6,370, IQR 4,859–8,264 mL, respectively, P < 0.001). Complete doses of NSAIDs were administered in 30.3% of ERAS and 16.4% of historical controls (P = 0.002).

Conclusion: Implementation of ERAS resulted in decreased administration of IVF and higher use of NSAIDs, but did not increase rates of AKI. Future studies are needed to reduce AKI and determine the long-term impact of AKI on renal function following surgery.

2260 - Poster Session
Hypermethylation testing to identify Lynch syndrome in endometrial cancer patients: Is it worth it?
Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA, University of South Carolina School of Medicine Greenville, Greenville, SC, USA, Carolinas Pathology Group, Charlotte, NC, USA

Objective: We sought to determine whether MLH1 promoter hypermethylation (HM) testing of endometrial cancer (EC) is a cost-effective triage strategy for Lynch syndrome (LS) testing.

Method: We constructed a decision analysis to compare cost-effectiveness of 3 screening strategies: (1) no immunohistochemistry (IHC) testing with referral for genetic testing (GT) based on Bethesda criteria (BC) alone; (2) IHC alone with no HM testing with referral for GT based on BC or abnormal IHC testing; or (3) IHC and reflex HM testing with referral for GT based on BC or abnormal IHC testing with negative HM. To evaluate the cost associated with each strategy, data from all consecutive patients with primary EC treated by gynecologic oncologists within a large system from 2013 to 2017 were used to populate the model. Patients were identified through the institutional cancer registry and departmental billing records; data were extracted from the medical record. Costs were obtained for each branch point at which reimbursement occurred. Cost/life-years saved and cost/quality-adjusted life-years (QALY) were calculated for each testing option based on published insurance reimbursement rates, cost data, and institutional reimbursement data. Results were compared using a one-way ANOVA for the 3 screening strategies.

Results: We identified 1,208 eligible patients. In our system, 282 patients had no IHC or HM; 876 had IHC but no HM; and 50 had IHC with reflex HM. Of the 282 patients with no IHC or HM, 33% complied with GT when indicated and 1 case of LS was identified. In the second group of 876 patients with IHC but no HM, 698 had normal IHC and GT was indicated in 45 of these patients with 0 cases of LS identified. In the 178 patients with abnormal IHC, 100 were compliant with GT, and 13 cases of LS were identified. In the last group of 50 patients with IHC and reflex HM, 1 had abnormal IHC without HM, and she underwent GT and had LS. Including downstream testing, the cost/case of LS identified was $4,000, $24,178, and $17,000, respectively. The cost/QALY gained in each modality was $3,235, $4,895, and $3,486, respectively. The percentage of patients referred for GT was 22%, 41%, and 22%, respectively.

Conclusion: The cost/QALY gained for each of the 3 testing algorithms was acceptable. Although IHC with or without HM was more expensive than no IHC testing, the number of unnecessary GT visits was lower when reflex HM was incorporated. The optimal cost-effective triage strategy to detect LS in patients with EC that preserves the scarce resource of GT appears to be IHC with reflex HM testing.

2301 - Poster Session
Interval debulking surgery is not worth the wait: A National Cancer Database study comparing primary cytoreductive surgery versus neoadjuvant chemotherapy
Y.A. Lyons, H.D. Reyes, M. McDonald, A.M. Newtson, E. Devor, D.P. Bender, M.J. Goodheart and J. Gonzalez Bosquet. University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Objectives: In recent clinical trials, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery was not inferior to primary cytoreductive surgery (PCS) followed by chemotherapy as initial treatment for advanced-stage epithelial
ovarian cancer. Better understanding of PCS and NACT outcomes will facilitate patient selection for these treatments. The aim of this study is to compare PCS and NACT surgical and survival outcomes in a large national database.

**Methods:** Data were extracted from the National Cancer Data Base for ovarian cancer from 2004 to 2015. Only patients with advanced FIGO stage (III–IV) epithelial ovarian cancer and known sequence of treatment were included: PCS = 26,717 and NACT = 9,885. Residual disease after treatment was defined based on recorded data: R0 was defined as microscopic or no residual disease, and R1 was defined as macroscopic residual disease. No size of residual disease was available. Multivariate Cox proportional hazard ratio was used for survival analysis. To compare 30- and 90-day mortality between groups, multivariate logistic regression analysis was utilized. Outcomes were adjusted for significant covariates.

**Results:** Patients who underwent PCS had better survival than patients who underwent NACT, even after adjusting for age, comorbid conditions, year of diagnosis, grade, stage, and residual disease after surgery ($P < 0.001$). PCS patients with R0 residual disease had the best median survival (62.6 months). NACT patients with R1 residual disease had the worst median survival (29.5 months). There was no difference between those with PCS and R1 (38.9 months) and those who received NACT and had R0 (41.8 months, HR = 0.93, 95% CI 0.87–1.0), after adjusting for age, comorbid conditions, year of diagnosis, grade, and stage. NACT patients had 3.5 times higher 30-day mortality after surgery than PCS patients (95% CI 2.37–5.39); 90-day mortality was similar for PCS and NACT patients in the multivariate analysis (HR = 1.23, 95% CI 0.99–1.51).

**Conclusion:** Based on this study, patients with advanced-stage epithelial ovarian cancer should be offered PCS regardless of tumor burden. NACT should be offered to those with medical comorbid conditions who are unfit for surgery.

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**2302 - Poster Session**  
**A cost analysis of the impact of enhanced recovery after surgery (ERAS) protocol in gynecologic oncology surgery**  
*University of Alabama at Birmingham, Birmingham, AL, USA*

**Objective:** This study aimed to determine the financial impact of an enhanced recovery after surgery (ERAS) protocol in gynecologic oncology patients.

**Method:** This study identified gynecologic oncology patients who were placed on the ERAS protocol after elective laparotomy from October 2016 to June 2017. A control group was identified from the year prior to ERAS implementation. Financial experts from the institution assisted in procuring cost data for these patient encounters, including payer status, charges, direct and indirect costs, and contribution margin. Length of stay (LOS) was also evaluated. SPSS Statistics v. 24 was used for statistical analysis.

**Results:** A total of 376 patients met criteria for inclusion: 179 in the ERAS group and 197 in the control group. Patient demographics were similar between the two cohorts. Payer status across the two groups was not statistically significant in patients with private insurance (control, 43.6%, vs ERAS, 41.9%). There was a significantly higher amount of Medicare patients in the control group (38.1% vs 31.5%, $P = 0.001$), but fewer Medicaid patients (6.1% vs 11.4%, $P = 0.001$) and self-pay patients (11.3% vs 15.5%, $P = 0.003$). Total charges ($45,288 vs $44,187$) and direct hospital costs ($5,334 vs $5,596$) were similar between the ERAS and control groups. However, overall contribution was decreased in the ERAS group ($8,426 vs $11,619$, $P = 0.008$). LOS was significantly lower in the ERAS group (2.9 vs 4.0 days, $P = 0.04$).

**Conclusion:** Implementation of the ERAS protocol in gynecologic oncology patients does not lead to increased costs for the patient or hospital system. The decreased contribution margin is likely due to a reduction in per-diem payments from the decreased LOS. However, at a high-volume institution, decreased LOS allows for more patients to be admitted.

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**2303 - Poster Session**  
**Minimally invasive surgical management of IA1 cervical cancer and effects on overall survival**  
1University of Kentucky Medical Center, Lexington, KY, USA, 2University of Kentucky College of Medicine, Lexington, KY, USA, 3University of Kentucky College of Medicine, Lexington, KY, USA

**Objective:** We sought to examine the all-cause mortality between patients who undergo minimally invasive (MIS) versus open extrafascial hysterectomy for stage IA1 cervical cancer.
Method: This study examined data from the National Cancer Data Base (NCDB) database for the years 2010–2012. Patients included in this analysis had stage IA1 cervical cancer treated with extrafascial hysterectomy. Additional inclusion criteria included squamous, adenosquamous, or adenocarcinoma histology. Patients were stratified according to hysterectomy approach, open or MIS (laparoscopic or robotic). Kaplan-Meier and Cox proportional hazard models were used to compare OS between the groups while controlling for age, grade, histology, and adjuvant chemotherapy/radiation.

Results: A total of 923 patients were included in the analysis. Of these, 388 (42%) underwent open hysterectomies and 535 (58%) underwent an MIS hysterectomy. Patients who underwent MIS procedures were on average younger ($P = 0.012$) and more likely to be privately insured ($P = 0.030$); however, no other significant differences were noted in race, histology, grade, or adjuvant therapy. Mean follow-up time was 49.5 months for open hysterectomies and 48.4 months for MIS hysterectomies. Mean survival for open hysterectomies was 79.7 months and for MIS 81.7 months. There was no significant difference in OS for patients undergoing MIS procedures compared to open procedures (OR = 0.721, 95% CI 0.321–1.615). See Figure 1.

Conclusion: Recent evidence indicates that laparoscopic or robotic hysterectomy is associated with higher recurrence rates and decreased survival compared to open surgery in patients in early-stage cervical cancer. In this large study of stage IA1 patients, no difference in survival was observed according to surgical approach. This demonstrates the previously demonstrated decreased survival in minimally invasive surgery for cervical cancer may not confer to stage IA1 disease.

Fig. 1.

2304 - Poster Session
Trends in hormonal replacement therapy among BRCA mutation carriers

Objective: Risk-reducing salpingo-oophorectomy (RRSO) is recommended to BRCA mutation carriers to prevent ovarian cancer by age 35 years or at completion of childbearing. Surgical menopause is a consequence, leaving many women symptomatic. Controversy exists around use of hormonal replacement therapy (HRT) in this population because of concern for increased breast cancer risk, although recent studies have proven its safety. We evaluated trends in HRT use among BRCA patients at a single institution.

Method: Women with BRCA1/2 mutations who underwent risk-reducing surgery between 2003 and 2018 were evaluated. HRT regimens utilized were captured. HRT was defined as estrogen (oral only, EO; transdermal patch, EP; vaginal, EV) or combined estrogen/progesterone therapy (oral only, transdermal, oral and other). Univariate tests were applied based on variable distribution, and associations between categorical variables were evaluated by $\chi^2$ test or Fisher exact test as appropriate for category size.

Results: A total of 155 patients underwent RRSO (BRCA1, 81, 53%; BRCA2, 71, 45%; BRCA1 and BRCA2, 3, 2%). Thirty-six patients (23%) had a concurrent hysterectomy. A total of 44 patients (28%) received HRT (s/p RRSO, $n = 35$, 23%; s/p hysterectomy with RRSO, $n = 9$, 6%). The most common symptoms were vaginal dryness (48%) followed by hot flashes (25%). The average age was 45 years, with patients younger than 50 years more likely to receive HRT ($P < 0.0001$) (Table 1). Among patients who received HRT, 11 (25%) had a history of breast cancer (stage 0–1, 11%); 8 (73%) had previous mastectomy; and
3 (27%) had lumpectomy. Vaginal estrogen therapy was most common among all HRT (EO = 18.2%, EP = 4.5%, EV = 50%, \( P < 0.0001 \)). Only 19 (43%) patients who received HRT had it administered immediately after RRSO (Table 1).

**Conclusion:** Despite recent studies evaluating the safety of HRT in BRCA carriers after RRSO, use of HRT has been underutilized. Among our cohort, younger women (<50 years) were more likely to receive HRT, yet only 43% were started at the time of RRSO prior to initiation of menopausal symptoms. Vaginal estrogen was the most commonly prescribed therapy, with less utilization of full-dose HRT (EO/EP or combined therapy) for definitive symptom management. Efforts to initiate HRT immediately at time of RRSO should be considered in this population to improve quality of life and patient satisfaction.

**Table 1.** Hormone replacement therapy in BRCA carriers

<table>
<thead>
<tr>
<th>Concurrent Hysterectomy performed</th>
<th>BRCA mutation post RRSO on HRT</th>
<th>( \text{p-value} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N = 44 )</td>
<td>( 9 ) (20.4%)</td>
<td></td>
</tr>
<tr>
<td>History of breast cancer</td>
<td>( 7 ) (63.6%)</td>
<td></td>
</tr>
<tr>
<td>Receptor positive</td>
<td>( 11 ) (25%)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>( 42 ) (95.4%)</td>
<td></td>
</tr>
<tr>
<td>Undergoing breast cancer screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at HRT initiation</td>
<td>( 45 ) yrs ( (34-72) )</td>
<td>( P &lt; 0.0001 )</td>
</tr>
<tr>
<td>Age of RRSO/HRT</td>
<td>( &lt; 50 ) yrs</td>
<td></td>
</tr>
<tr>
<td>( &gt; 50 ) yrs</td>
<td>( 35 )</td>
<td></td>
</tr>
<tr>
<td>( 9 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRT prescribed</td>
<td>( \text{immediately post RRSO} )</td>
<td>( 19 ) (43%)</td>
</tr>
<tr>
<td>HRT type and route</td>
<td>( \text{oral} )</td>
<td>( P = 0.05 )</td>
</tr>
<tr>
<td>Estrogen only</td>
<td>( 23 ) (52.3%)</td>
<td></td>
</tr>
<tr>
<td>Transdermal</td>
<td>( 2 ) (4.5%)</td>
<td></td>
</tr>
<tr>
<td>Vaginal*</td>
<td>( 22 ) (50%)</td>
<td>( P &lt; 0.0001 )</td>
</tr>
<tr>
<td>Overall</td>
<td>( 32 ) (72.7%)</td>
<td></td>
</tr>
<tr>
<td>Estrogen/Progestosterone</td>
<td>( \text{oral} )</td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>( 4 ) (9.1%)</td>
<td></td>
</tr>
<tr>
<td>Transdermal</td>
<td>( 2 ) (4.5%)</td>
<td></td>
</tr>
<tr>
<td>Oral + IUD</td>
<td>( 5 ) (11.3%)</td>
<td></td>
</tr>
<tr>
<td>Oral + Transdermal</td>
<td>( 1 ) (2.3%)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>( 12 ) (27.3%)</td>
<td></td>
</tr>
</tbody>
</table>

\*Vaginal cream/ring/tablet

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**Breast cancer surveillance following ovarian cancer in BRCA mutation carriers**

I. Cassa\(^a\), C. John\(^a\), J. Gillen\(^b\), K.N. Moore\(^a\), C. Walsh\(^a\), A.J. Li\(^b\), B.J. Rime\(^a\), B.Y. Karlan\(^a\) and F. Amersi\(^a\). \(^a\)Cedars-Sinai Medical Center, Los Angeles, CA, USA, \(^b\)The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, <The University of Oklahoma, Norman, OK, USA>

**Objective:** Patients with BRCA1 or BRCA2 mutations are at increased risk of developing both breast cancer (BC) and epithelial ovarian cancer (EOC). The incidence of BC after a diagnosis of EOC is not well known. Optimal breast cancer surveillance for BRCA mutation carriers following a diagnosis of EOC has not been defined.

**Method:** An Institutional Review Board approved, multiinstitutional retrospective chart review was performed. Patients with BRCA-associated EOC diagnosed between 1990 and 2015 were identified without a prior history of bilateral mastectomy. All women were treated with combination chemotherapy for EOC. Demographic and clinical data were collected. Descriptive statistics and univariate analyses were performed.

**Results:** A total of 186 patients with BRCA-associated EOC were included (140 BRCA1, 45 BRCA2, 1 patient with both BRCA1 and BRCA2). Sixteen (8.6%) women were diagnosed with BC following EOC: 3 with recurrent BC and 13 with a new BC diagnosis at a median of 38 months following EOC diagnosis. Annual mammography was performed in half of women and annual MRI in 25% of women. Twenty-two (12%) women underwent risk-reducing mastectomy (RRM) a median of 22 months following EOC. Breast cancer was most commonly detected on mammogram in 7 (44%) patients, followed by clinical examination 5 (31%) and 4 (25%) occult BC at RRM. Seven (44%) women had DCIS; the remaining (56%) had invasive ductal...
carcinoma. Fourteen (88%) had early stage (0–2) disease. At a median follow-up of 7 years, 6 (38%) women with BC following EOC have died from recurrent EOC and 1 (6%) from recurrent BC. See Table 1.

**Conclusion:** The risk of metachronous BC following EOC in BRCA mutation carriers is low. A majority of these BC are early stage and will be diagnosed with mammogram and clinical examination. OS in BRCA mutation carriers is dominated by EOC-related mortality. BC surveillance in BRCA mutation carriers following a diagnosis of stage III–IV EOC should prioritize nonsurgical strategies.

### 2306 - Poster Session

**Incidence and characteristics of 30- versus 90-day readmission following surgical intervention in ovarian cancer patients**

A.L. Mardock, Y. Sanaiha, S.E. Rudasill, D.H. Wong, A.K. Sinno, P. Benharash and J.G. Cohen. UCLA David Geffen School of Medicine, Los Angeles, CA, USA

**Objective:** The aim of this study was to compare the frequency and characteristics of 30-day versus 31–90 day readmission following surgery for ovarian, fallopian tube, or primary peritoneal cancer.

**Method:** This retrospective study of the Nationwide Readmissions Database characterized 90-day readmissions among adult women undergoing surgical cytoreduction for these cancers 2010–2015. Readmission was defined as a patient’s first postoperative hospitalization within the calendar year. \( \chi^2 \) univariate analysis compared patient cohort demographics and reasons for readmission, identified by diagnosis-related group codes. Multivariate regression identified independent predictors of readmission.

**Results:** Of an estimated 76,652 patients, 10,264 (13.4%) had 30-day readmission, and 6,942 (9.1%) were readmitted between 31 and 90 days. Compared to 31–90 day readmissions, 30-day readmission patients were more likely to have concurrent hysterectomy (73.8 vs 69.4%, \( P < 0.01 \)) and less likely to have laparoscopic surgery (5.5 vs 7.1%, \( P < 0.01 \)). The 30-day and 31–90 day readmission cohorts saw no difference in proportion of readmissions associated with gastrointestinal obstruction, female reproductive malignancy, metabolic or nutritional disorders, septicemia, or pulmonary embolism (Table 1). The 30-day readmissions were more frequently associated with postoperative or post-traumatic infection, while 31–90 day readmissions were more frequently associated with kidney and urinary tract infections or major hematologic and immune diagnoses (Table 1). Independent predictors of any 90-day readmission included pulmonary circulation disorder (OR = 1.29, 95% CI 1.07–1.55), metastasis (OR = 1.22, 95% CI 1.11–1.35), weight loss (OR = 1.15, 95% CI 1.01–1.32), fluid and electrolyte disorders (OR = 1.15, 95% CI 1.05–1.25), and diabetes (OR = 1.11, 95% CI 1.01–1.22).

**Conclusion:** The 30-day readmissions are often used to measure quality of surgical care. However, readmission rates remain high during the 31–90 day postoperative period in ovarian cancer patients. Given the high risk of 31–90 day readmission, future studies may benefit from including data for 90-day readmission. Prospective study is merited to assess the benefit of increased surveillance beyond the initial 30 days after ovarian cancer surgery.
Table 1. Proportion of 30-day and 31-90-day readmissions associated with various diagnosis-related groups

<table>
<thead>
<tr>
<th>Diagnosis-Related Group of First Readmission</th>
<th>30-Day Readmission</th>
<th>31-90-Day Readmission</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>G.I. obstruction</td>
<td>672</td>
<td>6.5%</td>
<td>396</td>
</tr>
<tr>
<td>Digestive disorder</td>
<td>1386</td>
<td>13.5%</td>
<td>479</td>
</tr>
<tr>
<td>Postoperative &amp; post-traumatic infection</td>
<td>1303</td>
<td>12.7%</td>
<td>223</td>
</tr>
<tr>
<td>Malignancy, female reproductive system</td>
<td>561</td>
<td>5.5%</td>
<td>339</td>
</tr>
<tr>
<td>Nutritional &amp; metabolic disorder</td>
<td>308</td>
<td>3.0%</td>
<td>263</td>
</tr>
<tr>
<td>Septicemia</td>
<td>421</td>
<td>4.1%</td>
<td>316</td>
</tr>
<tr>
<td>Major hematologic or immune diagnosis</td>
<td>133</td>
<td>1.3%</td>
<td>442</td>
</tr>
<tr>
<td>Kidney &amp; urinary tract infection</td>
<td>197</td>
<td>1.9%</td>
<td>205</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>243</td>
<td>2.4%</td>
<td>184</td>
</tr>
<tr>
<td>Digestive malignancy</td>
<td>238</td>
<td>2.3%</td>
<td>152</td>
</tr>
</tbody>
</table>

2307 - Poster Session

**Surgical stage IA clear cell ovarian cancer: Is adjuvant chemotherapy necessary?**

D.A. Klein, J.K. Chan, D.S. Kapp, A.K. Mann and C.I. Liao. aUniversity of California, San Francisco, San Francisco, CA, USA, bCalifornia Pacific and Palo Alto Medical Foundation/Sutter Health Institute, San Francisco, CA, USA, cStanford University, Stanford, CA, USA, dPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, eKaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

**Objective:** The aim of this study was to identify the benefit of adjuvant chemotherapy in surgically staged I clear cell ovarian cancer patients.

**Method:** Demographic and clinicopathologic data were extracted from the National Cancer Data Base PUF 2015 between 2004 and 2014. χ², one-way ANOVA, Kaplan-Meier, and Cox regression analysis were used for statistical analyses.

**Results:** Of 2,000 stage I clear cell ovarian cancer patients, the median age was 55.4 (range 24–89) years. Percentages of white, black, American Indian/Alaska Native, Asian/Pacific Islander, and other/unknown were 85.7%, 2.9%, 0.3%, 8.9%, and 2.3%, respectively. Location of treatment was as follows: Northeast, 22%; Midwest, 26%; South, 27%; West, 19%; and academic centers, 59%; and community hospitals, 41%. All patients underwent surgical staging with lymph node dissection, and 49.7%, 1.3%, and 45.6% had stage IA (n = 994), IB (n = 26), and IC (n = 912) disease, respectively. Of these patients, 80.8% received chemotherapy. Younger age (P = 0.012), white race (P < 0.01), academic center (P < 0.01), New England (P < 0.01), and stage IC disease (P < 0.01) were more likely to have chemotherapy. The use of chemotherapy increased from 70.2% (2004) to 85.9% (2014) (annual percentage change = 2.3%, P < 0.05). The 5-year OS was 85.6% for the cohort and 89.1%, 72%, and 82.5% for stage IA, IB, and IC, respectively. Chemotherapy was associated with an improvement in survival of those with stage IA (90.5% vs 83.8%, P = 0.026), stage IB (77.8% vs 57.1%, P = 0.296), and stage IC (83% vs 80.3%, P = 0.68). On multivariate analysis, lower substage (HR = 0.57, 95% CI 0.35–0.93, P = 0.03) and use of chemotherapy (HR = 0.44, 95% CI 0.25–0.77, P < 0.01) were independent predictors for improved survival.

**Conclusion:** Our data suggested that chemotherapy was associated with an improvement in OS in surgically staged I clear cell ovarian cancer. The use of chemotherapy has increased over time and was higher in younger age, white race, academic centers, and New England.

2308 - Poster Session

**Surgical stage 1 mucinous ovarian cancer: Does chemotherapy impact survival?**

Objective: The aim of this study was to determine the role of adjuvant chemotherapy in patients with surgical stage I mucinous ovarian cancer.

Method: Demographic and clinical data from the National Cancer Data Base from 2004 to 2014 were analyzed using χ², independent sample t test, Kaplan-Meier, and Cox regression.

Results: Among 2,041 stage I mucinous ovarian cancer patients with survival data (mean age 51.6 ± 14.4 years), most had stage IA 1,340 (66%), stage IB 22 (1%), or IC 598 (29%) disease; NOS 81 (4%). Most patients were white (1,786, 88%), black (113, 6%), or Asian/Pacific Islander (100, 5%). Most (1,047, 64%) patients did not receive chemotherapy; however, those with a Charlson/Deyo score of 1, higher substage, and higher grade received cytoreductive surgery, and malignant ascites were more likely to undergo chemotherapy (P < 0.05). Use of chemotherapy did not significantly change over the study period. In the cohort, the 5-year OS was 89.7%, and 90.0%, 90%, and 86.6% for stage IA, IB, and IC, respectively. Of stage IC patients, 69% received CT compared to only 21% for stage IA disease (P < 0.001). The 5-year OS for all patients did not differ in those who had chemotherapy versus observation (89.6% vs 89.9%, P = 0.461). In a subset analysis based on stage of disease, chemotherapy did not improve survival over observation in stage IA (89.6% vs 89.9%, P = 0.906), stage IB (90.0% vs 90.0%, P = 0.505) and stage IC (97.4% vs. 98.6%, P = 0.363). On multivariate analysis, those with older age (HR = 1.02, 95% CI 1.01–1.03), higher Charlson/Deyo score of 3 or more (HR = 29.25, 95% CI 9.43–90.78), poorly differentiated (HR = 2.32, 95% CI 1.39–3.88), and lymph vascular invasion (HR = 4.18, 95% CI 1.52–11.49) had a poorer survival; however, chemotherapy did not have an impact on outcome (HR = 0.80, 95% CI 0.55–1.17).

Conclusion: Our data showed that chemotherapy was not associated with improved survival in surgically staged I mucinous ovarian cancer patients.

2309 - Poster Session
Quality of life (QoL) in ovarian cancer patients following hyperthermic intraperitoneal chemotherapy (HIPEC) versus intraperitoneal (IP) chemotherapy
T. Dellinger, S.J. Lee, V. Sun, N.H. Ruel, X. Liu, W.C.M. Lin, M. Kebría and E.S. Han. City of Hope, Duarte, CA, USA

Objective: Both intraperitoneal chemotherapy (IPC) and hyperthermic intraperitoneal chemotherapy (HIPEC) have demonstrated significant OS benefit in ovarian cancer (OC) patients during primary treatment. Data on comparison of health-related quality of life (HR-QOL) following these treatments are scarce.

Method: Primary and recurrent OC patients were prospectively enrolled in a single-institution phase I trial to evaluate safety and QOL of HIPEC. HR-QOL was assessed via FACT-O questionnaires at baseline, and 3, 6, 9, and 12 months after HIPEC. A retrospective cohort of primary and recurrent OC patients who underwent IPC via modified Armstrong regimen at the same institution were evaluated for HR-QOL at 6–12 months following treatment via FACT-O. Comparison of QOL test scores was conducted using the Student t test. A general linear (ANOVA) model was used to study self-reported instrument results and patterns over time.

Results: From 2014 to 2018, a total of 18 OC (10 recurrent, 3 primary) patients were enrolled and underwent HIPEC, of which 13 were evaluable for HR-QOL in 2018. One hundred percent completed questionnaires at baseline, 81.3% at 3 months, 50% at 6 months, 62.5% at 9 months, and 43.8% at 12 months. QOL FACT-O total scores decreased at 3 months for all OC patients following HIPEC, but rose by 6 months, with return to baseline or better by 9 months. For recurrent OC patients, QOL scores decreased again at 12 months, coinciding with a median PFS of 13.4 months. A total of 11 (primary and recurrent) OC patients were identified from a previously published IPC cohort. QOL scores were similar between the historical IPC group and the HIPEC group in this trial for both FACT-O total scores and all subscores (emotional, physical, functional, social), except for ovarian-specific symptom index subscore, which was significantly worse in the HIPEC group (P = 0.04).

Conclusion: HIPEC and IP chemotherapy demonstrate similar HR-QOL at 6–12 months following therapy, although HIPEC patients reported worse ovarian-cancer specific symptoms.
Objective: The objective of this investigation was to understand when in the disease course do patients with ovarian cancer participate in clinical trials and how does this affect their clinical outcomes in a large tertiary center.

Method: With Institutional Review Board approval, we conducted a retrospective review of all women treated for ovarian cancer at our institution from 2010 through 2015. Clinical variables were extracted including presence and timing of clinical trial participation. Data were correlated utilizing univariate and multivariate parametric and nonparametric testing, and survivals were analyzed using the Kaplan-Meier method.

Results: We identified 391 women treated for ovarian cancer, of whom 68% were diagnosed with stage III or IV disease. Overall survival in this cohort was 5.5 years. The majority (91%) underwent surgery as an upfront (77%) or interval (23%) intervention, and timing of surgery was not associated with likelihood of trial participation. Of the entire cohort, 62 patients (16%) participated in a clinical trial. Examining only the patients with recurrent cancer, 26% participated in trials. Patients with recurrent ovarian cancer ($n=220$) and stage III or IV disease were more likely to participate in a trial. Median length of time from diagnosis to initiation of clinical trial was 1.5 years, and median time from initiation of trial to death was 2.4 years. In the recurrent setting, median OS for clinical trial participants was 4.8 years compared to only 2.6 years in nonclinical trial participants ($P<0.001$). Toxicity was the cause for trial cessation in 20% of trial participants, and this was associated with worse OS ($P=0.01$). Removal from trial secondary to progressive disease, however, was not associated with worse OS. Patients who received more than 4 lines of chemotherapy were more likely to have participated in a clinical trial ($P<0.001$) than those who received fewer than 4 lines. See Figure 1.

Conclusion: In the tertiary care setting, patients with advanced recurrent ovarian cancer who participate in clinical trials are likely to live longer with their disease than those who do not participate in clinical trials. Removal from trial secondary to toxicity rather than removal due to progression of disease is likely a poor prognostic indicator in this patient population.

Fig. 1. Overall survival in recurrent cohort by trial.
Objective: The aim of this study was to assess the utility of a commonly applied adverse outcome prediction algorithm, the LACE score, to predict readmission or patient death within 30 days on a gynecologic oncology service.

Method: We evaluated all patients who underwent a medical index admission to an academic gynecologic oncology service in 2017. The primary outcome evaluated was admission or death within 30 days of the index admission. For each patient, we calculated the component and composite scores of the LACE index, a risk prediction tool developed in a general medicine population that incorporates length of stay, acuity of admission, Charleson comorbidity score, and number of emergency department visits within the last 6 months. A high score (≥10) indicates an increased risk of death or readmission within 30 days. Patients who did not have all LACE components recorded, who died during their index admission, or who were discharged to hospice care were excluded. Logistic regression models were fitted with the composite LACE score as well as with the individual score components. We then calculated the area under the receiver operating characteristic curve (AUC) with 95% CI.

Results: Among 83 patients who underwent a medical index admission in 2017, 42 (50.6%) died or were readmitted within 30 days. The LACE score in the study population ranged from 10 to 19 with a median of 13 (IQR 12.5–15). The model using only the composite LACE score had an AUC of 0.54 (95% CI 0.41–0.66), demonstrating poor predictive ability. This finding is likely secondary to similarities of both acuity and Charleson comorbidity score among all included patients. Length of stay and number of emergency department visits had better discriminative power. The component LACE model had an AUC of 0.71 (95% CI 0.60–0.82), demonstrating a moderate predictive ability. See Figure 1.

Conclusion: Readmission and death within 30 days of admission are important quality indicators in health care. All patients in this gynecologic oncology cohort met high-risk LACE criteria. Establishing adequate predictive means to identify patients at increased risk and implement appropriate interventions is necessary. Further efforts will be directed at refinement of the predictive model in the gynecologic oncology population.

Fig. 1.

2312 - Poster Session
Combination of gemcitabine and nab-paclitaxel is active against recurrent ovarian cancer: Single institution retrospective review
A.G.M. Azzouqa and G. Colon-Otero. Mayo Clinic Florida, Jacksonville, FL, USA
Objective: Ovarian cancer is the deadliest gynecological cancer in the United States with 14,000 deaths annually. Current standard of care for platinum-resistant disease includes single-agent liposomal doxorubicin, topotecan, or the combination of paclitaxel with bevacizumab. These treatments are associated with a PFS of less than 6 months. Our objective was to evaluate the activity of gemcitabine and nab-paclitaxel in patients with platinum-resistant or refractory ovarian cancer, as well as evaluate safety and side effect profile.

Method: This was a retrospective review of patients with ovarian cancer treated at the Mayo Clinic in Florida from 2012 to 2018 treated with gemcitabine and nab-paclitaxel. The combination of gemcitabine and nab-paclitaxel was given at 800 mg/M² IV and 80 mg/M² IV, respectively, on days 1, 8, 15, and every 28 days. A total of 22 patients were identified, and their records were reviewed; 17 patients were platinum-resistant and 5 patients were platinum-sensitive.

Results: Seven out of 22 patients responded (overall response rates 31.8%). Overall response rate was 29.4% for platinum-resistant (5/17) compared to 40% for platinum-sensitive (2/5). PFS was 12.26 months for the whole group and 13.3 months for the platinum-resistant subset. No grade 3–5 nonhematologic toxicity was observed. This was a heavily pretreated group of patients with a median number of 2 previous treatments (range 1–6 previous treatments). OS at 24 months was 36% with a 50% overall survival at 12 months. See Figure 1.

Conclusion: The combination of gemcitabine and nab-paclitaxel is a safe and effective treatment for relapsed platinum-resistant/refractory ovarian cancer with superior results compared to historical control (PFS = 13.3 months compared to less than 6 months). This well-tolerated combination is a reasonable treatment option for these patients.

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2313 - Poster Session
Electronic medical records underestimate long-term postoperative opioid use after hysterectomy for endometrial carcinoma or hyperplasia
N.J. Jajala1, A. Chakraborty2, M.A. Wojtowycz2, W.D. Bunn1,2 and M.J. Cunningham1,2. 1SUNY Upstate Medical University, Syracuse, NY, USA, 2GYN Oncology of CNY, PC, East Syracuse, NY, USA

Objective: Prescription of opioids for postoperative pain may lead to long-term use, but reported rates vary from <1% to 38%. The wide variation may be related to the methods used to assess opioid use. Our objective was to assess the accuracy of
EMR data by comparison with state registry records of opioids dispensed in patients undergoing hysterectomy for endometrial hyperplasia (EH) or endometrial carcinoma (EC).

**Method:** Women undergoing hysterectomy for EH or EC between August 2017 and February 2018 were included in a retrospective cohort study. Patients were followed for 180 days postoperatively. Opioid use was assessed by EMR and I-STOP. EMR included patient reported use and prescription records. I-STOP included a record of all narcotics dispensed in New York state for the preceding 12 months. Data were obtained by chart review and query of I-STOP, and proportions were compared using the Fisher exact test.

**Results:** Sixty-six patients were included, 57 with EC and 9 with EH. Mean age was 62 years and mean Charleson comorbidity index 4.2. Fifty-seven (86%) underwent laparoscopic surgery. Endometrial carcinoma was stage I in 46 (80%), with 15 (22%) receiving adjuvant radiation and/or chemotherapy. Three patients had subsequent surgeries; there were no accidents or injuries during the follow-up period. Eighty-five percent reported no opioid use prior to surgery. Initial postoperative opioid use was recorded by EMR for 63 patients and by I-STOP for 53 patients (95% vs 80%, \( P < 0.05 \)). Fifteen percent of patients did not fill narcotics prescribed. There was a trend toward underreporting of opioid use in the EMR compared with I-STOP between 31 and 90 days postoperatively (4.5% vs 10.6%, NS). Between 91 and 180 days postoperatively, opioid use was recorded by EMR in 2 patients and by I-STOP in 10 patients (3% vs 15%, \( P < 0.05 \)). I-STOP indicated a trend toward less long-term opioid use following laparoscopy versus laparotomy (12.3% vs 33%, NS). Seven percent of opioid-naïve patients filled at least 1 narcotic prescription between 91 and 180 days postoperatively.

**Conclusion:** EMR records significantly overestimated initial opioid use and underestimated long-term use when compared with records of narcotics actually dispensed. This could result in underestimation of the overall impact of postoperative opioid prescriptions if EMR is the assessment tool used. Further studies should be based on verifiable databases of filled prescriptions.

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2314 - Poster Session

**Changes in surgical volume and outcomes over time for women with ovarian cancer**

A. Buskwofie\(^a\), L. Chen\(^b\), J.Y. Hou\(^c\), C.M. St. Clair\(^c\), A.I. Terga\(^c\), F. Khoury Collado\(^c\) and J.D. Wright\(^c\). \(^a\)New York-Presbyterian Hospital, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA, \(^b\)Columbia University College of Physicians and Surgeons, New York, NY, USA, \(^c\)New York-Presbyterian/Columbia University Medical Center, New York, NY, USA

**Objective:** Many studies over the past decade have sought to understand the relationship between procedural volume and surgical outcomes in gynecologic malignancies. However, how this information has affected current referral patterns and outcomes is unknown. We sought to examine the changes over time in surgeon and hospital procedural volume and their associated relationship to outcomes for patients with ovarian cancer.

**Method:** The New York Statewide Planning and Research Cooperative System database was used to identify all women diagnosed with ovarian or primary peritoneal cancer who underwent exenteration, debulking, hysterectomy, or oophorectomy in any hospital in New York state between 2000 and 2014. The number of surgeons and procedures performed each year, as well as estimates of annualized surgeon and hospital volume, was examined. Multivariate models were used to examine the association between surgeon volume and intraoperative, surgical site, and medical complications, as well as prolonged length of stay and excessive charges (>75th percentile for each). Trends over time were compared.

**Results:** A total of 25,044 women were identified, including 19,441 (77.6%) who underwent exenteration/debulking. Over time, the number of hospitals and surgeons performing ovarian cancer exenteration/debulking surgery has significantly decreased. The surgeon volume decreased from 452 surgeons performing an average of 3 cases/year in 2000 to 197 surgeons performing an average of 6 cases/year in 2014 (\( P < 0.003 \)). Hospital volume also decreased in a similar fashion. After accounting for multiple covariates, increasing surgeon volume was found to be associated with decreased mortality, with women who saw high-volume surgeons being 42% less likely to die (HR = 0.58, 95% CI 0.41–0.81). In addition, utilization of high-volume surgeons was independently associated with decreased length of stay (HR = 0.90, 95% CI 0.82–0.99) and decreased total charges (HR = 0.84, 95% CI 0.72–0.97).

**Conclusion:** Over time, care of patients with ovarian cancer has been concentrated to fewer surgeons and fewer hospitals. Our data suggest the utilization of high-volume surgeons results in decreased mortality.
Can a phone call keep postoperative patients from the emergency room? An evaluation of postoperative endometrial cancer patients.
S.S. Leea, J. Leeb and L.R. Boyda.
New York University School of Medicine, New York, NY, USA, The University of Texas Southwestern Medical Center, Dallas, TX, USA

Objective: Cost-effective postoperative care for endometrial cancer relies on addressing complications and lowering emergency department visits and readmissions. Patients seen in the emergency department but subsequently released without hospital admission present an opportunity for cost savings. Patients seen in safety net hospitals may have less social support, leading to higher emergency department visits and readmissions. We sought to evaluate factors associated with postoperative emergency department visits following surgery for endometrial cancer.

Method: All patients undergoing hysterectomy for endometrial cancer by gynecologic oncologists between 2013 and 2016 at both a private and a public hospital were included in the study. Outcomes clinically associated with emergency department visits during the 30- and 60-day postoperative periods were analyzed using comparative and multivariate analyses.

Results: Four hundred and twelve patients were included. During the 30-day postoperative period, 38 patients were seen in the emergency department: 19 (4.6%) were readmitted to the hospital (RAH) and 19 (4.6%) patients were treated and released (TAR). During the 60-day postoperative period, 49 patients were seen in the emergency department: 26 (6.3%) were RAH and 23 (5.6%) were TAR. RAH patients had the highest number of phone calls and outpatient visits both 30 and 60 days postoperatively (Table 1). In the 30-day postoperative period, compared to patients who did not present to the emergency department, TAR patients had fewer clinic visits than RAH patients (1.33 ± 0.03 vs 1.16 ± 0.12, respectively). Receiving care at a private hospital was associated with decreased rates of TAR visits within 30 days (OR = 0.351, 95% CI 0.129–0.956), adjusting for number of clinic visits, home nursing services at time of discharge, and American Society of Anesthesiologists’ classification system.

Conclusion: Readmitted patients have the highest number of phone calls and outpatient visits, which may reflect the true acuity of these patients. Patients who were TAR had a lower number of clinic visits within 30 days. These data can aid in care planning as well as cost modeling for payment models in endometrial cancer.

Impact of research findings and NCCN guidelines on use of bevacizumab for newly diagnosed ovarian cancer in the United States
S. Jorge, H.J. Gray, B.A. Goff and K.M. Doll.
University of Washington Medical Center, Seattle, WA, USA

Objective: Despite the multitude of clinical trials, the recent changes to FDA approval, and the high cost of administration, there has been no national analysis of bevacizumab (BEV) use among women with ovarian cancer (OC). Our goal was to determine whether a national pharmaceutical database could capture time trends in use and the nonclinical predictors of BEV use in the United States among newly diagnosed OC patients.

Method: Using the Truven Health MarketScan® databases, which cover approximately 240 million lives, we identified women ages 18–65 years with newly diagnosed OC from 2007 to 2014. All who underwent cancer-directed surgery and platinum-based chemotherapy within 3 months of diagnosis were included, with at least 1 year of continuous enrollment surrounding diagnosis. The proportion of women receiving BEV was calculated relative to the total number of new diagnoses each year. Logistic regression was used to determine the association between BEV use and various predictors.

Results: Among 17,037 new cases of OC, 1,405 (8.2%) received BEV within 6 months of diagnosis. The proportion of patients who received BEV increased 2.4-fold during the study period, from 5.3% in 2007 to 12.6% in 2014. However, the use of BEV plateaued between 2010 and 2012. The inflection points in the trend curve correspond to publication of randomized trials and society recommendations, as illustrated in Figure 1. In multivariate analyses, women who resided in the southern United States were more likely to receive BEV (OR = 1.31, 95% CI 1.10–1.56, P < 0.01). Among the subset of women whose treatment providers were known (n = 4,945), those treated by medical oncologists were more likely to receive BEV than those treated by gynecologic oncologists (OR = 2.18, 95% CI 1.65–2.88, P < 0.001). Cost data will be available at the meeting.

Conclusions: Analysis of the use of high-cost therapies in ovarian cancer will be critical to assessing the impact of novel research findings and appropriateness of use in a cost-conscious setting. We demonstrated that BEV use, prior to FDA
approval, was most sensitive to National Comprehensive Cancer Network guideline changes rather than research findings. Overall, the use of BEV for the upfront treatment of OC more than doubled between 2007 and 2014. Treatment by a medical oncologist and residing in the southern United States were associated with increased likelihood of receiving BEV during this time prior to FDA approval.

Fig. 1. Proportion of patients with newly diagnosed OC who received BEV within 6 months of diagnosis by years (2007-2014)

2317 - Poster Session
Assessment of the false negative rate of preoperative imaging in cervical cancer patients undergoing primary radical surgery
A. Staley, K. Tucker, P.A. Gehrig and L.H. Clark. University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Objective: Patient selection for primary radical surgery is paramount to avoid the use of adjuvant radiation treatment and its associated adverse effects in cervical cancer. The use of preoperative imaging could help identify those best suited for surgery versus primary radiation; however, no standard of care has been identified. We aim to describe the false negative rate and false positive rate of preoperative imaging at a single institution prior to radical surgery for cervical cancer.

Method: A retrospective chart review of all patients who underwent radical hysterectomy for early-stage cervical cancer from January 2010 to December 2017 at a single tertiary care center was performed. Patient demographics and clinicopathologic information, including imaging, surgery, adjuvant treatment, and disease outcomes, was recorded from electronic records. Descriptive statistics were used.

Results: One hundred and nine patients were identified who underwent preoperative imaging. Ninety-four (86%) had no suspicion for metastatic disease, and 15 (14%) had suspicion for metastatic disease on preoperative imaging. Of these 94, 19 (20%) had a false negative study with metastatic disease identified on final surgical pathology with 18 (95%) receiving imaging within 6 weeks of surgery. Regarding imaging modality, 68% (13/19) had PET/CT; 26% (5/19) had an MRI; and 1 patient had a PET/CT and diagnostic CT. Of the 19 who had false negative imaging, disease was found to be in the pelvic lymph nodes in 11 patients (58%), parametria in 7 (37%), vaginal extension in 3 (16%), and uterine extension in 3 (16%). Sixty-three percent (12/19) underwent conization prior to surgery. Only 1 of these 12 patients (8%) had a tumor >2 cm on cone
specimen. Only 1 (8%) had positive lymphovascular space invasion on cone. Of the 15 with possible metastatic disease on imaging, 60% had a false positive study with no metastatic disease identified on final surgical pathology.

**Conclusion:** Preoperative imaging is a commonly utilized tool to help identify cervical cancer patients who are optimal candidates for radical surgery. In this sample, the false negative rate of preoperative imaging was 20%. Further study is needed to explore preoperative testing that may more accurately identify patients who are optimal surgical candidates for cervical cancer treatment.

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**2318 - Poster Session**

**Provider characteristics and adherence to cervical screening best practice guidelines at an academic health system**


**Objective:** We sought to characterize cervical cancer screening practice patterns at the provider level for a single academic health system.

**Method:** In this observational cohort study, we identified women aged 30–65 years who underwent index cervical cytology, high-risk HPV co-testing between 2007 and 2017 and second testing between 2012 and 2017. Two serial co-tests defined a “paired co-test.” Patients with any diagnosis of dysplasia or gynecologic malignancy prior to second screen were excluded. Provider-level factors were collected to assess their impact on the time interval between paired co-tests. Univariate and bivariate parametric analyses were performed.

**Results:** We identified 90 providers who performed 23,157 paired co-tests, with a median interval of 13 months (range 3–45 months) between co-tests. Providers performed a median of 356 screens per year. Physicians had the shortest median interval between co-tests, followed by nurse practitioners, and midwives (13, 14, and 15 months, respectively, \( P < 0.001 \)). During the study period, the mean screening interval increased from 14.6 months (2012–2014) to 18.1 months (2015–2017, \( P < 0.001 \)). Female providers had longer mean screening intervals than males (16.8 vs 14.3 months, \( P < 0.001 \)). Academic physicians had longer mean screening intervals than private practitioners (16.2 vs 15.1 months, \( P < 0.001 \)). Internal medicine and family medicine practitioners had longer screening intervals than obstetrics/gynecology-trained practitioners (17.4 vs 15.4 months, \( P < 0.001 \)). The median screening interval per individual provider was calculated; the median across providers was 14 months (IQR 13–15.5, range 6–38).

**Conclusion:** Despite guidelines recommending a co-testing interval of 5 years in low-risk populations, the average co-testing interval for this population at an academic center was only slightly more than 1 year. While screening intervals improved over time, the majority of providers did not adhere to best practice guidelines. By identifying those providers with poor adherence to screening guidelines, increased education and resources may be better targeted.

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**2319 - Poster Session**

**BRCA screening patterns, demographics, and clinical characteristics among women with second-line ovarian cancer: Results from the Adelphi Disease Specific Cancer Programme**

M.I. Monberg, J.P. Hall, R. Moon, O. Higson, K. McLaurin and T. Dalvi. *aMerck & Co., Inc., Kenilworth, NJ, USA, bAdelphi Real World, Manchester, United Kingdom, cAstraZeneca, Gaithersburg, MD, USA

**Objective:** Three poly(ADP-ribose) polymerase inhibitors (PARPis) are approved within the United States and/or the European Union in second-line (2L) ovarian cancer (OC): olaparib, rucaparib, and niraparib. This analysis describes BRCA-screening patterns, demographics, clinical characteristics, and the use of PARPis as maintenance within a real-world sample of 2L OC.

**Method:** This cross-sectional study included patients undergoing active treatment for OC. Data were collected from 2,496 patient forms between December 2017 and March 2018 from 340 oncologists and gynecologists across the United States (\( n = 630 \)), France (\( n = 407 \)), Germany (\( n = 400 \)), Italy (\( n = 363 \)), Spain (\( n = 261 \)), and the United Kingdom (\( n = 335 \)). In addition to providing demographic and clinical characteristics, physicians also reported reasons for choice of maintenance therapy.

**Results:** Of 1,315 patients receiving 2L at the point of data abstraction, 17% (\( n = 219 \)) were actively receiving 2L maintenance. In Europe, 62% of all 2L patients had been screened for BRCA compared with 46% in the United States, but PARPi usage was
not different between Europe and the United States. Among patients receiving 2L maintenance, 47% (n = 103) received a PARPi-containing regimen and 53% (n = 116) received a non-PARPi-containing regimen. The most common non-PARPi maintenance regimens were bevacizumab (42% of non-PARPi maintenance patients, in combination or as monotherapy), platinum (35%, in combination or as monotherapy), and liposomal doxorubicin (7%, monotherapy). Compared with non-PARPi maintenance patients, more patients receiving a PARPi had serous histology, were screened for BRCA, were BRCA positive, had a complete response to 1L regimen, and received a platinum as 2L treatment (prior to maintenance). See Table 1.

Conclusion: Despite guidelines recommending testing, a significant percentage of 2L OC are not currently screened for BRCA, especially in the United States. Nonetheless, decisions related to PARPi use in 2L maintenance appear to be driven by BRCA status, histology, and response to 1L.

Table 1.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Total patients</th>
<th>Total patients receiving 2L maintenance at point of data abstraction</th>
<th>2L maintenance patients receiving a PARPi at point of data abstraction</th>
<th>2L maintenance patients not receiving PARPi at point of data abstraction</th>
<th>2L treatment patients at point of data abstraction</th>
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<tbody>
<tr>
<td></td>
<td>1315</td>
<td>219</td>
<td>103</td>
<td>116</td>
<td>1096</td>
</tr>
<tr>
<td>Mean age</td>
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<td>60.8</td>
<td>61.8</td>
<td>58.9</td>
<td>63.8</td>
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<td>Serous histology</td>
<td>63%</td>
<td>59%</td>
<td>74%</td>
<td>47%</td>
<td>64%</td>
</tr>
<tr>
<td>Family history of OC</td>
<td>10%</td>
<td>18%</td>
<td>27%</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Screened for BRCA (% of total number)</td>
<td>53%</td>
<td>57%</td>
<td>83%</td>
<td>33%</td>
<td>52%</td>
</tr>
<tr>
<td>Positive for BRCA (% of those screened)</td>
<td>28%</td>
<td>59%</td>
<td>70%</td>
<td>34%</td>
<td>22%</td>
</tr>
<tr>
<td>Received 1L maintenance, n (%)</td>
<td>585 (44%)</td>
<td>119 (54%)</td>
<td>50 (49%)</td>
<td>69 (56%)</td>
<td>465 (43%)</td>
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<td>1L outcome (to treatment or maintenance)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>46%</td>
<td>46%</td>
<td>71%</td>
<td>23%</td>
<td>46%</td>
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<tr>
<td>Partial response</td>
<td>27%</td>
<td>35%</td>
<td>19%</td>
<td>48%</td>
<td>25%</td>
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<tr>
<td>Stable disease</td>
<td>8%</td>
<td>5%</td>
<td>4%</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td>Disease progression</td>
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<td>7%</td>
<td>2%</td>
<td>12%</td>
<td>16%</td>
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<tr>
<td>2L treatment contained a platinum</td>
<td>59%</td>
<td>66%</td>
<td>85%</td>
<td>49%</td>
<td>57%</td>
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<tr>
<td>Reasons for choice of 2L maintenance therapy</td>
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<td></td>
<td></td>
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<tr>
<td>High response rate</td>
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<td>29%</td>
<td>35%</td>
<td>24%</td>
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<tr>
<td>PFS benefit</td>
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<td>60%</td>
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<td>53%</td>
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<tr>
<td>Side effects profile</td>
<td>31%</td>
<td>42%</td>
<td>21%</td>
<td>27%</td>
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<tr>
<td>Improves quality of life</td>
<td>19%</td>
<td>37%</td>
<td>27%</td>
<td>27%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

2320 - Poster Session
Evaluation of superficial versus deep inguinal lymph node dissection in squamous cell carcinoma of the vulva
J.N. Mattsona, J. Emersonb, A. Kulkarnib, A. Underwoodc, G. Sunb, S.L. Mottb, K.M. Robisona and E.K. Hill5. aGynecologic Oncology, Iowa City, IA, USA, bWomen & Infants Hospital, Brown University, Providence, RI, USA, cUniversity of Iowa, Iowa City, IA, USA, dWomen & Infants Hospital, Brown University, Providence, RI, USA

Objective: Our objective was to evaluate difference in recurrence rates, OS, and postoperative morbidity of superficial (above the cribriform fascia only) versus deep (above and below the cribriform fascia) inguinal lymph node dissection (LND) in squamous cell carcinoma (SCC) of the vulva.
Method: A retrospective cohort of 167 patients with vulvar SCC who underwent inguinal LND at the University of Iowa Hospitals & Clinics or Women & Infants Hospital from 1999 to 2017 were analyzed. Demographic, surgical, recurrence, survival, and postoperative morbidity data were collected. \(\chi^2\) and Fisher exact tests were used in comparison analysis, and Kaplan-Meier curves were used to analyze survival and recurrence data.

Results: There were 280 groin dissections in our cohort of 167 patients; 182/280 (65%) of inguinal dissections were deep, and 98/280 (35%) superficial. There was no difference in recurrence rates (vulvar, groin, and distant) between the 2 cohorts, and in particular, groin recurrence rates for deep versus superficial dissections were similar (5.6 vs 1.7%, \(P = 0.42\)). There was also no difference in OS survival between the 2 cohorts (\(P = 0.76\)). A significant difference in the rate of overall postoperative morbidity was found between deep and superficial LND (74.5 vs 54.2%, \(P = 0.01\)). This included increased rates of lymphedema (44.9 vs 22.9%, \(P = 0.01\)), readmission (27.6 vs 6.3%, \(P < 0.01\)), and infection (41.8 vs 25.0, \(P = 0.05\)), which were all significantly higher among patients undergoing deep LND.

Conclusion: In patients with SCC of the vulva, superficial inguinal LND had no significant difference in groin recurrence or overall survival when compared to deep inguinal LND. However, those who received a deep nodal dissection did have significantly increased overall morbidity, including lymphedema, readmission, and infection. When sentinel lymph node mapping fails or is contraindicated, our data suggest that a superficial inguinal LND has similar recurrence and survival outcomes with a reduction in overall morbidity when compared to a deep LND.

2321 - Poster Session
Resource utilization in the final 30 days of life for Medicare patients with ovarian cancer: An opportunity for improvement
H.J. Smith, M.I. Liang and W. Huh. University of Alabama at Birmingham, Birmingham, AL, USA

Objective: The objective of this study was to assess management of Medicare patients with ovarian cancer during the final days of life, specifically evaluating hospital admissions, utilization of palliative care and hospice resources, and total spending.

Method: This was a pre-intervention evaluation for a quality improvement project with the intent to improve end-of-life care for ovarian cancer patients at a comprehensive cancer center. Medicare administrative data were used to identify all patients with ovarian cancer who received at least 1 dose of chemotherapy and had a subsequent death claim filed in the period between July 2016 and December 2017. Total cost of care during the last 30 days of life was obtained from Medicare claims. Information regarding treatment history, hospital admissions, and hospice referrals was obtained by review of the electronic medical record. Groups were compared using two-tailed \(t\) test.

Results: There were 18 Medicare patients with ovarian cancer who met inclusion criteria. The mean age was 74 years (range 66–86 years). All but 1 patient had recurrent disease, and the majority of patients had been heavily pretreated with a mean of 4.6 lines of chemotherapy (range 1–7). Half of the patients had an inpatient admission in the last 30 days of life, all for uncontrolled symptoms of disease. The primary indication for admission was nausea/vomiting in 5 patients (55.6%) and dyspnea in 4 patients (44.4%). The majority of patients (83%) were on hospice at the time of death; however, the mean length of time on hospice was only 22.2 days (range 1–59 days). Only 2 patients had a documented goals-of-care discussion prior to their death or day of hospice referral. The total cost of care in the last 30 days for these 18 patients was $157,773. Mean cost per patient was significantly higher in the patients who had an inpatient admission in the last 30 days of life ($14,683 vs $2,847, \(P = 0.001\)).

Conclusion: While the majority of these ovarian cancer patients were on hospice at the time of death, the average time from hospice referral to death was approximately 3 weeks. Half of the patients had an inpatient admission for symptom control during their final 30 days, which was associated with a substantial increase in cost. Earlier hospice referral may avoid hospital admissions at the end of life and result in both better symptom control and decreased cost of care.

2322 - Poster Session
Relative importance of diet and physical activity in cancer survival: An analysis of the US national health and nutrition examination survey
J.K. Chan, a A.K. Mann, b A. Koh-Bell, c J.E. Chan, c and D.S. Kapp, d aCalifornia Pacific Medical Center, San Francisco, CA, USA, bPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, cCalifornia Pacific and Palo Alto Medical Foundation/Sutter Research Institute, San Francisco, CA, USA, dStanford University School of Medicine, Stanford, CA, USA
Objective: The aim of this study was to evaluate the impact of diet and physical activity on cancer mortality in women.

Method: Data were extracted from the Third U.S. National Health and Nutrition Examination Survey (NHANES III) on all respondents from 1988 to 1994. χ², multivariable Cox regression, and Kaplan-Meier estimates were employed for statistical analyses. Healthy Eating Index (HEI), based on intake of different food groups and nutrients, was used as a measurement of diet quality. Physical activity was defined based on metabolic equivalent (MET) intensity levels, and categorized into low and high based on American Heart Association guidelines.

Results: Of 3,196 women (median age 55 years, range 42–89 years), 87% were white, 9% black, and 3% Hispanic. Twenty-seven percent were obese (BMI ≥30 kg/m²), while 73% were non-obese (BMI <30.0 kg/m²). Twenty-two percent reported eating healthy diet, 69% needs improvement, and 8% poor diet. Self-reported physical activity were divided into 20% inactive, 53% not meeting criteria, and 28% meeting guidelines. Diet and lower physical activity were both correlated with increased cancer mortality. Those with a healthy diet and high physical activity had a significantly lower mortality rate compared to those with poor diet and low physical activity (P = 0.02). On multivariate analysis, both healthy diet (HR = 0.63, 95% CI 0.43–0.93, P = 0.02) and lower physical activity (HR = 1.37, 95% CI 0.91–2.06, P = 0.13) were found to be independent predictors for decreased cancer mortality. Of note, those who have a healthy diet but low physical activity have a lower risk of cancer mortality compared to patients with unhealthy diet but high physical activity (P = 0.01)

Conclusion: Our data suggest that poor diet and low physical activity are associated with the risk of cancer mortality. It appears that eating well is has more of an impact on cancer survival than exercising.

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2323 - Poster Session
Implementation of routine clinical collection of electronic patient reported outcomes in patients with gynecologic malignancy

R.M. Clark a,b and M.G. del Carmen a,b,c. aHarvard Medical School, Boston, MA, USA, bMassachusetts General Hospital/Harvard University, Boston, MA, USA, cMassachusetts General Hospital, Boston, MA, USA

Objective: The purpose of this study was to describe the initial experience with broad implementation of electronic patient-reported outcomes (PROs) at a large teaching hospital.

Method: PRO questionnaires were built on an EPIC and Citrix platform and could be completed by iPAD at clinic or at home via a portal. All patients received the EORTC QlQ-C30 and then self-identified whether they were there for an issue regarding their ovaries, uterus, cervix, or vulva/vagina or “I don't know.” Surveys were then administered for respective disease sites (EORTC OV28, EORTC Cervix, EORTC Uterus, FACT V), as well as the PROMIS Emotional and Instrumental Support questionnaires. Medical patients were assigned questionnaires every 90 days, whereas surgical patients were assigned both preoperative and postoperative questionnaires. Results were immediately available in the patient’s medical record.

Results: Within 90 days, 266 patients had completed a questionnaire. The overwhelming majority of patients who responded identified as white (96%) and primarily English-speaking (94%). Collection rates varied significantly by surgeon (18%–70%, P < 0.05). If a patient initiated a questionnaire, there was a 100% completion rate. Completion rates varied by visit type: new patients who had been referred specifically to a physician (100%), general new patients (58%), patients presenting for chemotherapy (20%), and postoperative patients (27%). Older patients (55 years or older) were more likely than younger patients to use the patient portal to complete their assigned PROs ahead of their clinic visit (P < 0.05). Patients older than 75 years had a 50% portal completion rate, whereas patients younger than 35 years had a 5% portal completion rate.

Conclusion: Implementation of routine clinical collection of PROs is feasible. Significant provider variation exists, indicating opportunity for quality improvements. Patients found the questionnaires feasible and acceptable, with 100% completion if survey was initiated. Patients who had requested a specific provider seemed more motivated to complete PROs. The lowest completion rates were in postoperative and chemotherapy patients, indicating that these cohorts may benefit from specific targeting. Older patients were most likely to use online portals for survey completion.

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2324 - Poster Session
**Objective:** Our study aims to compare universal tumor testing (UTT) to personal and family history as screening tools to identify Lynch syndrome (LS) among women diagnosed with endometrial cancer (EC).

**Method:** This was a retrospective study of all patients who underwent surgery for EC between January 1, 2016, and May 31, 2018, identified through the institutional tumor registry and cross-referenced with the Department of Pathology database to ensure complete case capture. Universal tumor testing with immunohistochemistry (IHC) staining for mismatch repair (MMR) proteins MLH1, MSH2, MSH6, and PMS2 was performed, regardless of patients’ personal or family cancer history or age. Positive IHC resulted in referral for genetic counseling (GC) as methylation testing has not proven to be efficient or cost-effective at our institution. Individuals at risk for LS meeting Amsterdam I or II criteria or revised Bethesda guidelines were identified and referred for GC.

**Results:** A total of 261 patients with EC underwent surgery during the study period. IHC staining for MMR proteins was performed in 194 women (74.3%) despite there being an institutional UTT policy. Sixty-six patients (34.1%) had a positive screening test and were referred for genetic evaluation (GE); 27 patients (40.3%) underwent GC, and 20 (30.3% of those with positive IHC and 74% of those who were counseled) elected to undergo testing, with 5 women (2% of all EC patients and 7.6% of those with positive IHC) diagnosed with LS through germline testing. When clinical criteria were applied, 30 individuals (11.5%) were identified to be at high risk for LS and were referred for GE. Of those 30 women, 13 (43.3%) received GC and testing, and 7 women were confirmed to have LS (2.7% of all EC patients and 23.3% of those with positive clinical criteria). Of the 89 women referred for GE, only 21 (31.5%) underwent GC and testing. See Figure 1.

**Conclusion:** Even with UTT, not all tumors are being tested. Systemic solutions are needed to improve the percentage of patients who will be referred for GC and to improve compliance with the referrals. For the most comprehensive detection of patients with LS, UTT should likely not replace clinical risk assessment but rather be used in combination with clinical assessment to identify these patients.

**Fig. 1.** Lynch syndrome (LS) Flowchart
The role of chemotherapy and radiation in AJCC surgical stage I uterine papillary serous carcinoma: A retrospective analysis of 4,970 patients
C.I. Liaoa, D.P. Mysonab, J.X. Shec, A.K. Mannfd, L. Delicg, A.J. Huangf, D.S. Kappg and J.K. Chane. aKaohsiung Veterans General Hospital, Kaohsiung City, Taiwan, bMedical College of Georgia, Augusta, GA, USA, cGeorgia Regents University, Augusta, GA, USA, dPalo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, eCalifornia Pacific & Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA, fCalifornia Pacific Medical Center, San Francisco, CA, USA, gStanford University School of Medicine, Stanford, CA, USA

Objective: The aim of this study is to determine the role of chemotherapy and radiation in surgically staged I uterine papillary serous cancer (UPSC).

Method: Data were obtained from the National Cancer Database (NCDB) from 2004 to 2014. One-way ANOVA, χ² test, Cox regression, and Kaplan-Meier analyses were used.

Results: Of 4,970 stage I UPSC patients, the mean age was 67 (range 27–90) years; 3,647 (73.4%), 1,055 (21.2%), 165 (3.3%), and 103 (2.0%) were white, black, Asian, and other/unknown, respectively. All 4,970 patients underwent lymph node dissection, and 1,424 of these had omentectomy with their surgical staging. According to the American Joint Committee on Cancer seventh edition for surgical staging, 3,766 (75.8%) were stage IA, 914 (18.4%) were stage IB, and 290 (5.8%) were undefined stage I. A total of 1,833 (36.9%) underwent no adjuvant treatment, 1,076 (21.6%) chemotherapy only (CT), 517 (10.4%) radiation only (RT), and 1,544 (31.1%) both chemotherapy and radiation (CT/RT) after surgery. In stage IA, OS was 83.2%. The OS for no treatment was 76.0% versus 89.7% for CT (P < 0.001), 79.1% for RT (P = 0.028), and 89.3% for CT/RT (P < 0.001). For stage IB, the OS was 69.5%. The OS for no treatment was 52.6% compared to 76.3% for CT (P < 0.001) and 50.0% for RT (P = 0.423), and CT/RT was 81.8% (P < 0.001). The use of CT/RT increased from 10.4% in 2004 to 38.7% in 2014 (annual percentage change 7.0%, P < 0.05). On multivariate analysis, younger age (HR = 1.04, 95% CI 1.03–1.06, P < 0.001), black race (HR = 1.36, 95% CI 1.02–1.82, P < 0.035), and higher substage (HR = 1.57, 95% CI 1.23–2.02, P < 0.001) were independent predictors of worse survival. Omentectomy (HR = 0.70, 95% CI 0.55–0.89, P = 0.004), CT (HR = 0.38, 95% CI 0.27–0.52, P < 0.001), and CT/RT (HR = 0.43, 95% CI 0.33–0.58, P < 0.001) were predictors for improved survival.

Conclusion: Our data suggest that the addition of chemotherapy to radiation is associated with an OS benefit in stage I UPSC. In line with this, the use of CT/RT to treat stage I UPSC cancers has increased over time.

Minimization of narcotics use after gynecologic surgery in a low resource setting with minimal use of neuraxial analgesia
A. Hari, K. Brennan, P.A. Akametalu, K. Dessources, C.H. Holschneider and A.K. Sinn. aUniversity of California, Los Angeles, Los Angeles, CA, USA, bDavid Geffen School of Medicine at UCLA, Los Angeles, CA, USA, cMemorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: We sought to analyze outcomes of a nonnarcotic multimodal perioperative pain regimen and determine supplemental narcotic use using morphine equivalence doses (MED) for patients undergoing gynecologic and gynecologic oncology surgery.

Method: This was a retrospective analysis of patients who underwent open (XL) or minimally invasive (MIS) gynecologic or gynecologic oncology surgery requiring admission at a public safety net hospital between August 2017 and April 2018. The multimodal nonnarcotic protocol included gabapentin 600 mg POx1 preoperatively and around the clock (ATC) acetaminophen, NSAIDs (ketorolac or ibuprofen), and gabapentin postoperatively. Supplemental narcotics were added as needed (PRN) or ATC. Spinal anesthesia was optional; no patients received patient-controlled anesthesia. Demographic, clinicopathological, and treatment data were collected. Postoperative total MEDs were normalized by length of stay (LOS). Average daily MEDs were stratified into minimal (0–9), occasional (10–19), and frequent use (≥20).

Results: Of 108 eligible patients, 65 patients had XL and 44 MIS. Median age was 47 (range 18–69) years. Median LOS was 2 days for XL and 1 day for MIS. Fourteen patients (13%) were on preoperative narcotics, and 90 patients (83%) received preoperative gabapentin. Only 10 patients had neuraxanalgesia (9%). Using this multimodal nonnarcotic pain regimen,
The median maximum POD 1 pain score was 2 for patients with minimal, 7 for patients with occasional, and 8 for those with frequent use ($P < 0.001$). Minimal, occasional, and frequent narcotic use was not significantly correlated with XL versus MIS ($P = 0.47$) or benign versus malignant diagnoses ($P = 0.56$). Preoperative gabapentin was associated with decreased LOS (2.1 vs 2.66 days, $P < 0.05$) and decreased median POD 1 maximum pain scores (6 vs 7.5, $P < 0.05$). Post-discharge narcotic refills were required for 6 patients (5%), none of which were in minimal users.

**Conclusion:** Multimodal nonnarcotic perioperative pain management allows for near complete avoidance of postoperative narcotic pain medications in over half of gynecologic/gynecologic oncology patients. This regimen controls postoperative pain well with minimal use of neuraxial analgesia and rare need for ATC narcotics.

**2327 - Poster Session**

**Factors influencing disease recurrence in women with borderline tumors of the ovary**

L. Scanlon$^{ab}$, J. Kim$c$, A. Nizam$^{ab}$ and G.L. Goldberg$^{ab}$. $^a$Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA, $^b$Hofstra - North Shore Long Island Jewish School of Medicine, Manhasset, NY, USA, $^c$Northwell Health, New Hyde Park, NY, USA

**Objective:** Borderline tumors of the ovary (BOT) make up approximately 15%–20% of all ovarian neoplasms. These tumors are typically considered indolent and have an excellent prognosis in women who are treated with conservative surgery. Conservative surgery for BOT plays an important role for fertility preservation in these women, and it is usually curative. However, recurrence rates can approach 30%. The aim of this study was to compare the intraoperative factors influencing outcomes and recurrence in women with BOT.

**Method:** An Institutional Review Board-approved study identified all our patients with BOT between January 2008 and May 2018. Demographics were obtained from medical records and tumor registry. Potential prognostic factors for recurrence were studied including histological subtypes, modality and type of surgical procedure, and intraoperative rupture of the tumor.

**Results:** A total of 157 patients were identified; 145 of these women (92%) had stage I and 12 had stage III disease. There were 18 recurrences noted in the study population (12%). The median age of the women who had recurrent disease was 44 years (range 22–79 years). Eighty-nine patients (57%) underwent minimally invasive surgical procedures compared to 68 (43%) who had a laparotomy. Fourteen (78%) of the recurrences occurred in the minimally invasive group ($P = 0.086$). Of the minimally invasive procedures performed, 15 (17%) were an ovarian cystectomy. Seven (47%) who had an ovarian cystectomy had a recurrence during the study period ($P = 0.03$). Nine (50%) who recurred had intraoperative rupture of the cyst ($P = 0.001$). The median time to recurrence was 25 months (range 4–94 months). There was no difference in the recurrence rates between serous and mucinous histology ($P = 0.537$). The presence of microinvasion and micropapillary features was associated with advanced stage at diagnosis but not recurrence risk ($P = 1$).

**Conclusion:** Our data suggest that the risk of recurrence of BOT was associated with minimally invasive surgery, ovarian cystectomy, and intraoperative cyst rupture. Our data also suggest that planning and counseling to select the appropriate surgical procedure with regard to the patient’s priorities and future fertility goals is important. It is important to minimize the anxiety associated with possible tumor recurrence and future fertility.

**2328 - Poster Session**

**Association between metabolic syndrome and endometrial cancer survival in a SEER-Medicare linked database**

J. Jin, S. Dalwadi, R. Masand, T.R. Hall, M.L. Anderson and M. Ludwig. Baylor College of Medicine, Houston, TX, USA

**Objective:** Metabolic syndrome (MS) is linked to increased endometrial cancer risk. This study examines the association between MS and endometrial cancer-specific survival (CSS) in early-stage (ES) and locally advanced (LA) disease.

**Method:** The Surveillance, Epidemiology End Result–Medicare linked database was used to identify patients with nonmetastatic endometrial cancer between 1992 and 2011 who underwent hysterectomy. Patients without complete stage or grade information were excluded. Patients were stratified into ES (stage I–II) or LA (stage III–IVa). MS status was determined through Medicare claims 1 year prior to diagnosis. The effect of MS on CSS was evaluated using univariate (UVA) and multivariate (MVA) Cox proportional hazards regression analyses.
Results: A total of 10,090 patients with endometrial cancer were identified; 86.6% of patients were ES, 13.4% were LA, and 16% had MS. MS was not associated with CSS on UVA. On MVA, age, adjuvant treatment, income, year of diagnosis, histopathology, race, comorbidity score, and MS were associated with CSS (all \( P < 0.01 \)). The presence of MS was associated with worse CSS in ES disease (HR = 1.31, 95% CI 1.09–1.57, \( P = 0.0026 \)); this difference did not exist for LA disease (HR = 1.16, 95% CI 0.90–1.48, \( P = 0.2367 \)). See Table 1.

Conclusion: In early-stage endometrial cancer patients older than 65 years, MS is associated with worse CSS. Control of MS may improve CSS in this population.

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2329 - Poster Session

A multi-centre prospective study comparing costs between robotics, laparoscopy and laparotomy in management of endometrial cancer

S.E. Ferguson\(^a\), T. Panzarella\(^b\), S. Lau\(^c\), L.T. Gien\(^d\), V. Samouelian\(^e\), H. Steed\(^f\), B. Renkosinski\(^g\), S. Kosa\(^h\) and M.O. Bernardini\(^i\).

\(^a\)University of Toronto, Toronto, ON, Canada, \(^b\)University of Toronto, Dalla Lana School of Public Health, Toronto, ON, Canada, \(^c\)McGill University - Jewish General Hospital, Montreal, QC, Canada, \(^d\)Université de Montréal - Hôpital Notre Dame, Montreal, QC, Canada, \(^e\)University of Alberta, Edmonton, AB, Canada, \(^f\)Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, \(^g\)Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Objective: To compare the immediate operating room, inpatient, and overall costs between three surgical modalities—laparotomy, laparoscopy, and robotics—among patients with endometrial cancer. The differences in costs between the three surgical modalities were also compared among patients with a BMI <40 and ≥40.

Method: A multicenter prospective observational study examined outcomes of women, with early-stage endometrial cancer, treated surgically. Costs were captured from a hospital perspective (reported in Canadian dollars). Resource use was collected for operating room costs including operating room time and equipment costs (surgical materials, medications, trochars, disposable equipment, and nursing time) and for inpatient costs (nursing time, imaging, bloodwork, transfusions, medications, disposable materials). All comparisons of continuous variables across cohorts were analyzed using an independent-samples Kruskal-Wallis test (data were tested for normality assumptions using a Kolmogorov–Smirnov test).

Results: The study sample included 520 patients, of whom 513, 488, and 482 had sufficient data to be included in the operating room, inpatient, and overall cost analyses, respectively (Table 1). The operating room costs were lowest for laparotomy and then laparoscopy and highest for robotics (median = $4,266.38 vs $5,209.27 vs $7,422.22, respectively, \( P < 0.001 \)). The inpatient costs were higher for laparotomy and laparoscopy compared to robotics ($5,881.61 vs $1,782.63 vs $1,726.31, respectively, \( P < 0.001 \)). The overall costs were highest for laparotomy, lowest for laparoscopy, with robotics in between ($10,298.20 vs $7,422.04 vs $9,162.20, respectively, \( P < 0.001 \)). For women with BMI ≥40, total costs were not statistically different among laparotomy, laparoscopy, and robotics ($10,291.50 vs $8,412.63 vs $9,002.48, \( P = 0.185 \)).

Conclusion: Among all patients, the overall cost was highest for laparotomy and lowest for laparoscopy with robotics between the two groups. Among patients with a BMI ≥40, there was no difference in cost between the 3 surgical modalities.

Table 1. Surgical, inpatient, and overall costs compared by surgical group among all patients, patients with BMI <40, and patients with BMI ≥40.
### Predictors of 30-, 60-, and 90-day hospital readmissions after ovarian cancer cytoreductive surgery: A nationwide readmissions database study


**Objective**: Patients with ovarian cancer (OC) have multiple comorbid conditions, undergo radical procedures, and are at high risk of readmission after cytoreductive surgery (CRS). Prior studies are limited in the ability to capture readmissions outside of the index hospital. Our study aim was to evaluate predictors of readmission for OC patients undergoing CRS on a national scale.

**Method**: The Nationwide Readmissions Database from the Healthcare Cost and Utilization Project was queried to identify all OC patients undergoing CRS during the period 2010–2015. CRS procedures were categorized using ICD-9 codes as simple pelvic (SP, removal of reproductive organs, lymph nodes, omentectomy), extensive pelvic (EP, addition of bowel or bladder resection), or extensive upper abdominal (EUA, addition of diaphragm stripping, splenectomy, pancreatectomy, and/or liver resection). Thirty-, 60-, and 90-day readmissions were identified. Multivariate logistic regressions were used to identify independent predictors for readmission.

**Results**: A total of 61,833 patients (weighted) were identified, and 20.6% experienced a 30-, 60-, or 90-day hospital readmission. Most readmissions (55%) occurred during the first 30 days. Teaching hospitals were more likely to perform EP or EUA CRS \((P < 0.001)\), and extent of CRS was adversely correlated with 30-, 60, and 90-day readmission rates \((P < 0.001)\). On multivariate analysis, predictors of 30-day readmission included length of hospital stay \((\text{OR} = 1.04)\), Elixhauser comorbid conditions \(> \text{2} \text{ (OR} = 1.39)\), and Medicaid \((\text{OR} = 1.30)\) or Medicare \((\text{OR} = 1.26)\) payer status (ref: private insurance), whereas SP CRS

<table>
<thead>
<tr>
<th>Cost CAN$</th>
<th>Laparotomy</th>
<th>Laparoscopy</th>
<th>Robotics</th>
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<tr>
<td><strong>Median</strong></td>
<td><strong>Median</strong></td>
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<td><strong>p-value</strong></td>
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<td><strong>(95.0% Lower &amp; Upper CL)</strong></td>
<td><strong>(95.0% Lower &amp; Upper CL)</strong></td>
<td><strong>(95.0% Lower &amp; Upper CL)</strong></td>
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<tr>
<td>All patients</td>
<td>4266.38 (4110.43, 4487.63)</td>
<td>5209.27 (5023.79, 5467.13)</td>
<td>7422.22 (7225.16, 7623.37)</td>
</tr>
<tr>
<td>Surgical</td>
<td>5881.61 (4897.79, 6147.61)</td>
<td>1782.60 (1695.47, 1916.00)</td>
<td>1726.31 (1689.93, 1790.67)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>10298.20 (9538.78, 10910.79)</td>
<td>7426.04 (7057.05, 7863.12)</td>
<td>9162.20 (8982.98, 9505.68)</td>
</tr>
<tr>
<td>Overall</td>
<td>4388.28 (4093.22, 4737.40)</td>
<td>5199.31 (4973.59, 5461.00)</td>
<td>7500.39 (7312.14, 7696.10)</td>
</tr>
<tr>
<td>BMI&lt;40</td>
<td>5850.55 (4897.79, 6164.39)</td>
<td>1774.55 (1682.11, 1858.73)</td>
<td>1696.00 (1641.53, 1753.67)</td>
</tr>
<tr>
<td>Surgical</td>
<td>10241.31 (9376.00, 10942.44)</td>
<td>7249.73 (6891.89, 7780.25)</td>
<td>9181.23 (9025.07, 9664.97)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>4197.02 (3677.86, 4487.63)</td>
<td>5524.63 (4775.38, 6816.41)</td>
<td>7225.16 (6814.52, 7648.22)</td>
</tr>
<tr>
<td>Overall</td>
<td>5584.28 (4444.31, 8389.55)</td>
<td>3042.07 (1783.35, 3109.85)</td>
<td>1794.51 (1742.09, 1923.35)</td>
</tr>
<tr>
<td>BMI&gt;40</td>
<td>10291.50 (8536.98, 15062.97)</td>
<td>8412.63 (7891.04, 10798.15)</td>
<td>9002.48 (8597.72, 9762.23)</td>
</tr>
</tbody>
</table>
(ref) was associated with a lower risk of readmission compared to EUA CRS (OR = 0.62). These trends were almost identical for 60- and 90-day readmissions.

**Conclusion:** Thirty-, 60-, and 90-day hospital readmission rates after OC CRS were high, especially for patients undergoing radical procedures. The true readmission rate after OC CRS is 20.6%, capturing index and nonindex hospital readmissions and both short- and long-term outcomes. Teaching hospitals performed significantly more radical CRS and had more readmissions than nonteaching hospitals, indicating that readmission may not be an appropriate marker for quality improvement without proper risk adjustment.

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**2331 - Poster Session**

**Brain metastases in patients with gynecologic cancers: National trends in incidence and management**

A.I. Tergasa, L. Chenb, C.M. St. Clair³, J.Y. Hou, F. Khoury Collado, A. Neugut, D.L. Hershman⁴ and J.D. Wright⁵.²⁶

- New York-Presbyterian/Columbia University Medical Center, New York, NY, USA
- Columbia University College of Physicians and Surgeons, New York, NY, USA
- Columbia University, New York, NY, USA

**Objectives:** Brain metastases (BM) from gynecologic cancers are considered a rare event. However, the incidence may be increasing because of improved survival rates. Standard-of-care management is unknown. The purpose of this study is to examine trends in incidence and management of BM in patients with gynecologic cancers (GC).

**Method:** The Premier Perspective Database was used to identify patients with uterine, ovarian, or cervical cancer and BM from 2006 to 2015. For the purposes of the trend analysis, only the index admission/visit was included. A Pearson correlation test was performed to assess the change in number of patients with GC and BM over time, with year/quarter as a linear variable.

**Results:** A total of 6,433 GC patients with BM were identified; 35% of patients had multiple admissions/visits. A total of 3,219 unique patient initial admissions/visits were included. There was a significant increase in number of patients with GC and BM from 2006 (7.9%) to 2014 (12.9%) (P < 0.001) (see **Figure 1**). The majority of these index admissions were urgent/emergent (65.3%) versus elective (27.5%) or unknown (7.2%). Median length of stay was 3 days (IQR 0–7 days). The majority were discharged home (66.6%) or transferred to another facility (21%). However, 9% were discharged dead. Of the 858 patients who underwent treatment during this index admission, 640 (74.6%) underwent whole brain radiation (WBRT), 155 (18%) underwent craniotomy, and 62 (7%) underwent multimodality treatment (various combinations of WBRT, craniotomy, and/or stereotactic radiosurgery). Overall, complication rates for each of these treatment modalities were low, ranging from 0 to 5.9% for WBRT, 0 to 6.4% for craniotomy, and 0 to 4.1% for stereotactic radiosurgery.

**Conclusion:** Brain metastases in patients with gynecologic cancers are becoming more common, with varying treatment approaches. These findings may have important implications regarding optimal surveillance for patients with gynecologic cancers, and further research is needed to determine standard-of-care treatment for this increasingly common clinical scenario.
Objective: We sought to evaluate the safety and cost savings of implementing presurgical testing guidelines in patients undergoing hysterectomy for endometrial cancer.

Method: Evidence-based presurgical testing guidelines were developed by a multidisciplinary team for institutional implementation. These guidelines were activated on the gynecologic surgery service at the ambulatory surgical unit of a comprehensive cancer center in January 2016. All patients with a diagnosis of endometrial cancer or complex atypical hyperplasia who underwent surgery at the ambulatory care center during the specified time periods were included in this analysis. Pre- and post-period analyses were performed with the pre-period defined as July 2014–December 2015 and the post-period as July 2016–December 2017. Rates of presurgical tests completed and the occurrence of perioperative adverse events were compared between the pre- and post-periods. Cost savings related to the reduction in presurgical testing performed in the pre- and post-periods were calculated and normalized in Medicare equivalent dollars per institutional protocol for cost analyses.

Results: A total of 749 hysterectomies were completed in the pre-period and 775 in the post-period. After implementation of presurgical testing guidelines, complete blood counts (CBC), coagulation testing (PTT), comprehensive metabolic panels (CMP), chest x-rays (CXR), and electrocardiograms (EKG) were reduced by 13.4%, 78.1%, 36.8%, 39.0%, and 15.5%, respectively (P values were all <0.001). Rates of perioperative cardiopulmonary adverse events were stable (0% vs 0%) across periods. Rates of perioperative hematologic adverse events were stable in the pre- and post-periods (3.3% vs 2.0%, P = 0.10). There were 0 deaths within 90 days after surgery in the post-period. There was a cost savings associated with this intervention that was proportional to the percentage of testing reduction.
**Conclusion:** Implementation of evidence-based presurgical testing guidelines is both safe and cost-effective in endometrial cancer patients. A team approach with multidisciplinary expertise is essential for successful guideline development and implementation. Use of streamlined testing guidelines is increasingly important as quality metrics and bundled payment schedules are a central component of the current landscape for health care policy and reimbursement.

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**2333 - Poster Session**

**Whole population BRCA screening is cost effective in Israel, even with varying prevalence of BRCA mutation**


aLis Maternity Hospital - Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, bTel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, cTASMC, Tel Aviv, Israel

**Objective:** Prevalence of BRCA mutation carrier state in Israel varies according to country of origin and reaches 2.5% among Ashkenazi Jews. Our objective was to investigate the cost-effectiveness of whole population screening for BRCA mutation in Israel.

**Method:** Lifetime costs of whole female population screening for BRCA mutation carrier state versus nonscreening were compared using a Markovian process decision analysis model. Model parameters and BRCA mutation prevalence in Israel were obtained from previously published data and survival curves of breast and ovarian cancer patients, respectively. Screening and other treatment-related costs were received from the Israeli Ministry of Health Pricing list according to specified codes. Quality-adjusted life years (QALYs), which reflect both quality and quantity of life lived and are used for cost-effectiveness analysis (1 QALY equates to 1 year in perfect health), were based upon utility values published in the literature. Sensitivity analysis was conducted with all variables to evaluate model uncertainty as well as Monte Carlo simulation. Analysis was done for varying degrees of BRCA prevalence.

**Results:** In the base case model the incremental cost effectiveness ratio (ICER) was $4,194 (U.S. dollars) per QALY gained and $4,246 (U.S. dollars) per 1 year gained in life expectancy. Discount rate and population prevalence of BRCA carrier are the most influential parameters. Even for a prevalence rate of 1%, the ICER is acceptable ($6,288 U.S. dollars per QALY) (Figure 1).

**Conclusion:** Whole population screening for BRCA mutations among Israeli women, even when including low-prevalence, non-Ashkenazi Jews in the algorithm, was found highly cost-effective and should be offered as part of general health screening strategies by national medical insurance providers. Such algorithm can be applied for other countries, depending on local prevalence of BRCA mutation and costs of screening and treatment.

![Fig. 1. BRCA whole population screening sensitivity analysis](image-url)
Objective: The reported HPV vaccine rates in Japan have dropped from 70% to near zero because of concerns of safety. We proposed to compare the regional and systemic safety profiles of HPV vaccine in Japanese versus whites in a meta-analysis to address these beliefs.

Method: Adverse reaction data were extracted from (1) Japanese national (Japanese regulatory agency open label phase III study), (2) Japanese international registration trial (NCT00543543 randomized study 001), and (3) European trial (NCT01304498 centers). A meta-analysis was performed to compare these events using a random mixed model effect.

Results: Of 526 patients who underwent 9 valent HPV vaccination, ages ranged from 9 to 26 years. One hundred (19.0%) were Japanese national trial; 127 (24.1%) Japanese were from international study 001; and 299 (56.8%) were Europeans. The rates of pain (93.0% vs 81.9% vs 89.3%), swelling (42.0% vs 44.9% vs 43.8%), erythema (33.0% vs 40.2% vs 34.1%), and systemic adverse event (14.0% vs 11.8% vs 20.7%) were comparable among the Japanese-national, Japanese international Merck, and European trials, respectively. More importantly, the rate of serious adverse events were not different at 0% vs 0% vs 0.3%. See Figure 1.

Conclusion: Our data suggest that the rate of adverse reactions and serious events were comparable between the Japanese and Europeans.
targeted year can undergo the examination the next year. In the present analysis, for the females who did not receive cervical cancer screening at the age of 20 years, the screening results from the following year, at age 21 years, were included.

**Results:** From 2011 to 2013, the cervical cancer screening targets at age 20 years were born in 1991 to 1993; thus in 2010, when public subsidies started, they were over the targeted ages for receiving the HPV vaccine. The incidence of CIN3 or worse (CIN3+) for these unvaccinated girls was 0.09% (7/7,872). On the other hand, among screening targets from 2014 to 2016, born in 1994 to 1996, where the vaccination rate was 79%, there were no cases of CIN3+. This reduction in incidence of CIN3+ in the vaccinated generation was statistically significant ($P = 0.016$). The screening rates were similar in both groups ($P = 1.0$).

**Conclusion:** For the first time, we have clearly shown the preventive effect of the HPV vaccine for CIN3+ in Japan. We also found that there will be a reduction in the risk for future cervical cancer in women with birth years enjoying past public subsidies for the HPV vaccine. The risk of cervical cancer morbidity, for girls born in 2000 or later, is expected to increase to the same levels as for previous generations of unvaccinated women because their vaccination rate is again almost 0%.

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2336 - Poster Session

**Evaluation of cervical cancer screening among women tested for HIV or diagnosed with sexually transmitted infections in sub-saharan africa: A cross-sectional study**

Y.H. Sallah. Yale University School of Medicine, New Haven, CT, USA

**Objective:** Cervical cancer is a leading cause of cancer-related mortality among women in sub-Saharan Africa (SSA) where screening has gradually increased but remains significantly lower than in developed countries. STI testing is an opportunity to integrate cervical cancer screening into patient care among high-risk populations. This study aimed to characterize cervical cancer screening rates among women tested for HIV or diagnosed with STIs in 5 African countries. In addition, sociodemographic determinants of screening uptake were explored.

**Method:** The Demographic Health Survey (DHS) is a nationally representative survey that uses a 2-stage, clustered sampling design to collect data on numerous health outcomes. Data from five sub-Saharan African countries including Cote d’Ivoire (2011), Lesotho (2014), Namibia (2013), Kenya (2014), and Zimbabwe (2015) were abstracted and weighted using DHS sample weights. Univariate analyses were conducted, and variables with $P < 0.2$ were included in a multivariate logistic regression model using SAS.

**Results:** Of the 25,948 women included, approximately 24% were ever screened for cervical cancer with the highest screening rate in Namibia (46%) and lowest in Cote d’Ivoire (3%). The mean age of participants was 32 years; 87% had at least a primary school education; 55% resided in a rural area; and 13% were covered by health insurance. Approximately 85% of respondents have been tested for HIV, and 3.6% had a confirmed STI in the past 12 months. After adjusting for covariates, women tested for HIV were 4.34 times more likely to have been screened for cervical cancer (aOR = 4.34, 95% CI 3.50–5.38). STI diagnosis within the past year was not statistically significantly associated with cervical cancer screening (aOR = 1.24, 95% CI 0.98–1.57). Wealthier women with higher levels of education and any health insurance coverage and living in urban areas were more likely to be screened (Table 1).

**Conclusion:** Cervical cancer screening in SSA is significantly higher among women tested for HIV. Although there was no difference in screening rates, only 25% of diagnosed women with an STI in the past year were screened suggesting missed opportunities to integrate STI testing/treatment with cervical cancer screening.
Impact of beta blockers on survival outcomes in ovarian cancer: A nationwide population-based cohort study
M.H. Baek and Y.H. Park. Hallym University Sacred Heart Hospital, Anyang, Korea, Republic of (South)

Objective: The impact of beta blockers (BBs) on survival outcomes in ovarian cancer was investigated.

Method: By using Korean National Health Insurance Service Data, Cox proportional hazards regression was performed to analyze HRs with 95% CIs adjusting for confounding factors.

Results: Among 866 eligible patients, 206 (23.8%) were BB users, and 660 (76.2%) were nonusers. Among the 206 BB users, 151 (73.3%) were nonselective beta blocker (NSBB) users, and 105 (51.0%) were selective beta blocker (SBB) users. BB use in patients aged ≥60 years, longer duration use (≥1 year), Charlson comorbidity index (CCI) ≥3, and cardiovascular disease including hypertension were associated with better survival outcome. These findings were observed in both NSBB and SBB. When duration of medication was analyzed based on number of days, NSBB (≥180 days) was associated with improved OS with a relatively shorter period of use compared to SBB (≥720 days). In multivariate Cox proportional hazards model, longer duration of BB medication (≥1 year) was an independent favorable prognostic factor for both OS and disease-specific survival in ovarian cancer patients.

Conclusion: In our nationwide population-based cohort study, BB use was associated with better survival outcomes in ovarian cancer in cases of long-term duration of use, older patients, and cardiovascular and/or other underlying disease (CCI ≥3).

Cervical Cancer Screening and Cytologic Results in Korean Women
J.M. Lea and K.B. Leeb. aKyung Hee University, Seoul, Korea, Republic of (South), bGachon University Gil Medical Center, Incheon, South Korea

Objective: The annual incidence of cervical cancer has been steadily declining from 1999 to 2010, after the introduction of Pap smear as a national screening program and the statistical portal system of the Korean Central Cancer Registry (KCCR). The

### Table 1. Sociodemographic and clinical characteristics associated with cervical cancer screening.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Screened (n=6,113)</th>
<th>Not Screened (n=19,834)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>2.1%</td>
<td>7.6%</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>25.6%</td>
<td>35.1%</td>
<td>2.68 (2.13-3.42)</td>
<td>2.11 (1.65-2.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary</td>
<td>51.5%</td>
<td>46.0%</td>
<td>4.18 (3.35-5.29)</td>
<td>2.81 (2.21-3.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Higher</td>
<td>20.7%</td>
<td>11.3%</td>
<td>7.13 (5.49-9.26)</td>
<td>3.38 (2.57-4.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>61.7%</td>
<td>48.3%</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>38.3%</td>
<td>51.7%</td>
<td>0.56 (0.51-0.62)</td>
<td>0.63 (0.55-0.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wealth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poorest</td>
<td>5.8%</td>
<td>12.0%</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poorer</td>
<td>11.1%</td>
<td>16.1%</td>
<td>1.41 (1.17-1.69)</td>
<td>1.19 (0.99-1.43)</td>
<td>0.072</td>
</tr>
<tr>
<td>Middle</td>
<td>15.2%</td>
<td>18.4%</td>
<td>1.66 (1.39-2.00)</td>
<td>1.18 (0.97-1.43)</td>
<td>0.0975</td>
</tr>
<tr>
<td>Richer</td>
<td>25.9%</td>
<td>24.3%</td>
<td>2.22 (1.87-2.65)</td>
<td>1.23 (1.01-1.50)</td>
<td>0.04</td>
</tr>
<tr>
<td>Richest</td>
<td>42.0%</td>
<td>29.2%</td>
<td>2.89 (2.43-3.44)</td>
<td>1.15 (0.92-1.43)</td>
<td>0.223</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never in a union/divorced/widowed</td>
<td>31.6%</td>
<td>30.7%</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/living in partner</td>
<td>68.4%</td>
<td>69.4%</td>
<td>1.09 (1.01-1.21)</td>
<td>1.16 (1.05-1.29)</td>
<td>0.0048</td>
</tr>
<tr>
<td>Covered by Health insurance</td>
<td>32.9%</td>
<td>33.1%</td>
<td>3.24 (2.93-3.59)</td>
<td>2.22 (1.98-2.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STI testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever tested for HIV</td>
<td>97.1%</td>
<td>87.6%</td>
<td>4.92 (3.96-6.11)</td>
<td>4.34 (3.50-5.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Had an STI in last 12 months</td>
<td>3.7%</td>
<td>3.5%</td>
<td>2.14 (1.82-2.52)</td>
<td>1.24 (0.98-1.57)</td>
<td>0.076</td>
</tr>
</tbody>
</table>
Objective of this study is to evaluate the recent trend of cervical cancer screening, and the association between the change of screening rate and the cytologic results in Korean women from 2010 to 2015.

Method: The National Health Insurance Cancer Screening Program for five common cancers was provided from the National Health Insurance beneficiaries. The data, including population, the screening rate, and the cytologic results for cervical cancer were obtained from the database of the National Health Insurance Service and the KCCR.

Results: The screening rate for cervical cancer has been steadily increasing, from 40.3% in 2010 to 54.2% in 2015 (Figure 1). In general, age-specific cervical cancer screening rates have steadily increased from 2010 to 2015. In 2015, the screening rate, 59%~63%, was highest between the ages of 40 and 60 years compared to 43%~48% in age groups younger than 30 years and older than 70 years. In the elderly age group, the screening rate was relatively low, 12%, especially in those who are older than 80 years (Table 1). The overall regional screening rate seemed to increase; however, compared to 53% in the area near Seoul, the screening rate was relatively low in some provinces, that is, Kangwon, Jeonnam, and Kyungnam (Table 2). During this period, the incidence of cytologic abnormalities suggesting pre-invasive lesion increased from 1.8% (46,259) in 2010 to 2.4% (89,753) in 2014, whereas the cytologic malignancy decreased from 0.037% (966) in 2010 to 0.017% (646) in 2014 (Figure 2).

Conclusion: The improvement in the screening rate of cervical cancer in Korean women seems to be the result of strategies made by the health sector, such as an organized screening program with participation encouragement. With the widespread use of effective screening tests based on the National Health Insurance Cancer Screening Program for cervical cancer and early detection with proper management of premalignant lesions of the cervix, the incidence of cervical cancer has decreased steadily. However, the total number of cervical pathology including pre-invasive lesion, as well as malignancy, has increased. This indicates that screening programs could be useful for early detection of pre-invasive lesion and prevent progression to malignancy.

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2339 - Poster Session
Assessing knowledge and competence in the management of ovarian cancer: A 3-year longitudinal analysis of CME outcomes data
D.R. Cameron and R. Caracio. Medscape Education, New York, NY, USA
**Objective:** Over the past 2 decades, considerable research has led to the U.S. FDA approval of 3 new PARP inhibitors. These advances challenge community oncologists, obstetricians, gynecologists, and other members of the multidisciplinary team to assimilate evidence and guidelines into practice. The objective of this study was to assess their knowledge and competency over time with respect to the management of ovarian cancer.

**Method:** From 2014 to 2017, we developed 20 continuing medical education (CME) activities for health care professionals who treat patients with ovarian cancer. We have reached over 82,000 learners to date. Pre- and post-assessment data from CME activities were categorized into themes and evaluated with respect to baseline data. Results summarize trends over time for oncologists and obstetricians/gynecologists.

**Results:** Based on the results of assessments conducted over 3 years, our analysis found that an increased proportion of oncologists and obstetricians/gynecologists: (1) understood concepts of PARP inhibitor utility in patients with BRCA1/BRCA2 mutations (from 55% at activity baseline to 86% post-assessment in May 2015); (2) selected BRCA testing for appropriate patients with ovarian cancer (from 48% at baseline to 67% post-assessment in September 2017); (3) identified potential adverse events associated with the use of PARP inhibitors (from 20% at activity baseline to 75% post-assessment in October 2017); and (4) understood outcomes from PARP inhibitor clinical trials (from 24% at activity baseline to 61% post-assessment in December 2017). In a nursing activity launched in 2017, knowledge and competence improved among nurses regarding the management of patients with BRCA-mutated ovarian cancer, with a more than 3-fold improvement in nurses’ ability to identify the need for BRCA1/2 testing in patients in whom ovarian cancer is newly diagnosed and recognize and manage treatment-associated adverse events.

**Conclusion:** This analysis demonstrates that the knowledge and competency of oncologists and other health care professionals improved over time in regard to the management of ovarian cancer (including understanding the clinical trial data and science behind emerging agents, which patients required BRCA testing, and the management of adverse events from novel agents), as measured through a longitudinal analysis of CME outcomes data from activities designed to achieve these ends.

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**2340 - Poster Session**  
**HPV types and lineages in Ugandan women with cervical cancer**  
**E.S. Wu, N.M. Mugisha, L.F. Xia, W. Phipps, A. Larsen, C. Nakisige and S.M. Schwartz.**  
*University of Washington Medical Center, Seattle, WA, USA, Uganda Cancer Institute, Kampala, Uganda, Fred Hutchinson Cancer Research Center, Seattle, WA, USA*

**Objective:** The aim of this study was to characterize the association between HPV DNA lineages and HIV status, and its impact on cervical cancer survival in Uganda.

**Method:** A prospective cohort of patients diagnosed with cervical cancer between July 2013 and February 2018 at the Uganda Cancer Institute was identified. Medical history, HIV test, and tumor tissue were obtained upon enrollment. HPV types were determined with Roche Linear Array and variants with PCR-based direct sequencing of the LCR/E6/E7 region. OS was assessed using Cox regression.

**Results:** HPV results are available for 241 patients. Median age was 48 (IQR 40–57) years. The majority (94%) had squamous cell carcinoma. At diagnosis, 40% were stage III–IV. HIV status was known in 212 patients, of whom 44% were HIV-positive (pos) and 56% HIV-negative (neg). Cervical cancer stage was similar between HIV-pos and HIV-neg patients. HPV was detected in 221 (92%) of samples. The distribution (not mutually exclusive) of HPV types was 46% HPV16, 23% HPV18, 12% HPV45, 5% HPV35, 4% HPV31, 4% HPV58, and 3% HPV33; 67% contained either HPV16 (44%), HPV18 (21%), or both (2%). Among the HPV16-positive tumors (n = 102), the distribution of lineages was 4% A, 67% B, 24% C, and 5% D. Among the HPV18-positive tumors (n = 1), the distribution of lineages was 12% A, 82% B, 2% C, and 4% D. The distribution of HPV type was similar by HIV status, but with HPV16, the distribution of lineages A or B versus C or D differed (P = 0.044), with 41% of HIV-pos patients compared to 22% of HIV-neg patients infected with lineage C or D. Median OS was 20 months. It was similar between HPV18 and HPV16 (20 vs 19 months, HR = 0.85, 95% CI 0.51–1.43). Among patients with HPV16-containing tumors, median OS was similar when comparing lineage A or B to C or D (18 vs 20 months, HR = 1.30, 95% CI 0.64–2.48).

**Conclusion:** The majority of cervical cancers in Uganda are associated with HPV16 and HPV18. HPV16 lineage distribution varied by HIV status, although no survival differences by lineage were detected.
2341 - Poster Session

Conditional relative survival of cervical cancer: Analysis of Korean central cancer registry data
J. Bae. Hanyang University College of Medicine, Seoul, Korea, Republic of (South)

Objective: Conditional relative survival (CRS) can complement the conventional 5-year relative survival that does not take into account the time the patient has survived after diagnosis. The purpose of this study was to evaluate the 5-year CRS and associated risk factors among Korean cervical cancer patients.

Method: We identified 78,606 cervical cancer cases with a diagnosis between 1996 and 2015 in the Korea Central Cancer Registry. The CRS rates were calculated according to age, history, treatment method, and stage at diagnosis.

Results: The relative survival rate for 5 years was 80.6%, and for 5 years the CRS increased for the first 2 years and remained stable at 94.3% after 5 years of survival. Patients younger than 40 years had the highest level (88.9%) in 5 years, while those 70 years or older had the worst CRS (55.0%) in 5 years. The localized disease had 91.9% CRS; local transferency had 72.3% CRS; and remote transitions were 27.0%.

Conclusion: Patients with cervical cancer showed an increase in CRS rates, which varied with age, histology, and stage at diagnosis. The CRS analysis therefore provides a more detailed perspective on survival over the years after the initial diagnosis or treatment.

2342 - Poster Session

Metabolic diseases and endometrial cancer risk: Malaysian experience
M.N. Shafiee, N.H. Abd Aziz, F. Ahmad, N. Abd Razak and N. Adeeb. UKM, KUALA LUMPUR, Malaysia

Objective: Globally, endometrial cancer (EC) incidence is on its rise. Hypothetically, metabolic diseases have a direct correlation to EC. Hence, this study was aimed at evaluating the link between metabolic syndrome and its constituent factors to EC in a gynecologic oncology center in Kuala Lumpur, Malaysia.

Method: The data were obtained in the Gynaecology Centre, UKM Medical Centre, Kuala Lumpur, between December 2008 and December 2013. A total of 238 patients with histologically confirmed EC within the study analysis were included in this study. There were 204 cases of endometrioid adenocarcinoma, 14 serous, 6 clear cell, and 14 carcinosarcoma. The primary outcome was the proportion of patients with type I and type II EC who had concurrent metabolic disorders. The secondary results include the association of metabolic syndrome with stages of EC, outcomes of treatment modalities, and survival rates.

Results: Metabolic syndrome was significantly associated with increased risk of endometrial carcinoma in type I EC (OR = 3.43, 95% CI 1.12–10.46, P < 0.05). Obesity increased the risk of type I EC (OR = 3.88, 95% CI 1.27–11.85, P < 0.05). There were no significant differences between both subtypes with other metabolic factors (diabetes mellitus, hypertension, high triglycerides, and low HDL levels). Univariate analyses found no significant effect of metabolic syndrome on the overall survival rate and disease-free survival rate.

Conclusion: Metabolic syndrome positively associated with increased risk of type I EC with obesity being the most influential risk factor. Effective prevention and intervention of these metabolic disorders might be essential in reducing the incidence of EC.

2343 - Poster Session

S. Ikeda, A. Yagi and Y. Ueda. *Tama-Hokubu Medical Center, Higashimurayama, Japan, *Osaka University Graduate School of Medicine, Osaka, Japan

Objective: Ovarian cancer is the most lethal gynecologic malignancy. It is the eighth most common cause of cancer in women in Japan, and the incidence tends to be increasing. The aim of this study is to perform a descriptive epidemiological analysis of ovarian cancer using a large population-based dataset from the Osaka Cancer Registry to clarify the trend and characteristics of ovarian cancer, including the histology-specific long-term trends in past 30 years.
Method: The histology-specific long-term trends in the age-adjusted incidence and survival rate of ovarian cancer in Osaka were examined, based on data from the Osaka Cancer Registry.

Results: A total of 14,644 cases of ovarian cancer were registered in Osaka from 1980 to 2012, including 2,877 serous adenocarcinoma, 1,496 mucinous adenocarcinoma, 1,351 clear cell carcinoma, and 988 endometrioid adenocarcinoma. The age-adjusted incidence rate has been increasing in all ages, especially in the 40s and 50s. In histological trend, the incidence of clear cell adenocarcinoma and endometrioid adenocarcinoma is strikingly increasing in the past 30 years. In survival, there is a definite improvement in 3 events, approval of CDDP, introduction of TC, and introduction of guidelines. Especially the first 2 years after the diagnosis, the treatment is effective and the improvement of survival is recognized. But it is still severe in the long term, and the survival rate continues to decrease even after 5 years.

Conclusion: The age-adjusted incidence of ovarian cancer has been increasing since 1980. It tends to increase in all ages, especially in the 40s and 50s. In histological trend, endometrioid adenocarcinoma and clear cell carcinoma are particularly increasing. It is suggested that there are many cases of malignancy transformation from endometriosis. Overall, the mortality rate is decreasing after 5 years. Development of more effective treatment is desired.

2344 - Poster Session
Distinct difference in research trends about gynecologic oncology between two koreas may reflect the different epidemiology of gynecologic malignancy between two groups of same species
S.H. Park. Incheon-sarang hospital, Incheon, Korea, Republic of (South)

Objective: This study aimed to investigate the current status of gynecologic oncologic disease in North Korea by analyzing research trends in obstetrics and gynecologic journals from North Korea and South Korea.

Method: Articles about gynecologic oncology in Pediatric Obstetric & Gynecology, a journal published in North Korea, from volume 1 in 2006 to volume 4 in 2016, were analyzed by using content analysis and frequency analysis. Articles were classified by disease origin and representative disease code (ICD-10). Obstetrics & Gynecology Science, a journal published in South Korea, was selected for a comparative analysis of research trends.

Results: Of the 3,361 articles that were reviewed, 117 were extracted from the North Korean journal and 513 were extracted from the South Korean journal. There is a distinct difference in research trends about gynecologic oncology between South and North Korea. Articles about gestational trophoblastic disease constitute 19% of the North Korean journal and 1.9% of the South Korean journal, whereas articles about uterine cancer constitute 3% in North Korea and 14% in South Korea. The most studied gynecologic oncologic disease in North Korea is cervical malignancy and in South Korea, ovarian neoplasia. In addition, there are no articles about endoscopic surgery for patients of gynecologic cancer in the North Korean journal.

Conclusion: This study presents an analysis of research trends about gynecologic oncology in North Korea, in which distinct differences were observed compared with South Korea. Distinct differences in research trends suggest the current status of the same gynecologic cancer is different between the two Koreas, which may provide the critical clue on different epidemiology of same gynecologic cancers between two groups of the same species.

Health Provider Wellness

2345 - Poster Session
Factors associated with obstetric and gynecology residents' decision to pursue fellowship
M. Greenwade, M. Palisoul, D.G. Mutch, A.R. Hagemann, C.K. McCourt, P.H. Thaker, K.C. Fuh, M.A. Powell and L.M. Kuroki. Washington University School of Medicine in St. Louis, St. Louis, MO, USA

Objective: To identify factors associated with obstetrics and gynecology (OB/GYN) resident decisions to pursue fellowships, with a specific focus on gynecologic oncology, and to report the role of mentee-mentor relationships, institutional characteristics, and other personal factors.

Method: A REDCap survey link was emailed to program coordinators of ACGME-accredited OB/GYN residency programs with a request to disperse to current residents. The 77-item survey asked about plans for fellowship and influencing factors.
Participants were stratified based on decision to pursue fellowship. The student t test was used to compare residents who were interested in pursuing a fellowship with those who were not in addition to those who expressed interest in a OB/GYN fellowship versus other subspecialties.

**Results:** Among 231 surveyed residents, 132 (41%) were interested in fellowships, and of these, 32 (14%) were interested in OB/GYN. Although there were no demographic differences between residents choosing fellowship versus generalist career tracks, trainees at academic programs were more likely to pursue fellowship ($P < 0.01$). Programs with >4 gynecologic oncologists were more likely to have residents interested in this subspecialty ($P < 0.01$). When questioned about specific institutional rotation experiences, residents pursuing OB/GYN were more confident than other respondents that they could find a research faculty mentor and were more likely to view OB/GYN attendings as involved in education, invested in resident success and well-being, and relatable ($P < 0.01$). Resident perception of burnout among attendings did not influence decision to pursue fellowship, but display of work-life balance and attending participation in social settings outside of work did play a role ($P = 0.02$). Across subspecialties, the most important factors considered when deciding to pursue fellowship included patient–doctor relationship ($P = 0.02$), desire for stronger surgical training ($P = 0.04$), opportunities for research ($P < 0.01$), and relatable mentors within the field ($P = 0.01$).

**Conclusion:** Medical students interested in gynecologic oncology should apply to academic residencies with >4 gynecologic oncologists. Strong and supportive mentor–mentee relationships influence OB/GYN residents’ decisions to pursue fellowship. As the need for specialists increases, programs should develop mentorship programs to support resident career development.

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**Practice-Changing Studies in Gynecologic Cancers and/or Their Precursors**

**2346 - Poster Session**

**Searching for an ideal cervical cancer screening model to reduce false negative errors in Korean women with high prevalence of cervical cancer**

*T. Song, Kangbuk Samsung Hospital, Seoul, Korea, Republic of (South)*

**Objective:** The aim of this study was to identify an ideal cervical cancer screening model to reduce false negative errors in Korea, which is characterized by high prevalence of cervical cancer.

**Method:** We conducted a cross-sectional study including 33,531 women who underwent routine cervical cancer screening in Korea. Colposcopic examinations were performed after abnormal results on their screening tests. Diagnostic capacities including sensitivity, specificity, and false negative rate of each screening scenario were analyzed at the CIN1 or worse (CIN1+) threshold with colposcopic biopsy results considered the gold standard.

**Results:** A total of 4,117 women had valid results for Pap cytology, human papilloma virus (HPV) tests, cervicography, and colposcopically directed biopsy and were included in this study. The disease prevalence of CIN1+ was 38.1%. Pap alone resulted in the highest false negative rate of 46.9%, followed by HPV alone at 25.1%, cervicography alone at 18.7%, Pap/HPV combined at 15.0%, Pap/cervicography combined at 6.9%, and Pap/HPV/cervicography combined at 2.9% in a sample of 1,570 women with CIN1+ lesions.

**Conclusion:** Cervicography demonstrated excellent performance for the detection of CIN or cervical cancer and markedly reduced false negative errors when used in combination with Pap cytology and HPV tests.

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**2347 - Poster Session**

**An investigation on the completeness of prophylactic salpingectomy intended for the prevention of ovarian cancer risk**

*L.W.H. Wong, J.L. Killeen and M.E. Carney. University of Hawaii, Honolulu, HI, USA*

**Objective:** To evaluate the completeness of salpingectomy intended for ovarian cancer risk reduction.

**Method:** Women without a history of ovarian cancer who were undergoing salpingoophorectomy were enrolled in this study. Salpingectomy was performed prior to oophorectomy. A blinded pathologist then examined the ovaries for the presence of
residual salpingeal tissue. Data collected included type of surgery (minimally invasive or laparotomy) and level of surgeon (attending or resident). Data were analyzed using Pearson’s χ² test.

**Results**: A total of 68 samples were examined among the 36 women enrolled. Only 5 ovaries (7%) had residual salpingeal tissue present after salpingectomy, which was statistically significant ($P = 2 \times 10^{-12}$). Of these 5 ovaries with residual salpingeal tissue, 3 (60%) were noted to be enlarged and inflamed, but there was no difference between level of surgeon (attending $n = 3$, resident $n = 2$, $P = 0.65$) or type of surgery (minimally invasive $n = 4$, laparotomy $n = 1$, $P = 0.18$).

**Conclusion**: Prophylactic salpingectomy has been heavily promoted based on the theory that serous tubal intraepithelial carcinoma is a precursor lesion for “serous ovarian carcinoma.” However, the validity of prophylactic salpingectomy has yet to be proven through adequate research. This blinded study is the largest study ever conducted to examine ovaries for residual salpingeal tissue after salpingectomy. In addition, this is the only study to compare learner versus attending outcomes in this setting. This study supports the continued clinical practice of prophylactic salpingectomy for ovarian cancer risk reduction.

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2348 - Poster Session
Use and outcomes of neoadjuvant chemotherapy for metastatic endometrial cancer

**Objective**: While primary cytoreductive surgery (PDS) is considered the standard of care for stage IV endometrial cancer, PDS is associated with significant morbidity and poor survival. Neoadjuvant chemotherapy (NACT) has been proposed as an alternative treatment strategy. We analyzed the use and outcomes of NACT for women with stage IV endometrial cancer.

**Method**: The National Cancer Data Base was used to identify women with stage IV endometrial cancer treated from 2010 to 2015. The cohort was limited to women ≤70 years with minimal comorbidity (comorbidity score = 0). Women were stratified by receipt of NACT or PDS. A propensity score analysis with inverse probability weighting was performed to balance the clinical characteristics of the groups. As the cohort displayed nonproportional hazards, survival was examined using flexible parametric Royston-Parmer models to account for time-varying hazards with use of NACT. An intention to treat (ITT) analysis was performed as well as a per protocol (PP) analysis that included only women who received treatment with both chemotherapy and surgery.

**Results**: Of a total of 4,890 women with stage IV endometrial cancer, NACT was utilized in 19.5% of patients. NACT use increased from 16.0% in 2010 to 23.9% in 2015 ($P < 0.001$). More recent year of diagnosis, Medicaid coverage, stage IVB disease, and serous histology were associated with use of NACT ($P < 0.05$). Use of NACT displayed a time-varying association with survival. In the ITT analysis, use of NACT was associated with decreased mortality for the first 3 months after diagnosis (HR at 2 months = 0.81, 95% CI 0.66–0.99). After 4 months, the survival curves crossed, and receipt of NACT was associated with increased mortality (HR at 6 months = 1.23, 95% CI 1.09–1.39). Similarly, in the PP analysis, use of NACT was associated with decreased mortality for the first 8 months after diagnosis (HR at 6 months = 0.79, 95% CI 0.63–0.98). After 9 months the survival curves crossed, and receipt of NACT was associated with increased mortality (HR at 12 months = 1.22, 95% CI 1.04–1.43).

**Conclusion**: Use of NACT for stage IV endometrial cancer is increasing. The relationship between use of NACT and survival is complex. Women treated with PDS are at increased risk of early death but have a more favorable long-term prognosis.

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2349 - Poster Session
Epigenetic therapy inhibits growth of ovarian cancer cells and reverses chemoresistant properties acquired from metastatic omental adipose-derived stem cells
J. Sookram, S.A. Brown and O. Ostrovsky. Cooper University Hospital, Camden, NJ, USA

**Objective**: 1. To examine the cytotoxicity of epigenetic drugs as single agents and in combination with paclitaxel/cisplatin. To investigate the ability of ovarian cancer cells to acquire chemoresistance in different omental microenvironments and whether the use of epigenetic drugs is able to counteract this chemoresistance.
**Method:** Cytotoxicity assays using IC50 (half maximal inhibitory concentration) values of epigenetic drugs, azacytidine (AZA) and suberoylanilide hydroxamic acid (SAHA), and chemotherapy agents, paclitaxel/cisplatin (PTX/CIS), were performed on human ovarian adenocarcinoma cell line Caov-3. Omental adipose-derived stem cells (OASCs) were isolated from omentum with/without metastases. Caov-3 was cultured with conditioned medium (CM) obtained from OASCs and subjected to different combinations of drug treatments. Control wells contained Caov-3 cultured with regular media. Cell viability was measured using MTT assay. Statistical analyses were performed using One-Way ANOVA method.

**Results:** Epigenetic drugs as single agents or in combination with classic chemotherapy agents showed significantly increased toxicity against ovarian cancer cell line Caov-3. Dual epigenetic therapy with AZA/SAHA and tetracocktail therapy containing all four drugs had a substantial 4-5 fold increase in cell death compared to classic chemotherapy with PTX/CIS. Conditioned media derived from OASCs isolated from metastatic omentum significantly promoted chemoresistance (~26-33% increase; p<0.05) against PTX/CIS compared to omentum without metastases and control containing regular media. Compared to PTX/CIS, use of epigenetic therapy resulted in up to a 40-fold reversal in chemoresistance acquired from CM of metastatic OASCs.

**Conclusions:** Use of epigenetic drugs significantly inhibited growth of ovarian cancer cells and successfully reversed acquired chemoresistance against classic chemotherapeutic agents. These results suggest that epigenetic drugs may have an important role in treating a subgroup of ovarian cancer patients that demonstrate resistance to initial chemotherapy containing taxane and platinum-agents.

**Fig. 1.**

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**2350 - Poster Session**

**Ofranergene obadenovec (VB-111) an anti-cancer gene therapy induces immunotherapeutic effect in platinum resistant ovarian cancer: Histopathology findings**


aSheba medical Center, Ramat Gan, Israel, bSheba Medical Center, Ramat Gan, Israel, cVBL Therapeutics, Modiin, Israel, dArizona Oncology (US Oncology Network), Phoenix, AZ, USA, eUniversity of Arizona College of Medicine Phoenix, Phoenix, AZ, USA, fMassachusetts General Hospital/Harvard University, Boston, MA, USA

**Objectives:** Ofranergene obadenovec (VB-111) is a targeted anti-cancer gene therapy with a dual mechanism: anti angiogenic/vascular disruption and induction of an anti-tumor directed immune response. Treatment with VB-111 in combination with weekly Paclitaxel has shown in a phase 2 trial to prolong overall survival in patients with recurrent platinum resistant ovarian cancer. A febrile post-dosing response was associated with improved survival supporting the role
of the immune system as part of VB-111’s mechanism of action. Here we present patients’ tumor biopsy data to further characterize the intratumoral immunologic activity of VB-111.

Methods: Post treatment biopsies were obtained from 3 patients with recurrent platinum-resistant ovarian cancer treated with intravenous VB-111 1x10^13 VPs every 2 months in combination with weekly paclitaxel; one patient in study NCT03398655 and two patients in study NCT01711970. Results were compared to pre-treatment specimens and to 12 untreated controls. H&E and Immunohistochemistry (IHC) was performed for CD8 and CD4 intratumoral T cells.

Results: Specimens taken before treatment with VB-111 showed no or minimal T cell infiltration in the tumor. One month after VB-111 treatment metastatic lesions demonstrated tumor infiltrated with CD8 (74 CD8+ cells/HPF) and CD4 T cells. At 4.5 months following first drug administration (post 3rd dose) a liver lesion showed (Figure 1) necrotic and fibrotic tissue with no viable tumor, lymphocytic aggregate, intensive staining for CD-8 (157 CD8+ cells/HPF), intense staining for CD-4 and pigmented macrophages.

Conclusions: Pathologic findings following VB-111 treatment suggest the induction of an Immunotherapeutic effect manifested as tumor infiltration with CD-8 T cells, and evidence of tumor necrosis. The presence of tumor-infiltrating lymphocytes is an important prognostic factor in ovarian cancer, and may contribute to the favorable survival outcome seen in the VB-111 phase II study. A pivotal phase III study evaluating the efficacy and safety of VB-111 in combination with weekly Paclitaxel compared to Paclitaxel and Placebo is currently ongoing.

**Fig. 1.**

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**2351 - Poster Session**

Clinical response and safety of apatinib monotherapy in recurrent or metastatic cervical cancer after failure of chemotherapy: An observational study

Y. Xiao, H. Cheng, X. Yu and L. Wang. Cancer Hospital of Zhengzhou University (Henan Cancer Hospital), Zhengzhou, China

**Objective:** To investigate the short-term efficacy and safety of apatinib in patients with recurrent or metastatic cervical cancer after failure of prior chemotherapy.

**Method:** A total of 40 patients with recurrent or metastatic disease received apatinib (500 mg/day) at our institute between June 2016 and June 2017. All patients received radiotherapy or surgery and at least one prior chemotherapy. The median age was 56 (32–73) years. Tumor histology was as follows: 32 squamous carcinoma, 6 adenocarcinoma, and 2 adenosquamous carcinoma. The most common metastatic site was pelvic cavity (29/40, 72.5%). Sixteen patients had history of hypertension. Clinical outcomes including objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS) were calculated. The adverse events (AEs) were also recorded and graded.

**Results:** The median duration of apatinib treatment was 7.8 months. During treatment, apatinib dose was reduced to 250 mg in 11 patients because of severe AEs. Treatment discontinuation occurred in 27 patients. All 40 patients were available for response evaluation: 5 achieved partial response; 21 patients achieved stable disease; and 14 had progressive disease, at best response, achieving an ORR of 12.5% and a DCR of 65%. Survival data were analyzed at a median follow-up of 14.0 (6.0–20.0
months); the median PFS was 4.3 months (95% CI 3.2–5.0) and median OS was 13.6 (95% CI 8.3–17.4 months) (Figure 1). A total of 14 grade 3 or 4 AEs occurred including leukopenia (5/40), hypertension (4/40), neutropenia (2/40), hemorrhage (2/40), and fatigue (1/40). There was no drug-related death.

**Conclusion:** This preliminary result indicated that apatinib may improve the disease control rate and delay disease progression in recurrent or metastatic disease, with well-tolerated toxicities, making it a promising therapeutic target for recurrent or metastatic cervical cancer treatment.

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**Fig. 1.**

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**2352 - Poster Session**

**Outcomes of whole genome and transcriptome sequencing (WGTS) in advanced gynecologic malignancies: Results from the personalized oncogenomics program (POG)**


*aBC Cancer, Vancouver, BC, Canada, bBC Cancer Genome Science Centre, Vancouver, BC, Canada, cBritish Columbia Cancer Agency, Vancouver, BC, Canada*

**Objective:** Advanced/recurrent gynecologic malignancies are a heterogeneous group of cancers with limited treatment options lacking predictive biomarkers. The personalized oncogenomics program (POG) is a British Columbia cancer investigational program that performs whole genome and transcriptome sequencing (WGTS) of recurrent cancers. A tumor
board identifies potentially predictive and actionable biomarkers. We analyzed the discussed actionable items and their impact on treatment decisions among patients with recurrent gynecologic cancers.

**Method:** Sixty POG participants with advanced gynecologic malignancies were successfully analyzed. WGTS results were used to identify germline and somatic mutations, copy number changes, structural alterations, and gene expression outliers. The POG tumor board defined actionable items as variants that could direct therapy using an investigational, off-label, or approved agent.

**Results:** Of all patients, 65% had tubo-ovarian carcinomas \( n = 39 \), 13% endometrial carcinomas \( n = 8 \), 8% uterine sarcomas \( n = 5 \), 10% cervical carcinomas \( n = 5 \), and 3% other \( n = 2 \). Disease comparator analysis changed or clarified the initial diagnosis in 4 patients; 83% \( n = 50 \) had actionable items, consisting mostly of gene expression changes \( n = 54 \), copy number variants \( n = 44 \), and mutations \( n = 40 \). Most common alterations involved DNA damage and repair, PIK3/AKT/mTOR and MAPK pathways (see Table 1). There were 23 patients (46%) who received treatments based on analysis results, including 13 off-label targeted therapies, 4 PARP inhibitors, 4 chemotherapies, and 2 immunotherapies. Median duration on treatment was 4 months, with the longest time on treatment in 2 cases of ovarian cancer: high-grade serous (24 months, olaparib), low-grade serous ovarian cancer (16 months, MEK inhibitor). 37 patients did not receive treatment based on POG due to lack of indication to start treatment \( n = 9 \), lack of actionable items \( n = 8 \), poor performance status including 3 deaths \( n = 8 \), lack of access to treatment \( n = 6 \), and patient/physician preference \( n = 6 \).

**Conclusion:** WGTS in advanced gynecologic malignancies can identify potentially actionable alterations that may elucidate treatment options.

**Table 1.**

<table>
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<tr>
<th>Disease (N)</th>
<th>PIK3CA/ AKT/mTOR</th>
<th>MAPK/ RAS/RAF</th>
<th>DNA repair/ HRD/ BRCA signature</th>
<th>High TMB/ PD-L1 expr</th>
<th>Cell cycle</th>
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<td>10</td>
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<td>8</td>
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<td>0</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

**2353 - Poster Session**

The effect of buffered lidocaine versus non-buffered lidocaine on pain scores during infiltration for vulvar biopsy: A randomized controlled trial

A. Kulkarni\(^a\), J. Villavicencio\(^b\), L.B. Beffa\(^a\), H. Mendez\(^a\), C. Luis\(^a\), C. Raker\(^c\), B. Cronin\(^a\) and K.M. Robison\(^a\). \(^a\)Women & Infants Hospital, Brown University, Providence, RI, USA, \(^b\)The University of Michigan Hospitals, Ann Arbor, MI, USA, \(^c\)Women & Infants Hospital, Brown University, Providence, RI, USA

**Objective:** The study objective was to compare pain scores on a visual analogue scale (VAS) during infiltration of local anesthetic for vulvar biopsies for women treated with buffered versus those treated with nonbuffered lidocaine.

**Method:** This was a double-blind, randomized controlled trial conducted at a single academic center in two clinics: general gynecology and gynecologic oncology. Eligible participants were women 18 years or older who required a vulvar biopsy for a noninfectious vulvar lesion, were able to read English or Spanish, and give informed consent. After enrollment, participants were randomized to one of two groups, buffered lidocaine or nonbuffered lidocaine. Using a VAS, pain scores were collected at three time points: baseline prior to intervention, at time of infiltration, and at completion of biopsy. Patients also completed an associated questionnaire prior to the procedure.

**Results:** One hundred and twenty-five patients were enrolled. Sixty-two were randomly assigned to the nonbuffered lidocaine control group and 63 to the buffered lidocaine intervention group. Mean age in the control and intervention groups was 57
and 61 years, respectively. The majority of patients were seen in the gynecologic oncology clinic: 76% in the control group and 79% in the intervention group. Baseline pain scores were similar in each group, with mean scores of 6.4 in the control group compared to 6.9 in the intervention group \( (P = 0.8) \). The control group had a mean pain score during infiltration of 42.2 versus 35.8 in the intervention group \( (P = 0.3) \). When comparing the mean change in pain from baseline to infiltration, the intervention group had a score of 28.9 versus 35.7 in the control group \( (P = 0.2) \). Sixteen percent of patients in the intervention group reported a VAS score of 0 for the entire procedure compared to 6.5% in the control group \( (P = 0.09) \).

**Conclusion:** Women who undergo vulvar biopsy often experience some pain during the procedure. In our study, for women who received buffered lidocaine, there was a trend toward lower mean pain scores at time of infiltration compared to the control group as well as a trend toward decreased change in pain scores from baseline to infiltration. More patients in the intervention group reported zero pain scores for the entire procedure compared to the control group. Buffered lidocaine may be a feasible option for anesthesia prior to vulvar procedures that may decrease patients’ discomfort.

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**2354 - Poster Session**  
**Adjuvant radiation or re-excision for early stage vulvar squamous cell carcinoma with positive or close surgical margins**  
S.M. Bedell, C. Hedberg, H. Pearson, A. Griffin, A. Bangdiwala and B.K. Erickson. *University of Minnesota, Minneapolis, MN, USA*

**Objective:** Given the rarity of vulvar cancer, there are limited data to guide adjuvant treatment in early-stage, high-risk disease. The objective of this study is to evaluate whether additional treatment with either re-excision or adjuvant radiation for stage I squamous cell carcinoma (SCC) of the vulva with close or positive surgical margins improves recurrence-free survival.

**Method:** Patients with pathology-confirmed SCC of the vulva who underwent primary surgical management between January 1, 1995, and September 30, 2017 were identified; those with FIGO stage 1A or 1B and positive or close surgical margins after primary surgical resection were included. Close margins were defined as less than or equal to 8 mm. Kaplan-Meier curves were generated and compared with the log-rank test. Multivariate analysis with Cox proportional hazards was performed to account for possible confounders, such as margins.

**Results:** Of the 152 patients with FIGO stage 1A and 1B SCC of the vulva, 59 (39%) had positive or close surgical margins. The median follow-up time was 24 months. Twenty-four patients received additional treatment with re-excision (20) or vulvar radiation (4); the remaining 35 patients received no additional treatment. There was no significant difference in age, race, or smoking status between treatment groups. Patients who had positive margins were more likely to receive additional therapy compared to patients with close margins (71% vs 29%, \( P = 0.01 \)). None of the 4 patients treated with adjuvant radiation therapy recurred or died from disease. A log-rank test showed that any additional therapy had significantly lower distant recurrence-free survival rates \( (P = 0.05) \), but local recurrence-free survival rates and overall survival rates were not statistically significant \( (P = 0.23 \text { and } P = 0.12, \text { respectively}) \). Subgroup analysis via log-rank test of the 42 patients with close margins only demonstrated no significant difference in local recurrence-free survival rates with additional treatment \( (P = 0.09) \).

**Conclusion:** Previous studies on adjuvant radiation for vulvar cancer have included all stages and make results difficult to interpret for early-stage disease alone. In our study, any additional treatment following primary surgical resection did improve the distant recurrence-free survival in stage 1A and 1B vulvar SCC, but did not improve local recurrence-free survival or overall survival. Larger studies are warranted.

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**2355 - Poster Session**  
**Survival differences in gynecologic high-grade serous carcinomas based on site of origin: Material or semantic?**  
M.A. Schwartz*, J. Huntley*, P. Hua*, S. Everest*, S. Li*, V. Kolev*, M.P. Hayes*, Y. Liu* and S.V. Blanck†. *Icahn School of Medicine at Mount Sinai, New York, NY, USA, †Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA*

**Objective:** The primary origin of most nonuterine (NU) gynecologic high-grade serous carcinomas (HGSC) is likely the fallopian tube (FT). Over time, the diagnosis of FT cancers has increased with a corresponding decrease in ovarian cancers. Prior studies have shown that women with FT-HGSC have improved survival compared to those with ovarian or peritoneal HGSC. We sought to determine whether survival outcomes differ for women with HGSC based on site of origin using updated 2014 guidelines for classification of gynecologic malignancies.
Method: Women with newly diagnosed NU-HGSC who underwent debulking surgery and received adjuvant treatment at a single academic institution from 2006 to 2017 were reviewed. Original histopathologic diagnoses and clinical data were abstracted from medical charts. Using 2014 WHO guidelines, we reassigned primary site (FT, ovarian, peritoneal tubo-ovarian) for all cases based on review of pathology reports. When reassignment was equivocal, a gynecologic pathologist determined site of origin. Kaplan-Meier and Cox proportional hazards were used to compare survival based on original and reassigned sites of origin.

Results: A total of 237 patients were included with a mean age of 63 years (SD = 10.7). The majority of patients were white (n = 188, 79%) and non-Hispanic (n = 210, 92%) and had advanced-stage disease (n = 201, 85%). The 5-year overall disease-specific survival was 62% (95% CI 53%–70%). The 5-year survival of those with FT, ovarian, and other (of whom all had advanced-stage disease and most received neoadjuvant chemotherapy) were 59%, 69%, and 36%, respectively (P = 0.06). After site of origin was reassigned, 5-year survivals (Figure 1) were 64%, 60%, and 26%, respectively (P = 0.24). In multivariate analysis, younger age (HR = 1.04, P = 0.002) and earlier stage (HR = 3.70, P = 0.005) were significantly associated with survival for both original and reassigned sites of origin. Adjusting for other variables, original site of origin was associated with survival (P = 0.05). However, once site of origin was reassigned, this finding was no longer significant (P = 0.76).

Conclusion: In NU-HGSC, site of origin does not have an impact on survival. Distinguishing anatomic origin of NU-HGSC is a semantic—not clinically relevant—exercise and abandoning the practice could simplify trial design, drug approvals, and patient counseling.

![Product-Limit Survival Estimates](image)

**Fig. 1.** Kaplan-Meier curve for death stratified by 2014 WHO reassigned site of origin (95% confidence interval). Log-rank test p-value=0.24.

2356 - Poster Session

The prognosis of epithelial ovarian cancer patients who are refractory after neoadjuvant chemotherapy

Objective: Neoadjuvant chemotherapy (NACT) followed by interval cytoreductive surgery has been rapidly applied to patients with advanced epithelial ovarian cancer. However, there is no standard consensus in treating patients who are refractory to NACT. We evaluated the patients who were refractory to NACT in an effort to determine potential clinical factors for predicting the patients who would benefit from avoiding NACT.

Method: We retrospectively reviewed 37 patients with epithelial ovarian cancer who showed progressive disease after receiving NACT between January 2001 and December 2016 at two tertiary centers in South Korea. We compared the patients who underwent cytoreductive surgery after NACT with those who continued chemotherapeutic treatment with different regimens without surgery. The primary aim was to compare overall survival, and the secondary aim was to compare the demographic and clinical characteristics between the two groups.

Results: A total of 37 patients showed disease progression after NACT. The median follow-up time was 13 months. The patients who received interval cytoreductive surgery after NACT showed a significantly longer overall survival compared to those who changed chemotherapeutic regimens (29 vs 8 months, P < 0.01). Patients with high-grade serous carcinoma showed longer survival than those with non-high-grade serous carcinoma (19.3 vs 10.3 months, P = 0.015). See Figure 1.

Conclusion: Surgery is a better treatment option for epithelial ovarian cancer patients who show progressive disease after NACT. After disease progression, the patients who are diagnosed with high-grade serous histology showed relatively longer overall survival. In patients who are refractory to NACT, their histology subtype ratio was different from that of the overall epithelial ovarian cancer patients group. Thus further study is needed to determine clinical factors that will respond more effectively to NACT.

![Figure 1](image-url)
Clinical outcomes of surgically unresectable endometrial cancers
J.L. Conway, J. Lukovic, S.E. Ferguson, J. Zhang, W. Xu, N. Dhani, A. Rink and K. Han. Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Objective: To determine outcomes of patients with unresectable endometrial cancer (EC) managed with definitive or neoadjuvant intent radiation (RT) and/or chemotherapy with or without surgery.

Method: Patients with unresectable FIGO stages II–IVA EC with bulky cervical, parametrial, or vaginal disease managed without upfront surgery from January 2000 to March 2018 were identified. Overall survival (OS) and disease-free survival (DFS) rates of patients treated with and without surgery were analyzed using the Kaplan-Meier method and compared using the log rank test. Multivariate logistic regression analysis was performed to identify factors independently associated with receipt of surgery. Multivariate Cox regression analysis was performed to identify factors independently associated with OS and DFS.

Results: Fifty-nine patients were identified, median age 63 years (range 37–88 years), and histology was endometrioid in 59% and nonendometrioid in 41%. Median follow-up was 2.2 years (range 0.3–9.8 years). Seventeen patients received neoadjuvant chemotherapy, 28 neoadjuvant RT, and 14 definitive RT. Forty patients’ disease became resectable after RT and/or chemotherapy; 39 patients underwent surgery. Overall, 18% (7/39) of patients developed a postoperative complication, and 10% (6/59) a severe (≥grade 3) complication. Patients treated with surgery had higher 3-year OS and DFS rates than those who were not (84% vs 41%, P < 0.001 and 56% vs 11%, P < 0.001, respectively) (Figure 1). On multivariate logistic regression, factors associated with higher odds of surgical resection included younger age (OR = 1.1, 95% CI 1.02–1.14, P = 0.013), endometrioid histology (OR = 3.7, 95% CI 1.05–12.5, P = 0.042), and earlier stage (OR = 4.1, 95% CI 1.08–16.7, P = 0.038). On multivariate Cox regression, younger age (HR = 0.9, 95% CI 0.88–0.98, P = 0.004), endometrioid histology (HR = 0.3, 95% CI 0.09–0.87, P = 0.028), and surgical resection (HR = 0.3, 95% CI 0.09–0.72, P = 0.010) were significantly associated with higher OS. Surgical resection (HR = 0.3, 95% CI 0.15–0.66, P = 0.002) was also associated with higher DFS.

Conclusion: Surgical resection following chemotherapy and/or RT for locally advanced, unresectable EC is associated with higher DFS and OS and more likely to be achieved in endometrioid subtypes.
2358 - Poster Session
Chemotherapy versus chemotherapy and radiation for stage III uterine cancer: Generalizability of cooperative group data to real world populations
S.K. Syeda, L. Chen, J.Y. Hou, A.I. Tergas, F. Khoury Collado, A. Melamed, C. St. Clair and J.D. Wright. aNew York-Presbyterian/Columbia University Medical Center, New York, NY, USA, bColumbia University College of Physicians and Surgeons, New York, NY, USA

Objective: Recent cooperative group data have suggested that chemotherapy alone is associated with similar survival and decreased toxicity compared to combination chemoradiation in women with stage III uterine cancer. Given the uncertainty of the generalizability of these findings, we compared the outcomes of women with stage III uterine cancer treated with chemotherapy alone to those treated with combination chemotherapy and radiation.

Methods: The National Cancer Data Base was used to identify women with stage III endometrioid, serous, and clear cell uterine cancer treated with either chemotherapy (with or without vaginal brachytherapy) or combination chemotherapy and external beam radiation (with or without vaginal brachytherapy) from 2004 to 2015. Survival was examined using Cox proportional hazards models and Kaplan-Meier analysis after propensity score analysis using inverse probability of treatment weighting to balance the clinical and demographic characteristics between the cohorts.

Results: Of the 18,456 patients identified, 9,456 (51.2%) received chemotherapy alone, while 9,000 (48.8%) received chemotherapy in combination with external beam radiation. Use of combination therapy was 54% in 2004, declined to a low of 45% in 2008, and then rose to 54% in 2015. Within the cohort, combination therapy was associated with a 24% reduction in mortality (HR = 0.76, 95% CI 0.72–0.81). Similar findings of decreased mortality were noted in subgroup analyses for both stage IIIA (HR = 0.79, 95% CI 0.66–0.94) and stage IIIC (HR = 0.77, 95% CI 0.72–0.82) tumors. Combination chemoradiation was associated with decreased mortality across all of the histologic subtypes.

Conclusion: Among women with stage III uterine cancer, combination chemotherapy and external beam radiation is associated with decreased mortality compared to chemotherapy alone.

2359 - Poster Session
Efficacy of second line chemotherapeutic regimens in persistent or recurrent epithelial ovarian cancer including fallopian tube cancer and primary peritoneal cancer: A multicenter retrospective study
H.P. Lee and Y.B. Kim. aSoon Chun Hyang University Hospital, Seoul, South Korea, bSeoul National University Bundang Hospital, Seongnam, South Korea

Objective: This study evaluated the efficacy of second-line chemotherapeutic regimens in persistent or recurrent epithelial ovarian cancer (EOC) including fallopian tube cancer and primary peritoneal cancer by analyzing multicenter medical data.

Method: We reviewed the clinical data of 398 persistent or recurrent EOC patients treated with second-line chemotherapy between January 2006 and December 2016. Patients were divided into three groups based on platinum-free interval at first recurrence from the first-line chemotherapy: platinum-resistant (less than 6 months), partially platinum-sensitive (6 to 12 months), and platinum-sensitive (more than 12 months) group. The second-line chemotherapeutic regimen was identified in each group, and the PFS for the second-line chemotherapy was compared.

Results: A total of 213 patients were eligible and analyzed for chemotherapy outcomes. The median age was 53 (23–81) years; 65 (30.5%) patients were platinum-resistant; 69 (32.3%) patients were partially platinum-sensitive; and 79 (37.1%) patients were platinum-sensitive. In the platinum-resistant and platinum-sensitive groups, there was no significant difference in PFS between regimens. On the other hand, in the partially platinum-sensitive group, taxane-containing regimens showed significantly longer PFS than other regimens (P < 0.05). In this partially platinum-sensitive group, the median PFS of taxane-containing regimens was 25.6 weeks (95% CI 14.0); S-phase inhibitor-containing regimens, 15.0 weeks (95% CI 12.0); topoisomerase 1 inhibitor, 16.1 weeks (95% CI 16.2); and topoisomerase 2 inhibitor, 13.0 weeks (95% CI 12.1).
Conclusion: The PFS of taxane-containing regimens is better than that of other regimens in the partially platinum-sensitive group. There was no significant difference in PFS between regimens in both the platinum-resistant and platinum-sensitive groups.

2360 - Poster Session
Clinicopathologic features of endometrial carcinomas from patients with Lynch syndrome, Lynch-like syndrome and intact DNA mismatch repair: A systematic review and meta-analysis

Objective: Screening for DNA mismatch repair (MMR) in endometrial carcinomas (EC) identifies patients at risk for Lynch syndrome (LS). Patients with MMR-deficient tumors and negative germline LS genetic testing have been described as having Lynch-like syndrome. We aimed to compare clinicopathologic features of EC in patients with intact MMR, Lynch-like syndrome, and LS.

Method: We conducted a complete systematic search of online databases PubMed, Embase, Medline, and the Cochrane Library between 1990 and 2018 to identify studies of EC patients undergoing tumor testing via MMR IHC or MSI and germline assessment for LS. A DerSimonian–Laird random-effects model meta-analysis was utilized to estimate the weighted prevalence of LS diagnoses.

Results: This comprehensive search produced 3,427 publications. After screening by three independent reviewers, 29 peer review studies met the inclusion criteria. Patients with intact MMR were the oldest at time of EC diagnosis, followed by Lynch-like syndrome and germline LS (59.2, 55.9, 51.4 years, respectively). Patients with intact MMR had the highest BMI followed by Lynch-like syndrome and germline LS (35.7, 33.3, 27.4, respectively). Patients with MMR-deficient tumors (Lynch-like or LS) were less likely to present with stage I disease compared to intact DNA MMR (intact MMR, 76%; Lynch-like, 60%; LS, 63%) and more likely to present with stage III disease (intact MMR, 9%; Lynch-like, 17%; LS, 19%). Patients with MMR-deficient tumors were less likely to present with grade I tumors compared to intact MMR (intact DNA MMR, 53%; Lynch-like, 38%; LS, 40%). Among our total population, 31% met family history criteria (Amsterdam and/or Bethesda criteria), 54% and 13% of LS and Lynch-like syndrome patients met family history criteria, respectively. See Table 1.

Conclusion: Our results demonstrate that patients with Lynch-like syndrome resemble patients with LS with earlier age at diagnosis, lower BMI, higher disease stage, and disease grade at time of EC diagnosis compared to patients with intact DNA MMR.
Table 1. Clinicopathic features of endometrial carcinomas in patients with intact MMR, Lynch-like syndrome and Lynch syndrome.

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=5741)</th>
<th>Intact DNA mismatch repair (n=4737)</th>
<th>Deficient DNA mismatch repair (n=924)</th>
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</thead>
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<tr>
<td></td>
<td></td>
<td>Lynch-like syndrome (n=704)</td>
<td>Lynch syndrome (n=220)</td>
</tr>
<tr>
<td><strong>Age</strong> Mean (range)</td>
<td>59.7 (42-65)</td>
<td>61.5 (57-65)</td>
<td>55.9 (34-65)</td>
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<td><strong>BMI</strong> Mean (range)</td>
<td>33.5 (30-36)</td>
<td>35.7 (34-37)</td>
<td>33.3 (31-35)</td>
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<td><strong>Stage</strong></td>
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<td></td>
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<tr>
<td>I</td>
<td>78%</td>
<td>76%</td>
<td>60%</td>
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<tr>
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<td>6%</td>
<td>6%</td>
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<td>III</td>
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<td>9%</td>
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<tr>
<td>IV</td>
<td>2%</td>
<td>3%</td>
<td>1%</td>
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<tr>
<td>Unknown</td>
<td>2%</td>
<td>7%</td>
<td>14%</td>
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<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
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<td>55%</td>
<td>53%</td>
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<td>30%</td>
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<td>19%</td>
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<tr>
<td>Unknown</td>
<td>2%</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Endometrioid</td>
<td>86%</td>
<td>87%</td>
<td>92%</td>
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<tr>
<td>Carcinosarcoma</td>
<td>2%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Serous</td>
<td>4%</td>
<td>7%</td>
<td>1%</td>
</tr>
<tr>
<td>Mixed</td>
<td>6%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Clear Cell</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
</tr>
</tbody>
</table>

2401 - Poster Session
Paraortic nodal radiation in the definitive management of cervical cancer
J.C. Sanders, T.C. Jones, S.W. Dutta, T.N. Showalter and K.D. Romano. University of Virginia, Charlottesville, VA, USA

**Objective:** To evaluate the safety and efficacy of paraortic (PA) nodal radiation (RT) in the management of cervical cancer.

**Method:** Patients with locally advanced cervical cancer treated with definitive external beam radiation and brachytherapy between 2004 and 2017 at a single institution were retrospectively reviewed. Clinical and treatment-related data were recorded, including age, stage, concurrent chemotherapy, and RT treatment parameters. Toxicity and clinical outcomes, including recurrence patterns, were also collected. Kaplan-Meier curves were generated to estimate local recurrence-free survival (LRFS), regional nodal recurrence-free survival (RNRFS), paraaortic nodal recurrence-free survival (PARFS), distant metastases free survival (DMFS), and overall survival (OS). Toxicities were graded using the Common Terminology Criteria for Adverse Events (CTCAE).

**Results:** A total of 284 consecutive patients were included with a median follow-up of 34 months and median age of 49 years. Detailed radiation records for 266 patients (94%) were available for review, with 90 (32%) receiving PA nodal coverage. The Kaplan-Meier estimated LRFS, RNRFS, PARFS, DMFS, and OS at 3 years were 85.5%, 90.2%, 94.2%, 82.6%, and 73.9%, respectively. Twenty-five patients (8.8%) experienced grade 3–4 toxicity, with no grade 5 toxicity. On logistic regression, PA nodal RT was not predictive for grade ≥3 toxicity (P > 0.05). PA nodal failure occurred in 11 patients (3.9%), including 3 with isolated PA nodal failure at time of first recurrence. None of these 3 patients received elective PA nodal coverage, and all 3 were salvaged with chemo-RT. Seven patients experienced both PA nodal failure and distant metastatic disease at the time of first recurrence, with only 2 of these patients having elective PA nodal coverage. One patient had locally persistent disease and then developed a PA nodal failure.

**Conclusion:** In this series, isolated PA nodal failures were rare with the addition of PA nodal RT, although this did not reach statistical significance because of the low number of events. With modern radiation techniques, severe late toxicities were uncommon and not related to the addition of a PA field. Our results indicate that elective PA nodal RT may safely be included, and further investigation is warranted to evaluate its role in modern practice.
2402 - Poster Session
Post hoc exploratory analysis of rucaparib in patients with platinum-sensitive recurrent ovarian carcinoma from the randomized, placebo-controlled phase III study ARIEL3: Effect of a deleterious germline or no germline BRCA mutation on efficacy

Objective: In ARIEL3 (NCT01968213), rucaparib maintenance treatment showed significant improvement versus placebo for the prespecified primary endpoint of investigator-assessed progression-free survival (PFS) and key secondary endpoint of blinded independent central review (BICR)-assessed PFS (Coleman et al. Lancet. 2017;390:1949-61). PFS improved with rucaparib in all 3 predefined, nested cohorts: BRCA mutation (germline, somatic, or unknown origin), BRCA mutation plus wildtype BRCA/wildtype BRCA/LOH, and intent-to-treat (ITT) population. In this post hoc exploratory analysis, we hypothesized that rucaparib would have greater benefit than placebo in subgroups associated with the presence or absence of a deleterious germline BRCA mutation.

Method: In ARIEL3, patients were randomized 2:1 to oral rucaparib (600 mg BID) or placebo. For this analysis, PFS was assessed in the subgroup of patients with a deleterious germline BRCA mutation in their tumor (germline BRCA mutation) and in patients with tumors without a deleterious germline BRCA mutation (no germline BRCA mutation).

Results: The visit cutoff dates for efficacy and safety were April 15, 2017, and August 15, 2017, respectively. In all subgroups, rucaparib significantly improved PFS versus placebo (Table 1) regardless of mutation status. Although the reduction in risk was numerically greater in the germline BRCA mutation subgroup (HR = 0.25, 95% CI 0.16–0.39) than in the no germline BRCA mutation subgroup (HR = 0.41, 95% CI 0.32–0.52), the reduction in risk between the two subgroups did not differ by a statistically significant margin. The safety profile of rucaparib versus placebo in the germline BRCA mutation and no germline BRCA mutation subgroups was consistent with the safety profile of rucaparib in the overall safety population reported previously.

Conclusion: In this post hoc exploratory analysis, the reduction in risk was numerically greater in the germline BRCA mutation subgroup than in the no germline BRCA mutation subgroup. In the no germline BRCA mutation subgroup, the observed improvement in PFS was not driven solely by the somatic BRCA mutation plus wildtype BRCA/LOH subgroup as demonstrated by the analysis of patients with wildtype BRCA tumors.
Fig. 1. *Cox proportional hazards model. †Stratified log-rank P value. ‡Patients with a tumor with a BRCA mutation of unknown origin had a tumor sample with a BRCA mutation according to Foundations Medicine’s T5 next-generation sequencing assay, but a blood sample was not available for central germline testing. §Given the small sample size, HRs were generated without the randomization stratification factors (ie, homologous recombination repair gene mutation status, time progression with penultimate platinum, and response to last platinum). ¶Somatic BRCA mutation + wild-type BRCA/high LOH + wild-type BRCA/low LOH + wild-type BRCA/LOH indeterminate. NR, not reached.

2403 - Poster Session
Prognostic factors associated with survival following platinum-based therapy in advanced/recurrent endometrial cancer
K.G. Essel¹, M.H. Vetter², D.W. Doo³, M. Greenwade⁴, M. Machiorlatta⁵, E. Evans⁶, B. Strope⁷, G. Opara⁸, S. Vesely⁹, M.A. Powell¹⁰, R.C. Arend¹¹, R. Salani¹² and K.N. Moore¹³. ¹The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, ²The Ohio State University, James Cancer Hospital, Columbus, OH, USA, ³University of Alabama at Birmingham, Birmingham, AL, USA, ⁴Washington University School of Medicine in St. Louis, St. Louis, MO, USA, ⁵The University of Oklahoma, Oklahoma City, OK, USA, ⁶The University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK, USA

Objective:

Method: In this multiinstitutional retrospective study, 155 patients with advanced or recurrent EC who received systemic chemotherapy were evaluated for baseline clinical characteristics. Prognostic factors predictive of response were identified using a logistic regression model. Adjusted Cox proportional hazards models using a backwards selection procedure were utilized to assess how covariates were associated with progression free (PFS) and overall survival (OS) in the presence of other variables. A predictive model was developed.
**Results:** Multivariate analysis identified 4 factors (African-American, type II EC, progressive disease following initial treatment, and multiple recurrent lesions) independently prognostic of poor response. Notably, adjuvant chemotherapy with initial radiation therapy did not affect prognosis. An additional 4 factors known to have prognostic significance (age ≥70 years, stage 3/4, presence of LVSII on uterine specimen, and depth of invasion ≥50%) were also included. A simple prognostic index was derived based on the total number of risk factors, and patients were classified into three risk groups: low risk (0–2 factors), mid risk (3–5 factors), and high risk (6–8 factors). Patients in the low-risk group experienced an overall response rate (ORR) of 96% to systemic chemotherapy with median PFS of 15.2 months and median OS of 29.6 months. Whereas patients in the high-risk group experienced an ORR of 50% to systemic chemotherapy with a median PFS of 12.3 months and median OS of 19.2 months.

**Conclusion:** A simple index based on 8 prognostic factors may have utility in clinical practice to identify women with advanced/recurrent EC who are not likely to respond to systemic chemotherapy. External validation of this predictive model is needed. Receipt of a prior radiosensitizer does not adversely affect response to subsequent chemotherapy following recurrence and should not be an exclusion factor for clinical trials evaluating systemic therapies.

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**2404 - Poster Session**

**Analysis of the endometrial stroma may play an important role in predicting progestin response in complex atypical hyperplasia or grade I adenocarcinoma**


*University of California, Los Angeles, Los Angeles, CA, USA, Spectrum Health Hospital Group/Michigan State University, Grand Rapids, MI, USA*

**Objective:** To determine whether stromal progesterone receptor expression and differential methylation in pretherapy endometrial biopsies correlate with response to hormonal therapy in a subset of patients with complex atypical hyperplasia or grade 1 adenocarcinoma.

**Method:** In this cross-sectional study, 27 patients with a confirmed diagnosis of complex atypical hyperplasia or grade 1 adenocarcinoma were treated solely with progestins. Fourteen of the 27 patients were categorized as progesterone sensitive, and 13 were resistant to therapy. Response to treatment was confirmed by subsequent biopsy or on final hysterectomy specimen. Immunohistochemistry for the progesterone receptor (PR) was performed on pretherapy biopsies, and a progesterone receptor expression score (PRES) was calculated for each cellular compartment (epithelium or stroma) by multiplying the percentage PR-positive nuclei by the intensity of staining. Whole genome bisulfite sequencing was used to identify differentially methylated regions (DMRs) in the epithelia and stroma of 5 sensitive and 5 resistant patients from this study cohort.

**Results:** Stromal PRES in pretherapy biopsies was significantly higher in the progestin responsive group (*P* = 0.001), and the most accurate in predicting treatment response (89%). There was no significant difference in the epithelial PRES between these groups. When the sensitive and resistant samples were compared, there were 245 DMRs identified in the stroma and 144 DMRs in the epithelium.

**Conclusion:** When epithelium and stroma in pretherapy biopsies were analyzed in this cohort of patients with atypical hyperplasia or adenocarcinoma, stromal progesterone receptor expression was more accurate in predicting response to progestin therapy. The DMRs identified between the sensitive and resistant groups involved response to estradiol, response to retinoic acid, and response to peptide hormone. These findings highlight the clinical significance in analyzing endometrial stroma. Further studies in a larger cohort are needed to validate these findings.

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**2405 - Poster Session**

**MSI-high due to MLH1 methylation is associated with worse recurrence-free and overall survival in endometrioid-type endometrial cancer: Implications for adjuvant therapy**

M. Avila, B. Fellman and R. Broaddus

*The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

**Objective:** Beyond advanced stage and grade at time of presentation, there are few reliable biomarkers that identify patients with endometrioid-type endometrial cancer at higher risk for recurrence or that have an impact on overall survival. The detection of MSI-high secondary to MLH1 gene methylation and subsequent loss of MLH1 protein is one of the most common molecular events in endometrioid carcinomas, occurring in 15%–20% of cases. While there is conflicting evidence on the
impact of MSI-high on clinical outcome, few have examined the role of MLH1 methylation specifically. The objective of this study was to determine whether MLH1 hypermethylation has an impact on recurrence and survival.

**Methods:** A retrospective review of 615 patients with endometrial carcinoma was performed. Clinical and pathological variables were extracted from pathology reports and electronic medical record. Tumors were screened via immunohistochemistry (IHC) for presence of the 4 mismatch repair (MMR) proteins with testing of MLH1 methylation when there was IHC loss of MLH1. Patients were separated into 3 groups: mismatch repair deficient-probable Lynch (dMMR-L), sporadic mismatch repair deficient with MLH1 hypermethylation (dMMR-S), and mismatch repair intact (iMMR).

**Results:** A total of 515 patients were categorized as endometrioid and 100 as nonendometrioid carcinomas. Of those with endometrioid-type carcinoma, 44 were dMMR-L, 86 were dMMR-S, and 385 were iMMR. Both the dMMR-S (28%) and dMMR-L (27%) groups had a higher incidence of presentation at stage III or IV compared to the iMMR patients (13%, \( P = 0.012 \)). Sites of recurrence (abdominal, extra-abdominal, local) did not differ between the 3 groups. Multivariate analysis showed that the dMMR-S group had significantly worse recurrence-free (\( P < 0.001, \text{HR} = 2.58, 95\% \text{CI} 1.52–4.38 \)) and overall (\( P < 0.001, \text{HR} = 3.76, 95\% \text{CI} 2.07–6.83 \)) survival (Figure 1a). This effect was especially pronounced in the stage I patients (Figure 1b). MMR deficiency had no impact on survival in the patients with nonendometrioid cancers.

**Conclusion:** In this cohort, tumors with presence of MLH1 hypermethylation have increased risk of recurrence and decreased overall survival compared to patients with MSS tumors. Importantly, MLH1 hypermethylation provides prognostic value in early stage disease. MLH1 methylation status should be taken into account in stage I patients for whom adjuvant therapy is a consideration.

**Figure 1a. Recurrence-free Survival and Overall Survival for All Stage Endometrioid Endometrial Cancer**

![Figure 1a](image1.png)

**Figure 1b. Recurrence-free Survival and Overall Survival for Stage 1 Endometrioid Endometrial Cancer**

![Figure 1b](image2.png)

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2406 - Poster Session

The effect of HPV testing in the detection of adenocarcinoma in situ and adenocarcinoma of the cervix


aUniversity of Minnesota, Minneapolis, MN, USA, bHealthPartners, Saint Paul, MN, USA
**Objective:** To evaluate a cohort of patients with adenocarcinoma in situ (AIS) or occult adenocarcinoma who were diagnosed based on cervical cancer screening tests and to determine whether method of diagnosis (HPV testing alone, cytology alone, or HPV and cytology) affects clinical outcome and management. Despite widespread screening, the incidence of cervical adenocarcinoma and its precursor, AIS, has continued to increase. As screening recommendations evolve, including the new option for primary HPV testing alone, it is important to assess whether screening is sufficient and to understand how method of detection may affect the clinical course of disease.

**Method:** This was a multicenter retrospective cohort study. We identified patients with AIS or occult carcinoma detected by routine screening between 2007 and 2017. Patients were divided into 3 cohorts based on which test led to their diagnosis: (1) HPV positive with normal cytology (HPV+/Pap−), (2) HPV negative with abnormal cytology (HPV−/Pap+), (3) HPV positive and abnormal cytology (HPV+/Pap+). Clinical demographics, treatment course, and surgical pathology were reviewed.

**Results:** A total of 130 patients were diagnosed with AIS (n = 108) or adenocarcinoma (n = 22) of the cervix based on abnormal screening tests. Sixteen subjects were HPV+/Pap− (12%), 11 were HPV−/Pap+ (8%), and 103 were HPV+/Pap+ (79%). Demographics were similar between groups, although HPV+/Pap− patients were slightly older and more likely to have used an IUD for contraception (33.3%) compared to HPV+/Pap+ (8.9%) and HPV−/Pap+ (9.1%) groups (P = 0.13). Rates of positive margins were highest in the HPV−/Pap+ group (63.6%) and similar in the HPV+/Pap+ (26.5%) and HPV+/Pap− (28.6%) groups (P = 0.05). Similar percentages of women in each group were offered fertility preservation (50.0%–61.3%, P = 0.79). After adjusting for differences in age and margin status, rates of definitive hysterectomy were similar between groups (52.1%–81.3%, P = 0.59).

**Conclusion:** We did not observe differences in clinical outcomes of lesions detected by abnormal HPV testing alone versus abnormal co-testing. Notably, in this study cohort, a significant proportion of AIS and adenocarcinoma was detected by both HPV alone (with normal Pap) and Pap alone (with negative HPV), arguing for continued HPV and Pap co-testing and against the options of HPV testing alone or cytology alone for cervical cancer screening.

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**2407 - Poster Session**

**Characteristics of uterine papillary serous cancer by next generation sequencing**

S.A. Ostby, B.M. Roane, A. Londono, R.C. Arend and C.A. Leath III. *University of Alabama at Birmingham, Birmingham, AL, USA*

**Objective:** To evaluate next-generation sequencing (NGS) testing outcomes among uterine papillary serous cancer (UPSC) for trends in mutated genes, therapeutic recommendations, and evaluation for possible associated *BRCA* germline mutations.

**Method:** Review of all patients with UPSC and NGS testing at a single academic center was performed between 2016 and 2018. Time to initiation of therapy, targeted drug therapy selection, and identification of underlying germline mutations were analyzed.

**Results:** Twenty patients diagnosed with UPSC underwent NGS in the study period. Median age at time of NGS testing was 60.0 years; most were Caucasian (65%) and had stage IV disease (n = 11, 55%). Previous treatment history included initial surgery, with an average of 2 prior lines of chemotherapy, and radiation in 50% of patients. Mean time from ordering NGS testing to the generation of the patient-specific report was 13 days and initiation of a targeted therapy in those ultimately pursuing treatment 189 days. NGS testing identified on average per patient 5.2 mutations for which the mean number of targetable mutations was 2.1 (range 1–4). Targeted therapy was recommended in all patients with an average number of 4.8 drugs per patient. Mutations in PIK3CA pathway were found most common (60%) followed by ERBB2 (30%). Targeted therapy was prescribed in 6 (30%) patients, with mean duration of therapy equal to 93 days. Most common targeted therapies included use of mTOR inhibitors (n = 4, 66.7%). Trastuzumab and rucaparib were used in 1 patient each. Discontinuation of therapy was most commonly due to progression on therapy (n = 4, 66.7%). There was 1 *BRCA* somatic mutation identified in a patient with negative germline testing.

**Conclusion:** NGS testing identified a targeted molecular therapy and was implemented most commonly for advanced-stage UPSC. Most commonly, PIK3CA mutations were found. There was not a suggestion for an association between *BRCA* mutations and UPSC with the use of NGS. Utilization of NGS testing in patients with UPSC provides additional treatment options beyond second-line therapy and offers insight into understanding these tumors on a gene level that could help with future clinical trials and management.
Objective: Women with epithelial ovarian cancer and a germline or somatic mutation in BRCA genes have a better prognosis. We sought to evaluate the clinical outcomes of patients with epithelial ovarian, fallopian tube, and primary peritoneal cancer (EOC) who developed brain metastases (BM) by mutation status.

Method: We identified patients with EOC and BM seen at our institution from January 2008 to July 2018. Charts were reviewed for relevant clinical characteristics and germline/somatic BRCA mutation status. Somatic and germline mutations were grouped for analyses. Survival analysis was done using Kaplan-Meier method.

Results: Of the 3,649 patients with EOC who presented to our institution, 91 had BM (2.5%). Of these, 76 had high-grade serous histology (84%). Germline and somatic BRCA status was available for 63 (69%) and 21 (23%) patients, respectively: 15 harbored BRCA1 and 6 BRCA2 germline mutations, and 1 had BRCA1 somatic mutation. Primary treatment, including use of intraperitoneal chemotherapy, did not differ by mutation status (P = 0.10). Median time to diagnosis of BM did not differ by mutation status: 34 months for BRCA mutation (range 0–85 months), 32 months for wildtype (WT) (range 0–96 months), and 24.5 months for unknown (range 4–80) (P = 0.39). Patients with BRCA mutation were more likely to have BM as the only evidence of disease at recurrence compared to WT patients (10/22 and 8/41, respectively, P = 0.04). There were no significant differences in treatment of BM by mutation status (P = 0.16). In the entire cohort, 7 patients received best supportive care (8%); 48 received radiation therapy (RT) only (53%); 33 underwent surgery and RT (36%); 2 had chemotherapy only (2%); and 5 had PARP inhibitor therapy in addition to one of the other treatment modalities (5%; these were all patients with BRCA mutations). Median overall survival from time of BM diagnosis was significantly longer for patients with BRCA mutation at 22 months (range 1–60 months) compared to WT (9 months, range 1–44 months) or unknown (6 months, range 1–71 months) (P = 0.03). See Figure 1.

Conclusion: BM were seen in only 2.5% of patients with EOC over the 10-year period. We show that germline and somatic BRCA mutation confer a significantly better prognosis for EOC with BM. Patients with mutation were more likely than WT patients to have isolated recurrence identified as BM and had longer OS. These data support pursuing more aggressive treatment in BRCA mutation ovarian cancer patients with BM.
2409 - Poster Session
Cancer biomarkers to improve performance of Xpert HPV for cervical cancer screening
L. Kuhn1, C. Svanholm-Barrie2, R. Saidur3, A.I. Tergas4, R. Boa5, J. Moodley6, S. Campbell7, D. Persing8, and L. Denny9. 1New York-Presbyterian/Columbia University Medical Center, New York, NY, USA, 2Cepheid, Solna, Sweden, 3University of Cape Town, Cape Town, South Africa, 4Cepheid, Sunnyvale, CA, USA, 5Groote Schuur Hospital, Cape Town, South Africa

Objective: We evaluated whether inclusion of cancer biomarkers improves performance characteristics of Xpert HPV testing as screening for cervical intraepithelial neoplasia grade 2 or greater (CIN2+).

Method: In a clinical study in Cape Town, South Africa, 418 HIV-negative and 426 HIV-positive women, aged 30–65 years, were recruited. All women had a cervical sample collected and underwent colposcopy and histological sampling with consensus pathology review. Cervical samples were tested on-site with Xpert HPV, a cartridge-based PCR that detects 14 high-risk HPV types in five channels: (1) HPV 16, (2) HPV 18, and 45, (3) HPV 31, 33, 35, 52, and 58, (4) HPV 51, and 59, and (5) HPV 39, 56, 66, and 68. A cycle threshold (Ct) value is generated for each channel. Cervical samples were also tested using real-time PCR to detect mRNA for CDKN2A, TOP2A, and MKi67. Results were reported as delta Ct values relative to internal controls. Multivariate logistic regression and receiver operating characteristic (ROC) curves were used to evaluate associations between Ct and delta Ct values for Xpert HPV channels and mRNA biomarkers with CIN2+.

Results: Ct values from channels detecting HPV 16, 18, 45, 33, 35, 52, and 58 were informative to predict CIN2+. The area under the curve (AUC) was 0.906 in HIV-negative and 0.870 in HIV-positive women. When sensitivity was set at 80%, specificity was 94.0% in HIV-negative and 82.7% in HIV-positive women. Delta Ct values for detection of mRNA for CDKN2A and MKi67 added significant improvement to the prediction of CIN2+ when included with the Ct values from the 3 informative Xpert channels. Including both HPV and biomarker parameters, AUC was 0.944 in HIV-negative and 0.913 in HIV-positive women. When sensitivity was set at 80%, specificity was 97.3% in HIV-negative and 89.6% in HIV-positive women.

Conclusion: Improvements in specificity of a round of screening using Xpert HPV can be achieved with the addition of cancer biomarkers.

2410 - Poster Session
Uterine sarcomas: Patterns of care, prognostic variables, and treatment effect
A. Shinde1, D. Akhavan2, A. Amini3, Y.J. Chen4, S. Beriwal5, S. Glaser6 and R.Li7. 1City of Hope, Duarte, CA, USA, 2Magee-Womens Hospital of UPMC, Pittsburgh, PA, USA

Objective: Optimal adjuvant therapy in patients with uterine sarcomas is uncertain. We evaluated the impact of adjuvant chemotherapy (CT), brachytherapy (BT), and external beam radiation (EBRT) in patients with high-grade endometrial stromal sarcoma (ESS), leiomyosarcoma (LMS), and undifferentiated uterine sarcoma (UUS).

Method: Patients with uterine cancer diagnosed from 2004 to 2015 were identified from the National Cancer Data Base. Patients who underwent upfront hysterectomy with ESS, LMS, or UUS histology, with stage IA–IVA disease were evaluated. Overall survival (OS) was compared using log rank Kaplan-Meier for univariate analysis (UVA), and Cox proportional hazards for multivariate analysis (MVA).

Results: We identified 4,942 patients. Median follow-up was 34 months. Patients received CT, BT, and EBRT in 36.3%, 6.8%, and 17.1% of cases, respectively. UVA did not show any benefit across all stages of disease for EBRT. CT worsened OS in all patients (3-year OS 53.4% vs 65.4%, P < 0.001). On subset analysis, stage III and IVA patients benefited from EBRT (stage III, 50.5% vs 32.1%; stage IVA, 38.9% vs 18.6%; P < 0.05). CT worsened OS in stage I patients (68.6% vs 71.9%, P = 0.044), and improved OS only in stage IVA patients (2-year OS = 41.6% vs 29.2%, P = 0.019). BT did not affect OS. MVA showed increasing stage of disease and UUS histology, and increasing tumor size worsened OS. Receiving CT was a borderline significant risk factor for worse survival (HR = 1.1, P = 0.05). EBRT improved OS (HR = 0.87, P = 0.018). BT had no effect. MVA stratified by stage showed improved OS with EBRT in stage II, III, and IVA patients (HR = 0.78, 0.58, and 0.26, respectively, P < 0.05 for all). CT was associated with worse OS in stage I patients, and only improved survival in stage IVA patients (HR = 1.16 and 0.42, P < 0.05). BT did not affect OS. MVA stratified by histology showed different effects. In hGESS, EBRT improved OS, while CT worsened OS (HR = 0.79 and 1.2, P < 0.05). In LMS, EBRT borderline improved OS (HR = 0.88, P = 0.060). In UUS, EBRT and CT improved OS (HR = 0.22 and 0.12, P < 0.05). See Table 1.
Conclusion: In this cohort of women with uterine sarcoma, observation appears to be appropriate for stage I patients. Stage II and III patients derive benefit with EBRT. Stage IVA patients benefit from both CT and EBRT. UUS benefits with EBRT and CT.

Table 1. Multivariable Cox Proportional Hazard Models for Overall Survival. EBRT = external beam radiation therapy. ESS = endometrial stromal sarcoma.
**Objective:** Prior studies have demonstrated that low-grade serous carcinoma of the ovary/peritoneum (LGSOC) is relatively chemoresistant in the adjuvant, neoadjuvant, and recurrent settings. While response rates of high-grade serous carcinoma of the ovary/peritoneum (HGSOC) to neoadjuvant chemotherapy (NACT) range from 70% to 90% in the literature, our prior work has demonstrated significantly lower response rates in LGSOC. We sought to update our prior work and evaluate response rates of women with LGSOC to NACT.

**Method:** Clinical data were abstracted on 35 patients from our institutional database with LGSOC treated from 2003 to 2018. Five patients (14%) were previously included in our aforementioned study of NACT in LGSOC. A single radiologist re-reviewed pre- and post-NACT imaging for response using RECIST criteria. Pre- and post-NACT CA-125 values were compared using paired t-tests. ER, PR, and Ki67 are being measured in a subset of cases for correlation with response; analysis is ongoing. Kaplan-Meier estimates of PFS and OS were performed.

**Results:** The median age was 56.0 years (21.9–86.6 years). The majority of patients (33/35, 94%) were diagnosed with stage III or IV disease. All patients received platinum-based regimens, the majority of which included carboplatin and paclitaxel (32/35, 91%) with a median of 4 cycles (range 3–9). Eighty-five percent (28/33) of patients underwent interval cytoreductive surgery. Fifty-four percent (15/28) of patients had residual disease present at the completion of surgery; 11/28 (39%) had no gross residual disease; and 2/28 (7%) did not have documentation of residual disease. Median pre-treatment CA-125 was 322.9 (range 14.9–2949.0); median post-treatment CA-125 = 150.0 (range 8.1–2614.0) (P < .001). Median decrease in CA-125 was 49.7%; 16/32 patients had >50% decrease in CA-125; and 3/35 (8.6%) had a partial response; 30/35 (85.7%) had stable disease; and 2/35 (5.7%) had progressive disease. Twenty-five patients (71.4%) received maintenance therapy for a median of 14 months; 23/25 (92%) received letrozole. Median OS for all patients was 47.43 months (95% CI 31.68–68.13) and median PFS was 19.97 months (95% CI 13.13–26.80).

**Conclusion:** This study provides further evidence of relatively low response rates of patients with LGSOC to NACT.

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**Objective:** To investigate whether select combinations of HPV genotypes, ascertained by Linear Array (LA) (lab-based, individual typing) and GeneXpert (GX) (point-of-care, grouped typing), can optimize sensitivity/specificity trade-offs to detect cervical intraepithelial neoplasia grade 2, 3, or cancer (CIN2+) in a South African screening population.

**Method:** We recruited women aged 35 to 60 years attending a community screening clinic (general population) and colposcopy referral clinic (high-risk population) in Cape Town. Each woman underwent a pelvic examination to collect cervical samples (tested by LA and GX for 14 high-risk HPV genotypes) and colposcopy-directed biopsy, LEEP, or ECC (reviewed by a pathologist for disease endpoint CIN2+). Multivariate logistic regression was used to determine HPV genotypes significantly associated with CIN2+ (P < 0.05). Guided by the multivariate results, we selected different HPV genotype combinations to calculate sensitivity and specificity. Type-specific prevalence and specificity were calculated using only data from the general population sample. Sensitivity was calculated combining data from the general and high-risk populations.

**Results:** There were 714 women (382 HIV–, 332 HIV+) from the general population and 404 women (200 HIV–, 204 HIV+) from the high-risk population included in the study. Prevalence for any HPV type was 29.7% by LA and 31.09% by GX (93.56% overall agreement, 0.85 kappa value). Type-specific prevalence by single/multiple infection for GX and LA is shown in Figure 1. Seven of the 14 HPV types (16, 18, 31, 33, 35, 52, and 58) were significantly associated with CIN2+. We included these 7 types in our combination analysis.

---

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types along with HPV 45 in calculations of selected typing. Sensitivity and specificity rates for full typing (all 14 HPV types) were similar to that of selected typing. For LA, sensitivity was 89.2% (full) versus 84.8% (selected). Specificity was 77.2% (full) versus 82.4% (selected). For GX, sensitivity was 91.6% (full) versus 89.2% (selected). Specificity was 75.3% (full) versus 80.2% (selected).

**Conclusion:** To optimize clinical performance of GX and LA for screening, HPV 16, 18, 45, 31, 33, 35, 52, and 58 should be included. HPV 45 was included for known links to adenocarcinoma. HPV 51, 59, 39, 56, 66, and 68 did not significantly improve sensitivity/specificity and could be considered for exclusion in screening tests.

**Fig. 1.** Type specific HPV Prevalence by Single/Multiple Infection.
**Method:** This was a retrospective analysis of 118 patients with cervical cancer who received a radical hysterectomy and ovarian transposition before pelvic irradiation from April 2012 to July 2017. A total of 105 patients underwent intensity-modulated radiation therapy (IMRT) with a limited radiation dose to the ovaries; 48 of these patients received unilateral ovary limitation, while 57 received bilateral ovary limitations. Patient follow-up regarding sex hormone levels (E2, follicle-stimulating hormone [FSH]) and menopausal symptoms was completed 1 year after their radiation therapy.

**Results:** Ovarian function was absent in 13 patients who received IMRT with no limitation on radiation dose to the ovaries. A total of 41 out of 105 patients (39.0%) who underwent IMRT with a limited radiation dose to the ovaries preserved their normal ovarian function. The percentage of patients with normal ovarian function was 33.3% and 43.9% in unilateral and bilateral ovaries limitation ($P = 0.318$), respectively. The cutoff dose of comparatively lower side ovarian maximum dose was 9.985 Gy (43.5% vs 3.8%, $P < 0.001$), and the cutoff mean dose was 5.32 Gy (45.6% vs 12.8%, $P = 0.001$). The average age of normal and abnormal ovarian function patients was 35.44 years and 39.09 years, respectively ($P < 0.001$).

**Conclusion:** Using IMRT, preservation of ovarian function was possible when the limited dose was as low as possible to the ovaries regardless of bilateral or unilateral limitation to the ovaries. The comparatively lower side ovarian maximum dose of less than 9.985 Gy and a mean dose less than 5.32 Gy could be better at preventing ovarian function. Ovarian function was better preserved in younger patients.

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**2414 - Poster Session**

**Primary cytoreductive surgery versus neoadjuvant chemotherapy for advanced-stage uterine malignancies**

G. Altwerger, K. Haines, G. Yadav, B. McNamara, H. Hosier, G. Menderes, G.S. Huang, M. Azodi, D.A. Silasi, A.D. Santin, E.S. Ratner, P.E. Schwartz, and B. Litkouhi. *Yale University School of Medicine, New Haven, CT, USA, Baylor College of Medicine, Houston, TX, USA*

**Objective:** The efficacy of neoadjuvant chemotherapy (NACT) for advanced-stage uterine cancer is not known. The purpose of this study is to compare NACT to primary cytoreduction (PCR) in both uterine serous (USC) and endometrioid (EAC) uterine cancer. Furthermore, prior research has shown increased rates of DVT/PE in ovarian malignancies treated with NACT; this study aims to evaluate the rate of DVT/PE in uterine malignancies treated with NACT.

**Method:** This is a single-institution retrospective study including uterine cancer stage IV USC and EAC grade 2/3 treated 2010–2017. Demographic data, stage, pathologic subtype, presenting symptom, ECOG, surgical approach, radiation, number of chemotherapy regimens, date of demise. Kaplan-Meier method, Wilcoxon rank sum tests, Cox, and logistical regression were used.

**Results:** A total of 51 patients with stage IV uterine cancer with a median age of 65 years were identified. The median OS of all stage IV patients was 41 months. The majority of patients had USC (53%); the remainder had EAC (47%). Patients undergoing PCR had a 52-month longer survival when compared to patients who underwent NACT (Figure 1A). In Cox proportional hazards regression model, age, BMI, presentation (vaginal bleeding vs systemic symptoms), radiation, ECOG, number of chemotherapy regimens, minimally invasive versus open, and DVT/PE were not independent prognostic factors for OS (Table 1). Interestingly, pathologic subtype was found to be an independent risk factor for OS (Table 1). When stratified for pathologic subtypes, USC showed no statistical difference in OS between PCR and NACT ($P = 0.3954$) (Figure 1B). Strikingly, the EAC histologic subtype showed a statistical difference between PCR versus NACT ($P = 0.0018$), 93 versus 41 months, respectively (HR = 3.926, 95% CI 1.1–14.44) (Figure 1C). Finally, by logistical regression analysis NACT was not an independent risk factor for development of DVT/PE ($P = 0.357, 95\% \text{ CI 0.48–7.655}$) in stage IV uterine cancer.

**Conclusion:** Patients with EAC undergoing PCR have longer OS when compared to NACT, whereas patients with USC have similar OS when treated with NACT or PCR. Given these findings, it is important to know the pathologic subtype when planning PCR versus NACT in advanced-stage uterine cancer. Last, NACT does not increase risk of DVT/PE when compared to...
2416 - Poster Session
Mutational landscape of gynecologic cancers identified by prospective clinical sequencing in a nationwide cancer network


Cancer Treatment Centers of America, Chicago, IL, USA, Cancer Treatment Centers of America, Newnan, GA, USA, Foundation Medicine, Inc., Cambridge, MA, USA, Cancer Treatment Centers of America, Phoenix, AZ, USA, Cancer Treatment Centers of America, Philadelphia, PA, USA, Cancer Treatment Centers of America, Tulsa, OK, USA

Objective: Tumor genomic profiling is a critical component of precision oncology allowing the detection of genomic alterations (GA) with the potential to be targeted therapeutically. We present an analysis of comprehensive genomic profiling (CGP) of a large series of gynecologic cancers (GC) assayed in a nationwide cancer network.
Method: A total of 870 patients with advanced GC were assessed by CGP by hybrid capture of up to 406 cancer-related genes on tumor tissue or for 62 genes on circulating tumor DNA ordered during clinical care for treatment decision making between January 2013 and May 2018. Clinically relevant GA were defined as associated with targeted therapies or mechanism-driven clinical trials. For 424 GC, tumor mutation burden (TMB) was calculated by counting mutations across a 0.8 to 1.11 Mb region (TMB high, ≥20 muts/Mb). Microsatellite instability status (MSI high, MSI intermediate, or MS stable) was assigned by a computational algorithm examining 114 intronic homopolymer loci for 454 cases. Treatment histories for 603 patients were obtained with Institutional Review Board-approved retrospective review.

Results: Median age was 56 years (range 18–94 years): 68% were Caucasian. Ovarian-type carcinomas predominated (52%). GA were identified in 96% (833/870) of GC, of which 603 (72%) had clinically relevant GA. PI3K/AKT/mTOR pathway (PIK3CA, AKT1/2/3, PIK3R1, PTEN, MTOR, STK11, FBXW7) clinically relevant GA were most common, present in 42.4% of GC. Clinically relevant GA in other targetable pathways were identified: 27% in MEK (KRAS, NRAS, Hras, BRAF, RAF1, GNAS, NF1, NF2), 10.5% in HRD (BRCA1/2, ATM, PALB2, BRIPI), and 9.0% in ERBB (ERBB2, ERBB3, ERBB4, EGFR). Thirty-two (7%) GC were MSI high or TMB high suggesting potential benefit from immunotherapy. Twenty-seven percent (163/603) of GC patients were ordered a genomically matched treatment; 64% (105/163) were agents that were FDA-approved in a different tumor type, and 23% (37/163) were through referral to a matched mechanism-driven clinical trial. With the access to TAPUR, the frequency of matched treatment through clinical trials increased over time from 2013 to 2018.

Conclusion: In a large series of GC assayed with CGP, 20% of patients received matched treatment, which was predominantly targeted therapy. The comprehensive sensitive and unbiased nature of CGP, coupled with a multidisciplinary molecular tumor board and staff dedicated to genomic interpretation, assisted in achieving a high frequency of patient participation in clinical trials and gene-directed treatment. Future analysis will explore outcomes for this subset of patients.

2417 - Poster Session
Risk of cervical and vaginal neoplasia after surgery for vulvar intraepithelial neoplasia or cancer: A 6-year follow-up study
T.R. Buchanan Jr., A.S. Zamorano, E. Liu, P.H. Thaker and L.M. Kuroki. Washington University School of Medicine in St. Louis, St. Louis, MO, USA

Objective: Current guidelines to continue cytology screening after hysterectomy are based on history of high-grade intraepithelial neoplasia of the cervix (CIN), but not of the vulva (VIN). Here, we aim to evaluate the utility of cytology among women, with and without prior hysterectomy, who underwent surgical management for VIN3+ disease by estimating the risk of high-grade cervical or vaginal intraepithelial neoplasia or cancer (CIN2+/VAIN2+) diagnosed during vulvar surveillance follow-up.

Method: Women who underwent surgery for high-grade VIN or vulvar cancer between 2006 and 2014 were identified retrospectively. Patients who underwent prior hysterectomy for any indication were included. Univariate and multivariate logistic regression analyses were used to identify clinical factors of abnormal cytology after surgical treatment for VIN and vulvar cancer.

Results: During our 8-year study period, 302 women were followed with surveillance exams after vulvar surgery over a median follow-up of 72 months. During that time, 100 (33%) women had abnormal cytology: 69 (23%) low-grade, 28 (9%) high-grade, and 2 (0.7%) carcinoma. Overall, 33% of women had a prior hysterectomy, but the risk of intraepithelial neoplasia or cancer was not significantly different from women with an intact cervix (9/99, 9%, VAIN2+ risk vs 15/203, 7%, CIN2+ risk). Correlates of high-grade cytology following treatment for VIN/vulvar cancer included non-white race (OR = 4.6, 95% CI 2.4–8.8), immunodeficiency (patients with human immunodeficiency virus or on immunosuppressive medications) (OR = 4.0, 95% CI 1.8–8.8), and prior abnormal cytology (OR = 4.4, 95% CI 2.1–9.3). The multivariable analysis shows that they remained significant (P < 0.01) (Table 1). Prior hysterectomy did not significantly decrease risk of abnormal cytology (OR = 0.87, 95% CI 0.5–1.6).

Conclusion: Women treated surgically for VIN/vulvar cancer have a 10% risk of at least high-grade cytology on surveillance screening. Prior hysterectomy does not mitigate the risk, as 9% will develop VAIN2+. Extrapolating from current guidelines, we recommend surveillance cytology screening at least 6–12 months after treatment, especially in women with a history of immunosuppression or prior abnormal cytology.
Table 1. Univariate and multivariate analyses assessing correlates of high-grade cytology after surgical treatment for vulvar intraepithelial neoplasia or cancer (N=302).

<table>
<thead>
<tr>
<th>Clinical Factors</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.980 (0.962-0.998)</td>
<td>0.03</td>
</tr>
<tr>
<td>Non-white race</td>
<td>4.565 (2.359-8.834)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cigarette smokinga</td>
<td>1.030 (0.600-1.767)</td>
<td>0.92</td>
</tr>
<tr>
<td>Immunosuppressionb</td>
<td>3.964 (1.785-8.801)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Prior abnormal Papc</td>
<td>4.438 (2.109-9.340)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior hysterectomy</td>
<td>0.869 (0.487-1.554)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

a Currently smoking only  
b Immunosuppression was defined as patients with human immunodeficiency virus or who were on immunosuppressive medications; data missing for 1 patient  
c Pap results available for 232 patients

2418 - Poster Session  
Gonadotropin receptors as targetable biomarkers in advanced, high-grade serous ovarian cancer  
aMoffitt Cancer Center-University of South Florida, Tampa, FL, USA, bH. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA

Objective: Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are probable risk factors for development of high-grade serous epithelial ovarian cancer (HGSOC). Gonadotropin-releasing hormone (GnRH) is released by the anterior pituitary and stimulates the production of FSH and LH. Reports suggest that endogenous production of GnRH by these malignant cells may provide an autostimulatory loop for cell growth. We hypothesized that targeted inhibition of gonadotropin hormone signaling would increase platinum cytotoxicity.

Method: Ascites samples were acquired from HGSOC patients at time of primary debulking surgery. Malignant cells of the ascites were cultured in the presence of increasing concentrations of cisplatin alone and in the presence of the GnRH antagonist, Degarelix, and evaluated for cisplatin-induced growth arrest using CellTiter96 cell survival assays. The relative protein levels of GnRH-R and FSH-R patient HGSOC cells were determined using Western blot analysis. Unpaired t-tests with Welch’s correction were used to determine whether cisplatin-induced HGSOC growth arrest was enhanced in the presence of Degarelix.

Results: HGSOC cells derived from the malignant ascites expressed various levels of GnRH-R and FSH-R. Further, in a subset of HGSOC cells, the cell growth inhibitory effects of cisplatin were enhanced in the presence of Degarelix. Densitometry analysis of immunobots suggested that Degarelix enhancement of cisplatin sensitivity was associated with increased relative expression of FSH-R but not GnRH-R on HGSOC cells.

Conclusion: HGSOC cells that exist in the malignant ascites express GnRH-R and FSH-R. Gonadotropin-signaling antagonism may be a beneficial addition to frontline platinum-based chemotherapy for a subset of HGSOC patients, and FSH-R expression may serve as a viable biomarker to select HGSOC patients most likely to benefit.

2419 - Poster Session  
Benefit of genome-driven treatment in gynecologic oncology patients  
aThe University of Chicago Medicine, Chicago, IL, USA, bNorthShore University HealthSystem, Chicago, IL, USA, cNorthShore University HealthSystem, Evanston, IL, USA

Objective: To review our experience of gynecologic oncology patients referred for tumor testing of somatic genetic mutations and to assess survival outcomes among patients who received targeted therapy.
**Method:** This was a retrospective chart review of gynecologic oncology patients referred for tumor testing of somatic genetic mutations from May 2013 to May 2018.

**Results:** Sixty-one patients were referred over the 5-year period, and 46 underwent somatic genetic mutation testing. Most had either ovarian or uterine cancers and had received a median of 3.7 previous chemotherapy regimens (range 0–14). The median number of mutations found was 3.5 (range 0–53); 82% had at least one actionable mutation. Twenty-five patients were started on a targeted medication (group 1), while 36 patients were not (group 2). In group 1, 96% had previously received a platinum agent, 36% in their most recent treatment. Four patients previously received immunotherapy, and 5 had received a PARP inhibitor. The most common drug started based on testing was everolimus (48%). The median time on a medication was 80 days. Clinical benefit rate (CBR = CR + PR + SD) was 32% and ranged from 8% to 60% by targeted therapy received. Only 8% discontinued drug for side effects; 88% stopped due to progressive disease. Twenty-one of 36 patients in group 2 had somatic mutation testing. Forty-two percent had no actionable mutation, and 38% opted for conventional chemotherapy despite having an actionable mutation. Fifteen patients never underwent testing; 5 preferred to remain off treatment (with no evidence of disease or stable disease), 5 opted for conventional chemotherapy without testing, and 5 went on hospice before their appointment. There was no difference in overall survival (OS) after somatic mutation testing (6.8 vs 6.1 months, \(P = \text{NS}\)) or OS after cancer diagnosis (47 vs 42 months, \(P = 0.4\)).

**Conclusion:** Somatic tumor mutation testing appears to provide novel treatment options for >80% of gynecologic oncology patients tested. The CBR in our cohort is comparable to that seen with traditional agents in a heavily pretreated population. Taking into account small numbers, the OS was similar between the two study groups, suggesting that targeted therapy may offer an alternative with a tolerable toxicity profile.

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**2420 - Poster Session**

**Anti-tumor effects of tetraarsenic oxide (TAO, As4O6) in human cervical cancer**

*M.S. Kim*, S.Y. Jeong, J.H. Kim, E.S. Paik, Y.Y. Lee, C.H. Choi, T.J. Kim, B.G. Kim, D.S. Bae and J.W. Lee. *Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South); Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

**Objective:** Current standard therapy for advanced or recurrent cervical cancer is combination chemotherapy with paclitaxel or topotecan based on cisplatin chemotherapy. However, this combination chemotherapy shows only a 27%~36% response rate. Therefore, there have been many efforts to discover other combination therapeutic agents for cervical cancer. Tetraarsenic oxide (TAO) showed the possibility of therapeutic effect in previous in vitro and in vivo studies with cervical cancer cell lines. The purpose of this study was to investigate the anticancer effect of TAO in an in vivo study using a patient-derived xenograft (PDX) mouse model and to reveal the mechanisms of TAO acting on tumor cells.

**Method:** We performed in vivo experiments with subrenal injection of three different squamous cell carcinoma PDX models of uterine cervix. TAO was administered to each group to compare the antitumor effect with control. We also performed in vitro studies using cervical cancer cell lines, in order to understand the mechanism of the anticancer effect of TAO. TAO was treated with SiHa, HeLa, and HUVEC cells, and Western blot was performed. In addition, to investigate the effect of TAO on cell migration, we performed MMP2 and ELISA assays using HUVEC and SiHa cells.

**Results:** In vivo studies with PDX mouse model, all three showed significant tumor volume reduction in the TAO-treated group. Furthermore, the tumor volume decreased more significantly in the cisplatin combination group than in the single-agent and control groups. In in vitro studies with SiHa and HeLa cells, TAO decreased the phosphorylation of Akt. In HUVEC cells, TAO decreased VEGF receptor 1 expression. Furthermore, the same results were obtained after processing with VEGF in HUVEC cells. Also, MMP2 was decreased in HUVEC cells.

**Conclusion:** TAO reduces tumor volume in cervical cancer PDX mice, which is more pronounced in the cisplatin combination group. TAO inhibits phosphorylation of Akt and decreases VEGF receptor 1 expression. However, these mechanisms differ depending on the cell line. These results indicate the reduction of VEGF-related signaling pathway plays an important role in the anticancer mechanism of TAO in cervical cancer.

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**2421 - Poster Session**

**Surgical cytoreduction in stage IVB serous endometrial carcinoma**
**Objective:** To evaluate oncologic outcomes in patients diagnosed with stage IVB serous endometrial cancer treated with upfront cytoreduction.

**Method:** We retrospectively identified all patients with newly diagnosed stage IVB serous endometrial cancer treated with upfront surgery at our institution from January 2005 to December 2015. Patients were analyzed according to residual disease status: 0 mm, ≤10 mm, or >10 mm. Patients selected to upfront chemotherapy were excluded. Survival curves were constructed using Kaplan-Meier analyses and compared with log rank test. Fisher exact and Kruskal-Wallis tests were used for comparison of association analysis.

**Results:** Of 85 patients identified, 72 (85%) underwent upfront debulking surgery and had extent of residual disease documented. Of these 72 patients, 61 (85%) underwent open surgery and 11 (15%) minimally invasive surgery. All patients had total hysterectomy and adnexectomy; 49/72 (68%) had upper and lower abdominal resections (liver, diaphragm, spleen, stomach, or bowel resections); 23/72 (32%) had only omental and nodal resections. Thirty-eight of 72 (53%) patients had 0 mm residual, 23/72 (32%) ≤10 mm residual, and 11/72 (15%) >10 mm residual disease. With a median follow-up of 60.2 months (range 0.5–137 months), 60 patients experienced recurrence. Across all groups, median age, race, BMI, and histologic subtype were comparable (**Table 1**). In the 0 mm, ≤10 mm, and >10 mm groups, the median PFS was 10.1 months (range 8–15 months), 11.4 months (range 8–17 months), and 10.1 months (range 3–14 months), respectively. Sixty-nine of 72 (96%) patients received postoperative therapy (POT); 67/69 (97%) received postoperative chemotherapy; and 2/69 (3%) combination chemotherapy and radiation therapy. Of the 3/72 (4%) patients who did not receive POT, 2 died from postoperative complications and 1 was lost to follow-up.

**Conclusion:** In this series of surgically treated patients with stage IVB serous endometrial cancer, upfront surgical cytoreduction to 0 mm residual disease was not associated with improved PFS. Our analysis is limited because there were fewer patients with >10 mm residual disease and because results were not compared with patients who had upfront chemotherapy. Expanding the numbers in our series through collaboration is warranted to further evaluate the impact of 0 mm residual on PFS.

**Table 1:** Patient Characteristics by residual disease at time of upfront debulking surgery.
Patients treated with primary debulking surgery for ovarian cancer require a unique set of reportable complications to accurately capture postoperative events.

O.T. Filippova\textsuperscript{a}, M.A. McKay Jr.\textsuperscript{b}, K. Long Roche\textsuperscript{a}, O. Zivanovic\textsuperscript{b}, Y. Sonoda\textsuperscript{a}, G.J. Gardner\textsuperscript{a}, D.S. Chi\textsuperscript{b} and V. Broach\textsuperscript{a}. \textsuperscript{a}Memorial Sloan Kettering Cancer Center, New York, NY, USA, \textsuperscript{b}Meharry Medical College, Nashville, TN, USA

<table>
<thead>
<tr>
<th></th>
<th>Total cohort</th>
<th>0mm</th>
<th>≤10mm</th>
<th>&gt;10mm</th>
<th>p-value</th>
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<td><strong>Age</strong></td>
<td></td>
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<tr>
<td>Median years (range)</td>
<td>66 (56-80)</td>
<td>66 (56-80)</td>
<td>66 (56-80)</td>
<td>55 (56-80)</td>
<td>0.85</td>
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<tr>
<td><strong>Race</strong></td>
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<td></td>
</tr>
<tr>
<td>White</td>
<td>52 (73.4%)</td>
<td>29 (76.3%)</td>
<td>13 (75%)</td>
<td>8 (72.7%)</td>
<td>1</td>
</tr>
<tr>
<td>Black</td>
<td>14 (20.3%)</td>
<td>7 (18.4%)</td>
<td>5 (25%)</td>
<td>2 (18.2%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>3 (4.3%)</td>
<td>2 (5.3%)</td>
<td>0 (0%)</td>
<td>1 (9.1%)</td>
<td></td>
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<tr>
<td><strong>BMI</strong></td>
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</tr>
<tr>
<td>Median kg/m² (range)</td>
<td>28.3 (19-48)</td>
<td>28.6 (19-46)</td>
<td>27.7 (19-35)</td>
<td>28.3 (19-48)</td>
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<td><strong>CA125</strong></td>
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<td>Median U/mL (range)</td>
<td>93 (7-7289)</td>
<td>45.5 (7-2155)</td>
<td>246.5 (19-3525)</td>
<td>46 (212-7289)</td>
<td>0.001</td>
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<td><strong>Histology</strong></td>
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<tr>
<td>Serous</td>
<td>64 (88.9%)</td>
<td>32 (84.2%)</td>
<td>22 (95.7%)</td>
<td>10 (90.9%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Mixed</td>
<td>8 (11.1%)</td>
<td>6 (15.8%)</td>
<td>1 (4.3%)</td>
<td>1 (9.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Procedure</strong></td>
<td></td>
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<tr>
<td>Robot</td>
<td>8 (11.1%)</td>
<td>8 (21.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.002</td>
</tr>
<tr>
<td>TLH</td>
<td>3 (4.2%)</td>
<td>3 (7.9%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>TAH</td>
<td>61 (84.7%)</td>
<td>27 (71.1%)</td>
<td>23 (100%)</td>
<td>11 (100%)</td>
<td></td>
</tr>
<tr>
<td><strong>Extent of resection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor: debulk lower/upper abdomen</td>
<td>49 (68.1%)</td>
<td>20 (52.6%)</td>
<td>22 (95.7%)</td>
<td>7 (63.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Omentum and nodes alone</td>
<td>23 (31.9%)</td>
<td>18 (47.4%)</td>
<td>1 (4.3%)</td>
<td>4 (36.4%)</td>
<td></td>
</tr>
<tr>
<td># Lymph Nodes resected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>11 (1-48)</td>
<td>12 (1-43)</td>
<td>9 (2-48)</td>
<td>5.5 (1-21)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Depth of myoinvasion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>22 (31.4%)</td>
<td>9 (24.3%)</td>
<td>9 (40.9%)</td>
<td>4 (36.4%)</td>
<td>0.55</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>20 (28.6%)</td>
<td>10 (27%)</td>
<td>6 (27.3%)</td>
<td>4 (36.4%)</td>
<td></td>
</tr>
<tr>
<td>&gt;=50%</td>
<td>28 (40%)</td>
<td>18 (48.6%)</td>
<td>7 (31.8%)</td>
<td>3 (27.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Lymphovascular invasion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>22 (31.9%)</td>
<td>14 (38.9%)</td>
<td>4 (18.2%)</td>
<td>4 (36.4%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Absent</td>
<td>47 (68.1%)</td>
<td>22 (61.1%)</td>
<td>18 (81.8%)</td>
<td>7 (63.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Extent of metastases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nodal</td>
<td>2 (2.8%)</td>
<td>2 (5.3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Lower abdomen (bowel/omentum /inguinal nodes)</td>
<td>41 (56.9%)</td>
<td>22 (57.9%)</td>
<td>10 (43.5%)</td>
<td>9 (81.8%)</td>
<td></td>
</tr>
<tr>
<td>Upper abdomen</td>
<td>29 (40.3%)</td>
<td>14 (36.8%)</td>
<td>13 (56.5%)</td>
<td>2 (18.2%)</td>
<td></td>
</tr>
<tr>
<td>Pelvic/Para-aortic nodes/ lower abdomen</td>
<td>43 (59.7%)</td>
<td>24 (63.2%)</td>
<td>10 (43.5%)</td>
<td>9 (81.8%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Upper abdomen</td>
<td>29 (40.3%)</td>
<td>14 (36.8%)</td>
<td>13 (56.5%)</td>
<td>2 (18.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Post-operative therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>67 (97.1%)</td>
<td>36 (97.3%)</td>
<td>21 (100%)</td>
<td>10 (90.9%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy/radiation therapy</td>
<td>2 (2.9%)</td>
<td>1 (2.7%)</td>
<td>0 (0%)</td>
<td>1 (9.1%)</td>
<td></td>
</tr>
<tr>
<td>No post op treatment</td>
<td>3 (4.2%)</td>
<td>1 (2.6%)</td>
<td>2 (8.7%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>
**Objective:** To explore the frequency of occurrence of an expanded set of adverse postoperative events in women undergoing primary debulking surgery (PDS) for ovarian cancer.

**Method:** All women treated with PDS for epithelial ovarian cancer at our institution between June 2015 and December 2017 were identified via a prospective database. Data were collected on reported surgical complications as well as additional postoperative events: reoperation within 30 days of surgery and between 30 and 90 days of surgery (90 day), readmission within 30 and 90 days, surgical complications within 90 days, time to postoperative chemotherapy, and need for postoperative rehabilitation or home nursing services. Appropriate statistical methods were utilized.

**Results:** During the study period, 280 were treated. Median age was 62 years (range 25–90 years); 157 (56%) were stage IIIC; 72 (26%) were stage IV; and 220 (79%) were high-grade serous. Complete gross resection was achieved in 210 patients (75%), and optimal resection (0.1–1 cm) in 50 (18%). Review of reported surgical complications data showed a median postoperative stay of 7 days (range 0–44 days), and 31 patients (11%) with a grade 3+ surgical complication. Considering additional postoperative events, 7 patients (3%) had a reoperation within 30 days and 3 (1%) within 90 days of surgery. Thirty patients (11%) were readmitted within 30 days and 27 (10%) within 90 days. Thirty-one patients (11%) had a reportable surgical complication within 90 days, with 8 (26%) grade 3+. Two patients had both a 30- and 90-day complication. Eight patients (3%) required subacute rehabilitation after surgery and 36 (13%) received home physical therapy; 111 patients (41%) required home skilled nursing visits. The median time to initiation of postoperative chemotherapy was 36 days (range 2-105 days), with 22% of patients (n = 61) starting chemotherapy >42 days. Median follow-up time was 20 months. There was no difference in PFS in patients who started chemotherapy ≤ or >42 days (P = 0.271).

**Conclusion:** Women treated with PDS undergo complex surgery and experience complications that are both unique and outside of the usual 30-day reporting window. Extending reporting to 90 days would capture an additional 14% of patients with postoperative complications. Further study is needed to evaluate how these additional postoperative events relate to survival.

2423 - Poster Session

**Management of surgical menopause in women undergoing risk-reducing surgery for elevated risk of ovarian cancer: Can we do better?**


**Objective:** To evaluate the counseling and management patterns surrounding surgical menopause in women undergoing surgical risk reduction (RR) for elevated risk of ovarian cancer.

**Method:** All women presenting to a gynecologic oncologist at our institution for discussion of surgical RR between June 2015 and April 2018 were identified using a prospective database. Data on patient and procedure factors and on menopausal counseling and management were collected via medical record review. For this study, women were considered eligible for hormone replacement therapy (HRT) if they had no personal history of breast cancer or other major medical comorbidity. Appropriate statistical analyses were used.

**Results:** Over 34 months, 615 patients were seen for consultation with the following mutation profile: 235 (38%) BRCA1; 219 (36%) BRCA2; 10 (2%) moderate penetrance mutations; 117 (19%) no known pathologic mutation; and 35 (6%) family history alone. Median age was 46 years (range 22–76 years). Consult only occurred in 259 patients (42%), while RR surgery was performed in 356 patients (58%) with the following procedures (see Figure 1): 240 (67%) RR BSO; 95 (28%) RR BSO with hysterectomy; and 18 (5%) interval salpingectomy (ISDO). Of the 241 patients who were premenopausal at the time of RR and underwent a procedure including a BSO, preoperative discussion of surgical menopause was documented in 200 (83%) and counseling regarding management documented in 165 (69%). Documentation of menopausal symptom assessment was present in 173 (72%) of postoperative notes. In this cohort experiencing surgical menopause, 130 (54%) were eligible for HRT, and management patterns were as follows: 33 (25%) were prescribed HRT; 7 (5%) nonhormonal therapy; and 84 (65%) referred to other provider for further management. Of the 33 patients prescribed HRT, all had a BRCA mutation, 22 (67%) BRCA1; 11 (33%) BRCA2; 15 (45%) had a hysterectomy and were treated with estrogen alone. There was no difference in discussion of surgical menopause (P = 0.687), management (P = 0.287), or HRT prescribing (P = 0.231) between female and male providers.
Conclusion: The use of HRT even in eligible patients after surgical risk reduction, is low, although surgical menopause is discussed during the majority of presurgical clinic visits. Factors inhibiting higher uptake of HRT need further investigation.

2424 - Poster Session
The use of a laparoscopic surgical algorithm to triage the timing of cytoreductive surgery in patients with low grade serous ovarian and peritoneal cancer
L.P. Cobb, B. Felmam, D.M. Gershenson, A.K. Sood, A.M. Nick, S.N. Westin, R.L. Coleman and N.D. Fleming. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bTennessee Oncology, Nashville, TN, USA

Objective: We have recently published our experience utilizing a laparoscopic scoring algorithm to triage patients with advanced ovarian cancer to immediate or delayed cytoreductive surgery (CRS) for the purpose of improving complete gross surgical resection (CGR) rates. In this study, we evaluated the subset of patients with low-grade serous ovarian/peritoneal cancer (LGSOC) to determine CGR rates and evaluate clinical outcomes.

Method: Laparoscopic assessment was performed prospectively on patients with suspected advanced-stage ovarian cancer from April 2013 to September 2017. Patients with a predictive index score (PIV) ≥8 received neoadjuvant chemotherapy (NACT), and patients with PIV score <8 were offered primary CRS. This subset analysis evaluated only the patients who were diagnosed with LGSOC. Univariate analysis was performed for effects on PFS.

Results: A total of 799 patients presented to our institution with presumed advanced-stage ovarian cancer, and 41 (5%) of these patients were diagnosed with advanced-stage LGSOC. Twenty-five of the 41 patients (61%) were candidates for laparoscopic scoring assessment for primary resectability, of which 17 patients had a PIV score of <8 and 8 patients had a PIV score of ≥8. Sixteen patients did not undergo laparoscopy due to the following: surgically unresectable (n = 7), no evidence of carcinomatosis on imaging (n = 5), and other (n = 4). Three patients with a PIV score <8 received NACT due to faculty declining primary surgery. In total, 36 patients underwent cytoreductive surgery; 21 (58%) underwent primary debulking; and 15 (42%) underwent interval debulking. CGR was achieved in 21/36 (58%), residual of ≤1 cm in 7/36 (19%), and >1 cm in 8/36 (22%). On univariate analysis for PFS, higher baseline CA-125 (P = 0.027), patients undergoing primary surgery compared to NACT (P = 0.006), and remaining tumor size >1 cm (P = 0.006) were significantly associated with PFS.

Conclusion: Laparoscopic scoring assessment for resectability in patients with advanced LGSOC is feasible and serves as a useful tool in personalizing decision making in the care of these patients. Primary cytoreductive surgery to minimal residual disease is associated with improved PFS outcomes compared to patients undergoing NACT or suboptimal surgery.

2425 - Poster Session
A phase II feasibility study of nab-paclitaxel and carboplatin in chemotherapy naïve epithelial neoplasms of the uterus
B. Pothisic, J. Lee, F. Musa, K. Lutz, E. Reese, S.V. Blank, L.R. Boyd, J.P. Curtin, X. Li, J.D. Goldberg and F.M. Muggia. aNew York University School of Medicine, New York, NY, USA, bNYU Langone Medical Center, New York, NY, USA, cWinthrop University Hospital, Mineola, NY, USA, dNYU Cancer Institute, New York, NY, USA

Objective: Few effective treatment options exist for women with advanced or recurrent endometrial cancer (EC). To explore a modification of the standard systemic treatment for advanced or recurrent EC, we sought to determine the feasibility of completing 6 cycles of nab-paclitaxel (Nab-P) and carboplatin. Unlike paclitaxel, Nab-P does not require any steroid or other premedication, an important consideration for patients with diabetes mellitus and in the investigation of combinations with immunotherapy. We prospectively evaluated safety and efficacy of a day 1, 8-dose schedule of Nab-P in combination with carboplatin day 1 q3weeks in patients with chemotherapy naïve EC.

Method: Patients with early-stage and high-risk, advanced primary, or recurrent EC with no prior platinum and taxane exposure were enrolled at a single institution. Patients received 6 cycles of day 1 Nab-P 100 mg/m² IV with carboplatin AUC 6 IV and day 8 Nab-P 100 mg/m² IV q21days. We evaluated percentage completion of 6 cycles with standard dose reductions, as well as toxicity per CTCAE v.4. Measurable disease was not required, and efficacy was assessed by PFS rate at 6 months.

Results: From 2016 to 2018, 23 subjects were enrolled; median age was 65 (43–73) years. Nineteen (82%) completed 6 cycles of the doublet therapy. Eight subjects (35%) were dose-reduced 1 level, and 5 (22%) were reduced 2 levels; only 1 subject withdrew due to toxicity. Twelve subjects (52%) had at least 1 grade 3/4 treatment-related adverse event, the most
common being anemia, 6 (26%); neutropenia, 4 (17%); and diarrhea, 2 (9%). Pre-existing neuropathy was an exclusion criteria, and 13 (57%) reported at least grade 1 neuropathy with treatment. After treatment, 3 (13%) deaths occurred with 2 due to disease progression and 1 to pulmonary embolism. At 6 months after treatment initiation, 19 (83%) had no evidence of disease or its progression; 4 (17%) had progressed. Kaplan-Meier analysis revealed a 6-month PFS rate of 80.5% (95% CI 65.1%–99.7%) (Figure 1).

**Conclusion:** The Nab-P/carboplatin day 1, 8 regimen met the prespecified criteria of feasibility with acceptable toxicity and efficacy. Use of Nab-P obviates steroid premedications, ideal for immune checkpoint inhibitors that target mismatch repair deficient advanced EC. A future phase II feasibility trial combining an anti-PD-1 agent with Nab-P and carboplatin is planned.

![Kaplan-Meier plot of progression free survival rate of 23 subjects.](image)

**Fig. 1.** Kaplan-Meier plot of progression free survival rate of 23 subjects.

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**2426 - Poster Session**

**Molecular driven endometrial cancer therapy (MODEL): A prospective paradigm using molecular tumor profiling to direct therapy in women with advanced/recurrent endometrial cancer**


*Duke University Medical Center, Durham, NC, USA, New York University School of Medicine, New York, NY, USA, Foundation Medicine, Inc., Cambridge, MA, USA, NYU Langone Health, New York, NY, USA*

**Objective:** To explore the feasibility of molecular tumor characterization in metastatic endometrial cancers (EC) to direct therapy using clinically actionable targets.

**Method:** In December 2017, our program prospectively instituted the Molecular Driven Endometrial Cancer Therapy (MODEL) paradigm to treat metastatic EC patients with selection of therapy based on molecular tumor characterization (in-house immunohistochemistry, IHC, or next-generation sequencing, NGS, FoundationOne©) at the discretion of the treating physician. Therapies and reported predictive IHC and genomic alterations (GA) biomarkers included bevacizumab (B-catenin, CTNNB1), trastuzumab (ERBB2), temsirolimus (TSC), immunotherapy (MSI, dMMR, and Tumor Mutation Burden, TMB), and hormone therapy (estrogen, ER) and progesterone receptor (PR) for advanced disease (MODEL1). PI3K/AKT/mTOR pathway and ERBB3 GA were also included for recurrent disease (MODEL2). A retrospective review of Foundation Medicine (FMD) and our institutional Endometrial Cancer Databases (IECD) was performed.

**Results:** Of 3,702 advanced EC in FMD (922 endometroid, 826 serous, 156 clear cell, and 40 mixed, 1,758 EC-NOS), 1,497 (40.4%) had at least one MODEL1 qualifying GA: ERBB2 (370, 10.0%); CTNNB1 mutation (660, 17.8%); TSC2 mutation (43, 1.2%); MSI-H (534, 14.4%), or MSS/TMB ≥ 20 (93, 2.5%). A total of 2,994 (80.9%) EC had MODEL2 qualifying GA: 2,836 (76.6%) had PI3K/AKT/mTOR and 115 (3.1%) ERBB3 GA. For MODEL1, 247 (6.7%) and for MODEL2 1,340 (36.2%) EC had alterations qualifying for more than 1 therapy arm (Table 1). Institutional results were similar with 33.8% (22/65) and 78.5%
(51/65) having least one clinically actionable targets for MODE1 and MODEL2, respectively. Twenty-two of twenty-three IECD patients were eligible and had tumor testing; 63.6% had at least one clinically actionable target; 40.9% (9/22) had ER/PR+ tumors (median ER 80%, range 20%–100%; median PR 40%, 10%–96%). The most common GA were in the PI3K/AKT/mTOR pathways (6/10, 60%). Seventeen percent have received biomarker-directed therapy. Tumor response and survival outcomes are being evaluated.

**Conclusion:** Treatment with clinically actionable genomically targeted drugs is feasible in metastatic endometrial cancer. Overlapping genomic alterations are common, and therapeutic prioritization is needed.

**Table 1.** Overlapping molecular features of studying patients (n=3702).

<table>
<thead>
<tr>
<th></th>
<th>TMB H/MSI H (n=627)</th>
<th>CTNNB1 (n=660)</th>
<th>ERBB2/3 (n=464)</th>
<th>TSC2 (n=43)</th>
<th>PI3K/AKT/mTOR (n=2842)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TMB H/MSI H</strong></td>
<td></td>
<td>184 (29.3%)</td>
<td>26 (3.9%)</td>
<td>8 (1.2%)</td>
<td>619 (98.7%)</td>
</tr>
<tr>
<td><strong>CTNNB1</strong></td>
<td>(n=627)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ERBB2/3</strong></td>
<td>(n=660)</td>
<td>61 (13.1%)</td>
<td>26 (5.6%)</td>
<td>6 (1.3%)</td>
<td>345 (74.4%)</td>
</tr>
<tr>
<td><strong>TSC2</strong></td>
<td>(n=464)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PI3K/AKT/mTOR</strong></td>
<td>(n=43)</td>
<td>16 (37.2%)</td>
<td>8 (18.6%)</td>
<td></td>
<td>43 (100%)</td>
</tr>
<tr>
<td></td>
<td>(n=2842)</td>
<td>619 (21.8%)</td>
<td>629 (22.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**2427 - Poster Session**

**Gastrointestinal adjuvant chemotherapy regimens improve survival outcomes in women with mucinous ovarian cancer**


aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bDavid Geffen School of Medicine at UCLA, Los Angeles, CA, USA, cJohns Hopkins Hospital, Baltimore, MD, USA

**Objective:** Mucinous ovarian cancer is a rare histologic subtype with poor response to gynecologic (GYN) chemotherapy regimens. We sought to determine whether a gastrointestinal (GI) regimen was associated with improved survival outcomes.

**Method:** Patients with mucinous ovarian cancer requiring adjuvant chemotherapy were included in this retrospective cohort study. Patients must have been evaluated at 1 of 2 included academic centers. Those who received neoadjuvant chemotherapy or did not have surgery were excluded. Gynecologic pathologists at each institution reviewed pathology to confirm tumor origin. Demographic and clinical information was extracted from the medical record. GI regimens were considered to be any chemotherapy regimen that contained 5-FU, capecitabine, irinotecan, or oxaliplatin. Bevacizumab treatment was allowed in either group. Summary statistics were used to compare demographic and clinical characteristics; Kaplan-Meier product-limit estimator and Cox regression were used to compare survival outcomes.

**Results:** Fifty-four patients were included in this analysis. The mean age was 44 years (SD 12.8), and the mean BMI was 28 kg/m² (SD 7.7). Of all tumors, 31% were grade 3, 24% were FIGO stage III or IV, and 87% of patients had an optimal tumor reductive surgery to R0. When patients were stratified by GI (n = 26, 47%) versus GYN regimens (n = 29, 53%) for their initial adjuvant chemotherapy, there were no differences in age, BMI, grade, stage, or tumor debulking status. Patients who received GI regimens were more likely to receive bevacizumab (54% vs 3%, P < 0.001). Unadjusted PFS analyses showed that receiving a GI regimen was associated with worse PFS (HR = 2.50, 95% CI 1.02–6.13, P = 0.04), as was increased stage and suboptimal tumor debulking. Unadjusted OS analyses showed that a GYN regimen was associated with worse OS (HR = 3.56, 95% CI 1.18–10.74, P = 0.02), as was advanced-stage and suboptimal tumor debulking. A comparison of GI versus GYN regimens in patients who did not receive bevacizumab demonstrated a persistent improvement in OS but not PFS with GI regimens.
Conclusion: The use of a GI regimen with or without bevacizumab was associated with improved survival outcomes and should be strongly considered in mucinous ovarian cancer patients requiring adjuvant therapy.

2428 - Poster Session
Identifying sonographic predictors of endometrial hyperplasia in asymptomatic women with incidental imaging findings
M.H. Pritcharda, L. Kucirkaa, G. Nicolea, E.J. Tanner IIIb, K. Patzkowskya, A.N. Faderb and A.L. Beavisb. aJohns Hopkins School of Medicine, Baltimore, MD, USA, bJohns Hopkins Hospital, Baltimore, MD, USA

Objective: There is equipoise regarding proper management of asymptomatic postmenopausal women with incidental sonographic findings concerning for endometrial pathology. We aimed to identify clinical and sonographic predictors of endometrial hyperplasia and cancer (EH/EC) in asymptomatic postmenopausal women.

Method: We identified 317 asymptomatic postmenopausal women at a single center who underwent endometrial sampling based on an incidental imaging finding from 2005 and 2015. We built multivariate logistic regression models to identify clinical and sonographic predictors of pathologic diagnosis of EH/EC. We generated a receiver operating characteristic (ROC) curve and calculated the area under the curve (AUC) to assess the discriminatory value of endometrial stripe for predicting EH/EC.

Results: Of 317 women, 5.4% (n = 17) had a diagnosis of hyperplasia or cancer. Clinical factors, including age, race, BMI, and diabetes, were not associated with detection of EH/EC. Thickness of stripe did not discriminate between those with and without EH/EC (AUC = 0.55). Sensitivity and specificity were maximized using a cutoff of 9 mm, but these were low at 53% and 51%, respectively. Presence of fluid on ultrasound was associated with a 3.91-fold higher odds of EH/EC (P = 0.03), even after adjustment for stripe thickness and presence of polyps. Among those with a stripe <9 mm, the presence of a polyp was associated with 4.87-fold higher odds of EH/EC (P = 0.04); however, there was no association between polyp and EH/EC among those with a stripe ≥ 9 cm.

Conclusion: Thickness of the endometrium >9 mm did not reliably predict an increased risk of EH/EC among asymptomatic postmenopausal women with an incidental sonographic finding. Fluid within the endometrial canal was the feature most predictive of EH/EC. Similarly, the presence of a polyp in the absence of a thickened endometrial stripe demonstrated an increased risk of EH/EC. These features should raise concern for EH/EC in postmenopausal women and prompt evaluation.

2429 - Poster Session
Identification of a subset of microsatellite-stable endometrial carcinoma with high PD-L1 expression and tumor-associated lymphocytes: A potential strategy for immune checkpoint blockade
M. Avilaa, S. Crumleyb, B. Fellmana and R. Broaddusa. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bHouston Methodist Hospital, Houston, TX, USA

Objective: Higher expression of PD-L1 and tumor-infiltrating lymphocytes has been linked to MSI-high tumors, including MSI-high endometrial cancer. Across various cancers, these markers have been associated with better therapeutic responses to immune checkpoint inhibitors. The clinical impact of PD-L1 expression in microsatellite-stable endometrial cancer has yet to be described.

Method: A total of 132 microsatellite-stable, FIGO grade 2 endometrioid adenocarcinomas with intact immunohistochemical expression of the 4 mismatch repair proteins were identified retrospectively. Tumor PD-L1 expression was assessed by immunohistochemistry. CD3 and CD8 immunohistochemistry was assessed using Aperio-based slide scanning to quantify tumor-associated lymphocytes. Tumor size, myometrial invasion, lymphovascular space invasion, stage, recurrence, and overall survival were derived from pathology reports and the electronic medical record.

Results: PD-L1 was positive in 48% (63/132) of the tumors. This positivity was typically weak and confined to a few tumor cells. A subset of tumors (21/63 PD-L1 positive cases, 33%; 21/132 total cases, 16%) showed very high PD-L1 expression (characteristics summarized in Table 1). High PD-L1 high was associated with significantly increased CD3+ and CD8+ lymphocytes. The majority of PD-L1 high patients were stage I or II (18/21, 86%) with higher rates of deep myometrial invasion and LVSI than those who were PD-L1 negative. Recurrences were found in 8/132 patients; 6 had weak PD-L1 tumor...
expression, and 2 were PD-L1 negative. No cases of tumor recurrence were identified in the 21 patients with high PD-L1 expression.

**Conclusion:** We identified a subset of mismatch repair intact, endometrioid endometrial carcinomas with high PD-L1 expression and increased numbers of CD3+ and CD8+ tumor-associated lymphocytes. Interestingly, tumor recurrences did not occur in this subset, despite the fact that deep myometrial invasion and LVSI were more common. These variables are commonly taken into account when considering adjuvant therapy in stage I patients. Therefore, knowing the PD-L1 expression and microsatellite instability status may be helpful in assessing the risk of recurrence. This also provides evidence for a varied spectrum of histopathologic features in microsatellite stable tumors that could be used to identify candidates for immune checkpoint blockade.

**Table 1:** Clinical and Pathological Characteristics Associated with High Tumor PD-L1 Positivity in Mismatch Repair Intact Grade 2 Endometrial Endometrioid Adenocarcinoma.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Tumor PD-L1 negative</th>
<th>Tumor PD-L1 High positive</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>60 (13); 82%</td>
<td>21 (13); 16%</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>59 (13)</td>
<td>58 (15)</td>
<td>0.06</td>
</tr>
<tr>
<td>Median (Minimum-Maximum)</td>
<td>50 (37-72)</td>
<td>59 (30-77)</td>
<td></td>
</tr>
<tr>
<td>Tumor stage (III)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>66 (66)</td>
<td>14 (86)</td>
<td>0.73</td>
</tr>
<tr>
<td>II</td>
<td>2 (11)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td>Aa (Spinal) invasion (III)</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>64 (64)</td>
<td>1 (64)</td>
<td>0.03</td>
</tr>
<tr>
<td>No</td>
<td>25 (36)</td>
<td>2 (11)</td>
<td></td>
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<tr>
<td>Myometrial invasion present or 250%, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>71 (36)</td>
<td>3 (44)</td>
<td>0.01</td>
</tr>
<tr>
<td>No</td>
<td>27 (64)</td>
<td>15 (25)</td>
<td></td>
</tr>
<tr>
<td>No applicable (no myometrial invasion)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVSI, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (11)</td>
<td>0 (86)</td>
<td>0.005</td>
</tr>
<tr>
<td>No</td>
<td>21 (66)</td>
<td>13 (82)</td>
<td></td>
</tr>
<tr>
<td>Metastasis to pelvic lymph nodes, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (11)</td>
<td>2 (11)</td>
<td>0.10</td>
</tr>
<tr>
<td>No</td>
<td>23 (63)</td>
<td>14 (92)</td>
<td></td>
</tr>
<tr>
<td>Metastasis to paraaortic/energy nodes, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>2 (18)</td>
<td>0.14</td>
</tr>
<tr>
<td>No</td>
<td>1 (10)</td>
<td>3 (20)</td>
<td></td>
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<tr>
<td>CD3 expression in S03</td>
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<td></td>
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</tr>
<tr>
<td>Overall</td>
<td>80 (90)</td>
<td>104 (74)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hotspot</td>
<td>257 (90)</td>
<td>185 (75)</td>
<td>0.03</td>
</tr>
<tr>
<td>Periphery</td>
<td>729 (93)</td>
<td>171 (74)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cervix</td>
<td>61 (90)</td>
<td>3 (20)</td>
<td>0.06</td>
</tr>
<tr>
<td>CD8 expression in S03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>390 (90)</td>
<td>404 (75)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hotspot</td>
<td>222 (90)</td>
<td>225 (75)</td>
<td>0.001</td>
</tr>
<tr>
<td>Periphery</td>
<td>303 (97)</td>
<td>66 (22)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cervix</td>
<td>379 (95)</td>
<td>721 (74)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
**Objective:** Endometrial cancer is a common gynecologic malignancy primarily treated with complete surgical staging, which may include complete pelvic and paraaortic lymphadenectomy. The role of lymphadenectomy, and its intraoperative indications, is controversial. Three factors are important in the decision to proceed with lymphadenectomy: myometrial invasion, maximum tumor dimension, and histology. There are no universally established guidelines, and these criteria are incorporated in various degrees in the decision to proceed with lymphadenectomy. This investigation assesses the use of intraoperatively measured maximum tumor dimension (MTD) with and without preoperative histologic grade.

**Method:** This study compared retrospectively endometrioid endometrial cancer (EEC) patients with intraoperatively measured MTD ≤2 cm to those with MTD >2 cm from January 1, 2002, to August 31, 2017. This assessment compared those with MTD ≤2 cm with endometrial biopsy (EB) grade 1–2 to patients with MTD > 2 cm with EB grade 3. Lymph node metastasis (LNM), recurrence, and survival were also compared.

**Results:** This study reviewed 222 patient cases. In tumors >2 cm, LNM occurred in 20% of cases, while in tumors ≤2 cm, LNM was found in 6% of cases (P = 0.04). Recurrence and mean survival based on last follow-up visit in these two groups were not statistically different (P = 0.78 and P = 0.36, respectively). Data demonstrated a trend that, when combined with preoperative EB FIGO grade, a higher proportion of patients with EB FIGO grade 3 and MTD >2 cm had LNM compared to those with EB FIGO grade 1–2 and MTD ≤2 cm (43% vs 11%, P = 0.06). LNM was found in 15% of cases in which lymphadenectomy was performed based on current practices, whereas if the criteria of EB FIGO 3 and MTD >2 cm were used, the incidence of LNM would have been 44% of cases. However, using this criterion, two patients would not have had their nodal metastases detected. Compared to the current practice, the sensitivity and specificity of the proposed criteria would be 60% and 81%, respectively. The PPV and NPV would be 43% and 90%, respectively.

**Conclusion:** The results indicate that MTD combined with EB FIGO grade can detect LNM in a higher proportion of cases when compared to current practice. MTD combined with EB FIGO grade may eliminate the need for frozen section sampling in a substantial number of cases.

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**Objective:** Olaparib (50 mg hard capsules, HC) is approved in the European Union as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (BRCAm) ovarian cancer (PSR-OC) who are in response to platinum-based chemotherapy. So far, only limited data on real-world olaparib treatment are available.

**Method:** The German prospective noninterventional study C-PATROL (NCT02503436) collects routine clinical and patient-reported outcome data in BRCAm PSR-OC patients treated according to label with olaparib with the recommended dose 800 mg daily for HC or 600 mg daily for film-coated tablets (FT). The second interim analysis (cutoff date 01FEB2018) for patients treated with olaparib HC reflects data on patient characteristics and safety by using descriptive statistics. Subgroup analyses were performed according to age (younger than 70 years and 70 years and older), comediations (yes and no), and baseline comorbid conditions (yes and no).

**Results:** A total of 165 BRCAm PSR-OC patients treated with olaparib HC and with ≥3 months follow-up were analyzed (median age, 61 years; ECOG ≤1, 92.7%; ≥2 relapses, 40.0%; ≥3 prior platinum chemotherapies, 40.0%). Data were stratified according to subgroups (younger than 70 years, 128 patients, vs 70 years and older, 37 patients; comediations, yes, 139 patients, vs no, 26 patients; and baseline comorbid conditions: yes, 80 patients, vs no, 79 patients). Of all patients, 89.7% had
adverse events (AEs, any grade). Nausea (44.2%), fatigue (34.6%), anemia (28.5%), and vomiting (17.0%) occurred most frequently, with anemia and vomiting being less frequent in patients 70 years and older and patients without comediations. These four AEs occurred first mainly within 3 months after start of treatment.

**Conclusion:** The second interim analysis indicates that under routine conditions treatment with olaparib, HC is well tolerated with a manageable toxicity profile also in patients with higher age, comorbid conditions, and comediations. The toxicity profile observed so far is in line with the results of the clinical trial program for olaparib in PSR-OC.

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**2432 - Poster Session**

CA-125 levels are predictive of survival in women with low grade serous ovarian carcinoma

T. Maya, D. Unninayar, M.Q. Bernardini, W. Xu and A.A. Tone. *Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada*

**Objective:** Low-grade serous ovarian carcinoma (LGSC) is a rare subtype of epithelial ovarian carcinoma. Cancer antigen 125 (CA-125) is glycoprotein commonly elevated in the serum of patients with high-grade epithelial ovarian malignancies. The significance of CA-125 in patients with newly diagnosed LGCS is unclear. We designed a study examining the prognostic value of baseline CA-125 levels in patients with newly diagnosed LGSC.

**Method:** A retrospective cohort analysis of 267 patients with LGSC (Silverberg grade 1) was undertaken through the Ovarian Cancer Association Consortium collaborative database. All patients had central pathology review. Patients' demographics included age, stage, CA-125 level, residual disease, chemotherapy, recurrence, and vital status. Univariate and multivariate analyses of PFS and OS using Cox proportional hazards model were performed, and Kaplan-Meier survival curves were generated. Optimal cutoff CA-125 values were determined by maximizing the log rank test.

**Results:** The median age at diagnosis was 55 years. The median CA-125 levels at diagnosis for all study patients was 223 IU/mL. For patients with stage I disease, median CA-125 was 36 IU/mL, and for patients with stages III–IV, median CA-25 was 312 IU/mL. PFS and OS were inversely related to CA-125 value (*P* < 0.001). To identify CA-125 levels predictive of poor survival, optimal cutoff tests of log CA-125 values were performed. In the full cohort, the optimal cutoff for PFS was CA-125 = 91 (log CA-125 = 4.51), and the optimal cutoff for OS was CA-125 = 162 (log CA-125 = 5.09) (*P* < 0.001). In stage I patients, the optimal cutoff for PFS and OS was 347 IU/mL. In advanced-stage patients, the cutoffs for PFS and OS were 330.9 IU/mL and 217 IU/mL, respectively. MVA showed significant association between CA-125 levels at diagnosis and survival outcomes.

**Conclusion:** This multicenter analysis indicates that elevated baseline CA-125 level at diagnosis was inversely associated with PFS and OS. Accurate documentation of CA-125 levels may provide important prognostic information in women with LGSC.

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**2433 - Poster Session**

Outpatient desensitization is an effective and safe management option for platinum hypersensitivity reactions: A single institution experience

M.H. Vetter, A. Khan, F.J. Backes, K. Bixel, D.E. Cohn, L.J. Copeland, J.M. Fowler, R. Salani and D.M. O’Malley. *The Ohio State University, James Cancer Hospital, Columbus, OH, USA, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA, The Ohio State University Medical Center, Columbus, OH, USA*

**Objective:** Platinum hypersensitivity reactions (HSR) occur at a rate of approximately 1% of all platinum administrations and can range in severity from mild to life-threatening. There is increasing interest in platinum desensitization (PD) protocols. Here, we report our expanded experience with outpatient PD in our gynecologic oncology population.

**Method:** This is a report from a multidisciplinary quality improvement initiative to develop a standardized outpatient PD protocol for patients with gynecologic malignancies. All patients with a gynecologic malignancy undergoing outpatient PD for platinum HSR from 2011 to 2017 were included. Given the exploratory nature of the study, descriptive statistics were performed.

**Results:** Eighty-seven patients underwent PD. Most patients were being treated for ovarian cancer (62.8%) and receiving carboplatin (71.3%) at time of initial HSR. Participants had received a mean of 10.8 prior platinum doses. Initial HSR was
categorized using a modified system as mild (17.2%), moderate low risk (27.6%), moderate standard risk (43.7%), or severe (11.5%), and a PD was assigned accordingly (Table 1). The shortened 4-step PD was the most commonly used (55.2%) followed by the standard 1-bag, 16-step protocol (41.0%) or a 3-bag, 16-step prolonged protocol (3.8%). In total, 557 desensitization cycles were attempted with 545 cycles successfully completed for a completion rate of 97.8%. Breakthrough reactions (BTR) occurred at a rate of 21.7% (121/557 PD cycles). Of the 58 patients who experienced BTRs, 55.2% (32/58 patients) had BTR isolated to the first PD cycle. Severe BTR reactions were rare occurring at a rate of 1.1% of all infusions. One patient was observed overnight following a BTR, and 1 ICU admission occurred for an adverse reaction to benzodiazepines. There was no anaphylaxis or deaths. The most common reasons for discontinuing PD were progression of disease (37.5%), completion of therapy (34.6%), or escalation (14.4%) of PD protocols due to continued BTR.

**Conclusion:** The treatment practices for platinum HSR are changing in specialized centers to outpatient PD. These data lend further support to the safe and effective PD utilizing a modified classification system and a standardized outpatient PD protocol.

**Table 1:** Reaction classification and subsequent desensitization protocol utilized.

*At the beginning of the series, patients with moderate (standard-risk) reactions underwent desensitization with the shortened protocol; however, this was changed to a standard PD in order to decrease incidence and severity of breakthrough reactions (BTR).

^A 3-bag, 16-step protocol is used for patients with either severe or persistent moderate (standard-risk) BTR.

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**2434 - Poster Session**

**Predictive factors of unexpected lymphatic drainage pathways in early-stage cervical cancer**


aHôpital Européen Georges-Pompidou, Paris, France, bCHU Vaudois, Lausanne, Switzerland, cHôpitaux Civils de Lyon, Bron, France

**Objective:** The purpose of this study was to describe sentinel lymph nodes (SLN) topography in patients with early-stage cervical cancer and to determine preoperative factors of atypical lymphatic drainage pathway.

**Method:** We analyzed the data of two prospective multicentric trials on SLN biopsy for cervical cancer (SENTICOL I and II) in women undergoing surgery for early-stage cervical cancer. SLN detection was realized with a combined labeling technique (patent blue and radioactive tracer). Patients having a radical surgery (radical hysterectomy trachelectomy) with bilateral detection were included.

**Results:** Between January 2005 and July 2012, 278 patients with 945 intraoperative detected SLNs fulfilled the inclusion criteria. The SLNs were mainly located in the ilio-obturator or external iliac area in 84.2%. The other localizations were 8.7% in the common iliac area, 3.5% in the parametrium, 1.5% in the promontory area, 1.4% in the paraaortic area, and 0.7% in other
areas. Sixty-two patients (22.3%) had at least 1 SLN in atypical area. In multivariate analysis, variables independently associated with the presence of 1 or more SLNs in atypical area were BMI ≥25 kg/m² (ORa = 0.36, 95% CI 0.15–0.85, \( P = 0.02 \)) and multiparity (ORa = 0.49, 95% CI 0.25–0.94, \( P = 0.03 \)). See Figure 1.

**Conclusion:** The SLNs search should begin in the ilio-obturator and external iliac area. Other territories should be explored in the absence of SLNs in this first level or as a complement. Pelvic dissection should be done only in case of absence of SLN in all territories.

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**Fig. 1.**

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2435 - Poster Session

**Women with anal cancer precursors: Clinical characteristics and concomitant genital tract neoplasia**

Y. Liu, M.P. Hayes, K. Sigel and M. Gaisa. *Icahn School of Medicine at Mount Sinai, New York, NY, USA*

**Objective:** Two thirds of high-risk human papillomavirus (hrHPV)-related anal cancers occur in women. Half of the cases present at advanced stages, underscoring a significant deficiency in anal cancer screening for women. We thus aimed to identify the clinical characteristics of women with anal precancerous lesions (i.e., anal intraepithelial neoplasia, AIN 2/3) and to determine whether their AIN 2/3 is associated with cervical, vulvar, and vaginal intraepithelial neoplasia (CIN/VIN/VAIN).

**Method:** We performed a retrospective study of women who had undergone high-resolution anoscopy examination and biopsy between 2010 and 2018. Patients with diagnosis of AIN 2/3 were included. Medical records were reviewed, and all colposcopic examination results were recorded.

**Results:** One hundred women with AIN 2/3 (median age 54 years, range 27–74 years) were identified. Among the subjects, 97 were HIV-positive. Anal hrHPV prevalence was 100%, including HPV16/18 (73%). Cervical hrHPV prevalence was 67%, including HPV16/18 (40%). For women with anal and cervical coinfection, hrHPV types were concordant in half of the cases. Forty-two women had concurrent or history of genital high-grade lesions, including CIN 2/3 (40), cervical adenocarcinoma in situ (2), VIN 3 (7), and VAIN 3 (2). Six had high-grade lesions at 2 genital sites. When comparing women who had...
AIN 2/3 alone and those who had high-grade lesions at both anal and genital sites, there was no statistical difference in clinical characteristics such as age, race/ethnicity, HIV status, smoking history, and HPV genotypes ($P > 0.4$). Among women with both AIN 2/3 and CIN 2/3, 11 (27%) developed anal lesions more than 10 years following the successful treatment of cervical lesions by LEEP or hysterectomy.

**Conclusion:** HIV-positive women and those with genital high-grade lesions are at great risk of developing anal cancer precursors. AIN 2/3 can present as an isolated lesion or after long intervals beyond the treatment of cervical lesions. Consequently, we recommend integrating anal cancer screening with the standard gynecological examination for all high-risk women.

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**2436 - Poster Session**

**Visceral-to-subcutaneous adipose tissue ratio is a poor prognostic factor in type 1 endometrial cancer patients**

K. Yamaguchi$^{a,b}$, M. Wada$^c$, K. Takakura$^d$ and I. Konishi$^{a,c}$.

$^a$National Hospital Organization Kyoto Medical Center, Kyoto, Japan,
$^b$Kyoto University, Kyoto, Japan, $^c$Kyoto University Graduate School of Medicine, Sakyo-ku, Japan

**Objective:** Obesity designated by BMI is a risk factor for type 1 endometrial cancer. Recently visceral-to-subcutaneous adipose tissue ratio (V/S ratio) as well as BMI was found to be associated with the increased incidence of several malignancies including endometrial cancer. However, the clinical effects on endometrial cancer have not been determined. The aim of this study is to identify the clinical impact of V/S ratio on endometrial cancer.

**Method:** A total of 148 endometrial cancer patients who were treated in Kyoto Medical Center from January 2012 to December 2016 were enrolled in this study. BMI, V/S ratio, abdominal circumstance, pathology, stage, and prognosis were assessed retrospectively.

**Results:** There was no significantly different distribution between type 1 and 2 among BMI, V/S ratio, abdominal circumstance, and complication with diabetes. Although BMI and abdominal circumstance were not related to FIGO stage, V/S ratio values in advanced-stage cases were significantly higher than those in stage 1 cases ($P = 0.0098$). Kaplan-Meier curves depicted that BMI and abdominal circumstance were not related to PFS and OS in both type 1 and 2 endometrial carcinoma cases. V/S ratio is not a prognostic predictor in type 2 endometrial cancer cases, whereas V/S ratio more than 0.5 is significantly poorer prognosis than V/S ratio less than 0.5 in type 1 endometrial cancer patients among both PFS and OS ($P = 0.0080$ and $P = 0.0053$, respectively). The Cox regression univariate analysis of PFS showed that V/S ratio was a significant prognostic factor ($P = 0.033$). For overall survival, there are no prognostic factors.

**Conclusion:** V/S ratio is a possible prognostic predictor in type 1 endometrial cancer cases. These findings lead to developing precision medicine in endometrial cancer patients.

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**2437 - Poster Session**

**CCNE1 and BRD4 expression and platinum resistance in high-grade serous ovarian cancers**

S.S. Petersena, A.J. Wilsonb and D. Khabelea.

$^a$University of Kansas Medical Center, Kansas City, KS, USA, $^b$Vanderbilt University, Nashville, TN, USA

**Objective:** CCNE1 (cyclin E) amplified and bromodomain and extraterminal 4 (BRD4) amplified ovarian cancers are associated with poor outcomes. The objective of this study was to determine whether mRNA and immunohistochemical (IHC) profiles of CCNE1 and BRD4 are associated with platinum sensitivity in serous ovarian cancers.

**Method:** Copy number analysis data were extracted from The Cancer Genome Atlas (TCGA) for high-grade serous ovarian tumors with BRD4 and CCNE1 (cyclin E) amplification. Immunostaining for cyclin E and BRD4 was performed in 130 serous ovarian tumors on a tissue microarray (TMA) IHC in 130 clinically annotated formalin-fixed paraffin-embedded serous tumors from Vanderbilt University Medical Center (VUMC). Staining intensity (1, weak; 2, moderate; 3, strong) and percentage of positive nuclei (0–100) were multiplied to yield an H score for Cyclin E and BRD4 expression. Pearson correlation coefficients were determined for mRNA expression of cyclin E and BRD4 in 307 TCGA tumors (RSEM V2 data extracted from the Broad Firehose database) and protein expression of cyclin E and BRD4 in 130 serous ovarian tumors. CCNE1 and BRD4 expression in relation to platinum sensitivity were evaluated using the Mann-Whitney $t$ test.
**Results:** TCGA demonstrated about 20% of high-grade serous EOC harbor amplifications in CCNE1 and BRD4. BRD4 amplification overlaps with CCNE1 amplification in 26/57 (46%) of high-grade serous EOC of the TCGA. Immunostaining for cyclin E and BRD4 in 130 serous ovarian tumors on a tissue microarray yielded intermediate to high staining of CCNE1 in 52.1% of tumors and intermediate to high staining of BRD4 in 71.6% of tumors. Protein expression by IHC between CCNE1 and BRD4 was positively correlated, r= 0.25 (P = 0.005). High expression of CCNE1 was associated with platinum resistance (P = 0.023). High BRD4 expression was not associated with platinum resistance (P = 0.95).

**Conclusion:** TCGA mRNA and TMA IHC expression analysis suggests that a subset of serous ovarian tumors has high levels of CCNE1 and BRD4 expression. High CCNE1 expression is associated with poor prognosis and platinum resistance. Future studies are warranted to evaluate the subset of tumors with elevated expression of both CCNE1 and BRD4 in relation to platinum resistance and clinical outcomes.

2438 - Poster Session

Lck inhibitors are an adjunctive therapeutic agent in platinum-resistant endometrioid tumors


*Cleveland Clinic, Cleveland, OH, USA, bThe Cleveland Clinic Foundation, Cleveland, OH, USA*

**Objective:** The membrane complement regulatory protein, CD55, drives chemoresistance in endometrioid carcinoma cells by activating LCK (lymphocyte-specific protein tyrosine kinase). This study sought to test LCK inhibitors as chemosensitizing agents for platinum-resistant endometrioid carcinoma cells.

**Method:** Platinum-resistant endometrioid carcinoma cell lines CP70 and HEC1a were cultured and pretreated with LCK inhibitor, either Saracatinib or PP2, or vehicle. Nontreatment controls were simultaneously cultured without pretreatment. Cells were then plated, and Cisplatin was applied the next day at several doses, with/without Saracatinib, PP2, or vehicle. Cell proliferation was assessed by CellTiter-Glo, with percentage survival normalized to the untreated control for each group. Caspase 3/7 Assay kit was utilized to assess apoptosis in parallel with CellTiter-Glo. Relative caspase activities were normalized to untreated controls in each group, with activity assessed from 30 to 120 minutes. Protein lysates were also obtained, and Western blot studies performed to assess phosphorylation status of LCK. For statistical analysis, numerical values were calculated by one-way ANOVA to assess statistical significance. For proliferation assays, IC50 was calculated using nonparametric values set to nonlinear fit curve as per statistical analysis performed with GraphPad Prism.

**Results:** In vitro studies validate our hypothesis that platinum-resistant endometrioid cancer cells pretreated with an LCK inhibitor, such as PP2, followed by cisplatin treatment leads to significantly decreased cell proliferation in a dose responsive manner, as shown in Figure 1. Increased sensitivity to cisplatin was due to increased apoptosis. We replicated these findings in additional lines including cisplatin-resistant ovarian and endometrial endometrioid adenocarcinoma cells. Preliminary immunoblot studies indicate a decrease in phosphorylated LCK in the LCK inhibitor-treated cells, normalized to total LCK.

**Conclusion:** Collectively, these studies identify LCK inhibitors as a potential adjunctive therapeutic agent in platinum-resistant endometrioid ovarian carcinoma. The combination chemotherapy would provide a therapeutic strategy to chemosensitize this subset of otherwise resistant ovarian cancer.
A novel peptide that restores p53 function may act synergistically with carboplatin in targeting high-grade serous ovarian cancers

T. Lai, A. Neal, T. Grogan, A. Soragni and S. Memarzadeh. University of California, Los Angeles, Los Angeles, CA, USA

Objective: While p53 mutations are ubiquitous in high-grade serous ovarian cancers (HGSOCs), a subset of these mutations results in aggregation of p53. The aim of this study is to determine whether combination treatment with a peptide-restoring mutant aggregating p53 (ReACp53) and carboplatin results in improved response in HGSOC.

Method: An in vitro high-throughput 3D organoid bioassay was used to test combination therapy with ReACp53 and carboplatin in 3 ovarian cancer cell lines and 7 primary patient samples. Chemo-naïve (n = 2), neoadjuvant-treated (n = 3), and platinum-resistant (n = 2) clinical samples were included for evaluation. Cell viability following treatment was used to determine response. Loewe synergy (LS) response surfaces were constructed to assess for synergistic, additive, or antagonistic interactions at various dose combinations in order to determine an overall delta score, called a LS score. A positive LS was suggestive of potential synergy. Whole exome sequencing was performed in parallel to identify specific p53 mutations that could serve as potential markers of response to combination therapy.

Results: Response to therapy was assessed in OVCAR-3 (R248Q), SKOV3 (P89fs), and SNU-119 (P151A) cell lines. Synergistic activity was observed in OVCAR-3 with a known aggregating mutation (LS 22.7), but not in SKOV3 (LS −4.7), or SNU-119 (LS −5.8). In the 7 primary patient samples, there was a wide range of responses to combination therapy (LS −37.8 to 29.1). A synergistic effect was observed in 1 chemo-naïve sample (LS 29.1) and 1 platinum-resistant sample (LS 16.8). This suggests that combination therapy with ReACp53 and carboplatin may be effective in a select group of HGSOCs regardless of platinum sensitivity.

Conclusion: ReACp53, a peptide that restores function of mutant p53, may work synergistically with carboplatin in targeting a subset of HGSOCs.
**Objective:** Programmed cell death protein (PD-1) and its ligand, PD-L1, are expressed in various solid tumors and play a key role in cancer cell evasion of the immune system. Anti-PD-L1 agents are a source of targeted immunotherapy for these tumors. We aimed to study the immune landscape of ovarian cancer (OC) microenvironment in a cohort of primary OC patients by measuring expression of PD-1 and PD-L1 genes using a single-cell RNA sequencing technique to explore the role of targeted immunotherapy.

**Method:** Viable tumors from 10 patients (8 primary ovarian cancer, 2 fallopian tube cancer) were collected at primary surgery and processed following standard protocols of single-cell RNA sequencing for gene expression profiling using 10X technology. Raw sequencing data were processed via CellRanger, and gene expression was quantified in the unit of unique molecule identifier (UMI) count. Customized Seurat analysis was done to decompose cell lineages for each patient. Total cell count, cell type distribution, and overall and percentage distribution of PD-1 and PD-L1 genes were then determined.

**Results:** A total of 30,535 single cells across 10 patients were sequenced. Three major subtypes of cell lineages (epithelial, 67%; stromal, 16%; immune, 12%) were identified. Ten patients showed expression of PD-1 and PD-L1 genes across some cell types (expression range, 0.0–18.5%) with UMI counts varying from 1 to 4 in any given cell. The immune cell lineage subtype (6 of 9 patients) consistently expressed both PD-1 and PD-L1. Interestingly, a small subset of patients showed highest expression values for PD-1 and PD-L1 in both their immune and epithelial cell subtypes. The PD-1 gene was highly expressed in only 1 patient in both epithelial and immune cells with a UMI count of 3, while PD-L1 gene expression was highest in 6 patients, within the epithelial cell lineage (UMI 3-4).

**Conclusion:** Single-cell RNA-sequencing on viable OC cells identified tumors demonstrating high gene expression of PD-1 and PD-L1 across tumor and immune cells. This could help identify patients most likely to benefit from immune therapy in the future and further understand the mechanism of immune evasion in ovarian cancer.

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**2441 - Poster Session**

**Intraoperative anesthesia considerations with utilization of hyperthermic intraperitoneal chemotherapy (HIPEC) in epithelial ovarian cancer**

A.M. Chichura, L.J. Moulton Chambers, A.B. Costales, P.G. Rose, C.M. Michener, H. Mahdi, M. Yao and R. DeBernardo. Cleveland Clinic, Cleveland, OH, USA

**Objective:** Hyperthermic intraperitoneal chemotherapy (HIPEC) can present perioperative metabolic and physiologic challenges. This study aims to examine the incidence of electrolyte and glycemic changes encountered intraoperatively and their association with postoperative complications in women with epithelial ovarian cancer (EOC) undergoing cytoreductive surgery (CRS) with HIPEC.

**Method:** This is a retrospective, single-institution study of 64 women with EOC who received CRS with HIPEC at the Cleveland Clinic between 2010 and 2018. Data collected included patient demographics, intraoperative metabolic parameters, arterial blood gases, and postoperative adverse events.

**Results:** The mean age at surgery was 61.5 years. The majority of women experienced electrolyte abnormalities (96.9%, n = 62) and required pressor support intraoperatively (92.2%, n = 59). Hyperglycemia (>200 mg/dL, 80.6%, n = 50), hypomagnesemia (<1.7 mmol/L, 48.4%, n = 30) were frequently seen. A blood transfusion was given in 60.8% (n = 31) of cases, and 60.9% (n = 39) of women required insulin intraoperatively. Intraoperative lactic acidosis (lactate >2.0) was noted in 81.3% (n = 52). Insulin administration was required in significantly more patients with lactic acidosis compared to those without (69.2% vs 25.0%, P = 0.005). In patients with intraoperative lactic acidosis, there were no significant differences in length of stay (median 6 vs 6 days, P = 0.82) or postoperative adverse events including reoperation (1.9% vs 8.3%, P = 0.34), ICU admission (9.6% vs 0.0, P = 0.57), anastomotic leak (5.8% vs 0.0, P = 0.99), respiratory failure (1.9% vs 0.0, P = 0.99), or death (0.0 vs 0.0, P = 0.99) compared to patients without lactic acidosis.

**Conclusion:** Administration of HIPEC during CRS for EOC is associated with high incidence of intraoperative electrolyte disturbances, lactic acidosis, and need for pressor support. In this cohort, intraoperative lactic acidosis was not associated with adverse postoperative outcomes; however, because of small sample size, it may not be able to detect a clinically significant difference. Further study is needed to optimize anesthesia care in women with EOC undergoing CRS with HIPEC.
Patterns of adjuvant therapy and outcomes in the treatment of stage II endometrial cancer: A National Cancer Database study

M.H. Vetter, K. Bixel and A.S. Felix. aThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, bThe Ohio State University Medical Center, Columbus, OH, USA, cThe Ohio State University, Columbus, OH, USA

Objective: Currently, use of adjuvant radiation (RT) via brachytherapy or pelvic RT is recommended for patients with surgically staged, low-risk stage II disease with the option of adding chemotherapy (CT) for high-risk disease. However, these recommendations are based on small numbers of stage II EC patients within larger randomized clinical trials or small retrospective reviews. The purpose of this study was to explore patterns of adjuvant therapy and outcomes in a large retrospective cohort of stage II EC patients.

Method: We queried the National Cancer Data Base for women with FIGO 2009 stage IIB or FIGO 2014 stage II ECs who underwent hysterectomy between 2004 and 2014. Adjuvant therapy was categorized as none, RT only, CT only, and RT plus CT. We used logistic regression to estimate ORs and 95% CIs for multivariate-adjusted associations between sociodemographic and tumor characteristics with receipt of adjuvant RT or CT. Cox regression was used to estimate multivariate-adjusted HRs and 95% CIs for associations between adjuvant therapy and overall survival.

Results: Our analysis included 11,872 women with stage II EC. Lower odds of receiving RT-only was observed among older women (OR for each 1-year increase in age = 0.98, 95% CI 0.97–0.99) and women with serous (OR = 0.73, 95% CI 0.64–0.83) or carcinosarcoma histology (OR = 0.60, 95% CI 0.52–0.69) compared with low-grade endometrioid. Older age was inversely associated with receipt of CT only (OR = 0.97, 95% CI 0.96–0.98), while diagnosis with high-grade histology (compared to low-grade endometrioid, ORs = 3.19–14.18) was associated with higher odds of receiving CT-only treatment. Compared with women who did not receive adjuvant treatment, receipt of RT (HR = 0.95, 95% CI 0.90–1.00) was significantly associated with improved OS, while CT alone (HR = 0.96, 95% CI 0.85–1.09) or combination CT and RT (HR = 0.97, 95% CI 0.89–1.05) was not associated with OS (Figure 1).

Conclusion: We observed lower odds of receiving adjuvant RT among women of older age or those diagnosed with serous or carcinosarcoma histology, while high-risk histology was associated with higher odds of receiving CT. Receipt of adjuvant RT was related to improved survival among women with stage II EC.

Fig. 1.
**2443 - Poster Session**

Comparison of outcomes with utilization of hyperthermic intraperitoneal chemotherapy (HIPEC) with paclitaxel and cisplatin versus cisplatin alone in women with epithelial ovarian cancer

A.M. Chichura, L.J. Moulton Chambers, A.B. Costales, P.G. Rose, C.M. Michener, H. Mahdi, M. Yao and R. DeBernardo. Cleveland Clinic, Cleveland, OH, USA

**Objective:** The aim of this study was to investigate disease outcomes, including PFS and OS and perioperative adverse outcomes, in women with epithelial ovarian cancer (EOC) receiving cytoreduction with hyperthermic intraperitoneal chemotherapy (HIPEC) with single-agent cisplatin (C) versus paclitaxel/cisplatin (PC).

**Method:** A retrospective, single-institution study of women with primary or recurrent EOC who received debulking and HIPEC with C or PC between the years 2010–2018 was performed.

**Results:** Among 56 women with EOC undergoing cytoreduction with HIPEC, PC was administered in 44 patients (78.6%) and 12 (21.4%) received C alone; 38.2% \((n = 21)\) had HIPEC at interval cytoreduction and 61.8% \((n = 34)\) had recurrent EOC. Usage of PC was significantly more frequent in platinum-sensitive versus platinum-resistant patients (89.5 vs 45.5%, \(P < 0.001\)). There were no significant differences in medical comorbid conditions, ethnicity, ASA score, or extent of surgery between the cohorts. While intraoperative acidosis (lactate > 2.0, 93.2% vs 66.7%, \(P = 0.01\)) and hypokalemia (88.6% vs 41.7%, \(P < 0.001\)) were more frequent among patients receiving PC versus C alone, there was no difference in need for pressor support (90.9% vs 91.7%, \(P = 0.99\)). Similarly, there was no difference in ICU admission (22.7 vs 16.7%, \(P = 0.65\)), hospital length of stay (median 5.0 vs 5.0 days, \(P = 0.90\)), or home discharge (79.5% vs 58.3%, \(P = 0.22\)) between the cohorts. Incidence of mild (22.7% vs 8.3%, \(P = 0.27\)), moderate (15.9% vs 0.0, \(P = 0.14\)), and severe postoperative complications (6.8% vs 16.7%, \(P = 0.29\)) were not different for those who received PC versus C alone. There was no significant difference in PFS at 3 years for women receiving C alone versus PC (46.2% vs 43.8%, \(P = 0.34\), HR = 0.58, 95% CI 0.19–1.76). Similarly, at a median follow-up duration of 29.2 months, 3-year OS was 45.0% for C versus 66.7% for PC \((P = 0.23, HR = 2.28, 95% CI 0.60–8.62)\).

**Conclusion:** Addition of paclitaxel did not significantly improve PFS or OS at the time of HIPEC compared to C alone. Similarly, PC did not increase incidence of adverse postoperative outcomes compared to C alone. Further study is needed to elucidate the optimal chemotherapy regimen for women with EOC receiving HIPEC.

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**2444 - Poster Session**

Use of adjuvant therapy and overall survival in stage II low-grade versus high-grade endometrioid endometrial carcinomas: A National Cancer Database study

M.H. Vetter\(^a\), K. Bixel\(^b\) and A.S. Felix\(^c\). \(^a\)The Ohio State University, James Cancer Hospital, Columbus, OH, USA, \(^b\)The Ohio State University Medical Center, Columbus, OH, USA, \(^c\)The Ohio State University, Columbus, OH, USA

**Objective:** With the recent data demonstrating molecular similarities between some high-grade endometrioid EC (EEC) and serous carcinomas, some practitioners are favoring the use of more aggressive adjuvant therapy than what has historically been used in the treatment of low-grade EEC. The purpose of this study was to ascertain the differences in treatment patterns and outcomes in patients with low-grade and high-grade EEC.

**Method:** We queried the National Cancer Data Base for women with stage II EEC (all grades) who underwent hysterectomy between 2004 and 2014. Patients with grade 1 and 2 EEC were classified as low grade, while those with grade 3 were classified as high grade. Treatment types included none, radiation (RT) alone, chemotherapy (CT) alone, and combination RT plus CT. Polytomous logistic regression was used to estimate ORs and 95% CIs for multivariate-adjusted associations between histology and treatment. Associations between treatment type and OS according to histology were examined with Kaplan-Meier plots, log rank tests, and Cox proportional hazards regression.

**Results:** Our analysis included 6,500 women with low-grade stage II EEC and 1,978 women with high-grade stage II EEC. Compared to women with low-grade EEC, women with high-grade EEC were more likely to receive CT only \((OR = 1.95, 95\% CI 1.40–2.72)\) and combination RT plus CT \((OR = 3.41, 95\% CI 2.75–4.22)\), while no difference in use of RT only was observed \((OR = 0.91, 95\% CI 0.81–1.02)\). There was no difference in survival between women with low- versus high-grade EEC. Treatment was significantly associated with OS among women with low- and high-grade EEC (Figure 1). RT only was significantly associated with improved OS in both low- \((HR = 0.84, 95\% CI 0.79–0.89)\) and high-grade EEC \((HR = 0.83, 95\% CI 0.73–0.94)\), while combination CT and RT was associated with lower OS in both groups \((low-grade EEC, HR = 1.24, 95\% CI 1.70–1.43; high-grade EEC, HR = 1.32, 95\% CI 1.09–1.59)\).
Conclusion: Women with low- and high-grade stage II EEC had similar OS. While patients with high-grade EEC were more likely to receive CT and combination therapy than their low-grade counterparts, RT-only treatment was associated with improved survival in both low- and high-grade stage II EEC patients.

Fig. 1.

2445 - Poster Session
Multiple lines of bevacizumab-based therapy in patients with pretreated recurrent tuboovarian carcinoma: Feasibility and effectiveness in the clinical routine
C. M. Kurbacher, V. Kallage, A. T. Kurbacher, S. Herz and J. A. Kurbacher. Gynecological Center Bonn-Friedensplatz, Bonn, Germany

Objective: Bevacizumab (Bev) is approved for the treatment of both advanced-stage primary and recurrent tuboovarian carcinoma (TOC) in combination with chemotherapy (Ctx) not including retreatment. This retrospective study sought to yield more concise data on both feasibility and effectiveness of multiple lines of Bev-based treatment in patients with recurrent TOC.

Method: From our database, a total of 90 patients with recurrent TOC (45 with platinum-sensitive or platinum-resistant disease each) receiving at least 1 line of Bev-based therapy in the clinical routine were identified. Of all patients, 37 (41.1%) had 1, 20 (22.2%) had 2, 13 (14.4%) had 3, and 20 (22.2%) 4–9 lines of Bev. A total of 225 courses of Bev-based treatment were administered: 58 (25.8%) as monotherapy (Bev), 63 (28.0%) in combination with conventionally dosed Ctx (Bev+cCtx), and 104 (46.2%) in combination with metronomic Ctx (Bev+mCtx). Time to progression (TTP) was calculated from the start of each Bev-based treatment until progression, and OS was calculated from the start of the first Bev-based treatment until death from any reason or loss to follow-up. Adverse effects of Bev were scored according to CTCAE vs 4.03.

Results: Bev-based treatment was well tolerated. Most frequent side effects were proteinuria in 50%, hypertension in 41%, gastrointestinal toxicity in 31%, and infection in 17% of treatments. G3-4 toxicities were rare and generally manageable with hypertension in 2.2%, bowel obstruction in 0.9%, small bowel perforation in 0.9%, nephrotic syndrome in 0.4%, and infection in 1.3% of treatments. Both TTP and OS were not significantly different between different types of treatment; TTP for Bev was 5.4 ms; for Bev+cCtx, 6.1 ms; and for Bev+mCtx, 6.3 ms. OS for Bev was 28.6 months; for Bev+cCtx, 31 months; and for Bev+mCtx,
21.4 months. TTP for platinum-resistant versus platinum-sensitive patients was 4.5 and 7.6 months ($P = \text{NS}$), and OS was 12.2 versus 20.0 months ($P = 0.044$). TTP was comparable between 1 and multiple lines of Bev: 1 line, 6.6 months; 2 lines, 6.3 months; 3 lines, 5.9 months; and $\geq$4 lines 3.7 months ($P = 0.130$). However, OS increased significantly with the number of lines of Bev: 1 line, 8.8 months; 2 lines, 16.8 months; 3 lines 25.4 months; and $\geq$4 lines, 36.6 months ($P = 0.0001$).

**Conclusion:** Retreatment with Bev was safe and effective in a real-world population of patients with recurrent TOC. Whereas the incidence of severe side effects did not increase by the line of Bev-based treatment, the number of Bev-based lines had a significant impact on overall survival. Thus, rechallenge with Bev may be a valuable option in the treatment of recurrent TOC.

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2446 - Poster Session
Withdrawn at author’s request

2447 - Poster Session
Intraperitoneal port cytology after completion of primary therapy for advanced stage ovarian cancer: A novel approach to a ‘second look’
K.V. Grettea, B.J. Longb, M.A. Finana and R.P. Rocconi.a Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA, bThe George Washington University, Washington, DC, USA

**Objective:** The aim of this study was to determine whether intraperitoneal (IP) port cytology predicts early recurrence and/or poor prognosis in patients with ovarian cancer who have completed primary therapy.

**Method:** A prospective study of patients with advanced-stage ovarian cancer undergoing IP port removal after debulking followed by IV/IP chemotherapy was performed. Ports were flushed with 10 cc of normal saline into ThinPrep fixative to be analyzed for cytology. Results were correlated with clinical factors and cancer outcomes. Survival was calculated using Kaplan-Meier curves and compared using log rank analysis.

**Results:** Effluent from 53 IP ports was analyzed, and patients were followed for a median of 62 months. Mean age was 58.5 years, with the majority of patients being white (90%), with stage 3 (62%), and serous histology (87%). Seven (13.2%) patients had positive IP cytology. POS and NEG groups were similar with regard to age, BMI, stage, grade, and GOG status. Patients with POS results had increased risk of recurrence (HR = 3.2, 95% CI 0.4–28.9) and death (HR = 6.5, 95% CI 0.7–58.8) and were more likely to recur before 12 months ($71\%$ vs $22\%$, $P = 0.007$). Compared to NEG, POS conferred a shorter median survival with PFS of 32 versus 7 months ($P = 0.02$) and OS of 84 versus 42 months ($P = 0.04$). See **Figure 1**.

**Conclusion:** IP port cytology is predictive of recurrence and survival in patients with ovarian cancer. This inexpensive test may serve as an adjunct to imaging and tumor markers to determine disease status at the completion of treatment. Further study should investigate the impact this may have on management.
Objective: The primary advantage of using neoadjuvant chemotherapy (NACT) when managing advanced ovarian cancer is that it reduces the morbidity of the cytoreductive procedure. Minimally invasive surgery (MIS) may be an option for women undergoing interval cytoreduction depending on the extent of surgery required. Our goal is to create a scoring system using preoperative factors to help predict the extent of surgery at the time of interval cytoreduction in advanced ovarian cancer.

Method: The prospective database of ovarian cancer patients at the University Health Network was used to study patients from 2007 to 2016 with stage III-IV ovarian cancer receiving NACT followed by interval cytoreduction. Patients were stratified into 3 groups based on surgical outcome: type 1, a basic procedure with optimal cytoreduction; type 2, a basic procedure with suboptimal cytoreduction; and type 3, a complex procedure involving either resection of upper abdominal disease or resection of intestine. Eleven clinical and 8 radiologic criteria were assessed, and a univariate followed by multivariate analysis was completed comparing the surgery types.

Results: One hundred and seventy patients met study inclusion criteria. A univariate analysis identified 4 significant criteria: the presence of prechemotherapy CT findings of porta hepatis disease ($P < 0.05$), post-NACT CT findings of porta hepatis disease ($P < 0.05$), and post-NACT CT findings of ascites ($P < 0.05$) were associated with a type 2 or 3 surgery, and a decrease in CA-125 of either 95%, 90%, or 80% from baseline ($P < 0.05$) is associated with a type 1 surgery. Two covariates remained significant on multivariate analysis: post-NACT CT findings of porta hepatis disease ($P < 0.05$) and a decrease in CA-125 of 95% from baseline ($P < 0.05$).

Conclusion: Two preoperative criteria showed significance in predicting the extent of surgery in our patient population. These criteria may be used to predict patients who benefit from an MIS approach at the time of interval cytoreductive surgery.
Objective: Hyperthermic intraperitoneal chemotherapy (HIPEC) is commonly used to treat peritoneal-based malignancies, including epithelial ovarian cancer. Following the publication of a randomized phase III trial showing an improvement in PFS and OS, we sought to review our experience.

Method: A retrospective study of women with EOC who were treated at the Cleveland Clinic with debulking and HIPEC between 2010 and 2018 was performed.

Results: Sixty-three women were eligible for analysis treated at the following time points: interval debulking (36.5%) and recurrence (63.5%). The majority of patients had serous cancers (81%) and were BRCA wildtype (75.6%). Mean ASA score was 3 in 75%, and Charlson comorbidity index was 0–4 in 84%. Chemotherapeutic agents used for HIPEC included cisplatin (98%), paclitaxel (76%), mitomycin-c (11%), and adriamycin (13%). A small bowel resection was performed in 7 (10.9%) and a large bowel resection in 15 patients (23.4%). A diversion was performed in 2 patients (9%). An optimal (<1 cm residual) debulking was accomplished in 95% of cases. Complications are shown in Table 1. In the neoadjuvant setting, 6 patients had a CR following neoadjuvant chemotherapy (3 cycles 73%, 4 cycles 18%). Mean number of days since last chemotherapy before HIPEC was 29.5 days with mean CA-125 prior to surgery being 36 U/mL. Seventy-eight percent of patients had a complete cytoreductive surgery to no gross residual disease. With a median follow-up of 5.1 months (2.8–7.5 months), there has been 1 recurrence. In the recurrent setting, the mean number of days since last chemotherapy before HIPEC was 41 days with a mean CA-125 prior to surgery being 33.5 U/mL. Seventy percent of patients were platinum-sensitive. With a median follow-up of 12.3 months (7.2–32.7 months), all but 1 patient has recurred with 62.5% having recurrences pelvic and extra-pelvic. Only 5% had extra-abdominal recurrences. Median PFS was 12.8 months (6.8–37.1 months) for all recurrent patients. One-year PFS and OS were 54.7% (37.3%, 72.1%) and 86% (74.4%, 97.5%), respectively, in the recurrent cohort. See Table 1.

Conclusion: In our experience, HIPEC is a feasible and safe option for patients with epithelial ovarian cancer in the interval and recurrent setting. Given the increasing interest in HIPEC and likely implementation, it is critical for programs to collect and perform institutional analyses of these data to ensure patient safety and maximize outcomes. An online registry would be an optimal forum to maximize data analysis.

Table 1: Adverse events in patients undergoing debulking and HIPEC.

<table>
<thead>
<tr>
<th>Adverse Event (AE)</th>
<th>Number of patients (n=64) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative AE*</td>
<td></td>
</tr>
<tr>
<td>Electrolyte disturbance</td>
<td>62 (96.9)</td>
</tr>
<tr>
<td>Hypotension- requiring pressor support</td>
<td>59 (92.2)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>26 (41.3)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>13 (20.3)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Postoperative AE**</td>
<td></td>
</tr>
<tr>
<td>Return to OR</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>VTE</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Gastrointestinal anastomotic leak</td>
<td>3 (4.7)</td>
</tr>
<tr>
<td>Genitourinary leak</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Ileus</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Superficial wound infection</td>
<td>3 (4.7)</td>
</tr>
<tr>
<td>Pelvic abscess</td>
<td>3 (4.7)</td>
</tr>
<tr>
<td>Readmission</td>
<td>4 (6.3)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>5 (7.8)</td>
</tr>
<tr>
<td>Fever</td>
<td>7 (10.9)</td>
</tr>
</tbody>
</table>

* From time of surgery to within first 24 hours postoperatively
** From 24 hours to 30 days postoperatively
Is there a difference between sBOT and mBOT?

**Objective:** The staging and surgical method for borderline ovarian tumors (BOT) is a controversial issue. Compared to malignant ovarian tumors, in BOT it is difficult to determine the surgical method because of development of tumors at an earlier stage and in younger women. This study aims to compare the serous (sBOT) and mucinous borderline ovarian tumors (mBOT) with respect to clinical-pathologic factors, disease-free survival (DFS), and recurrence.

**Method:** This is a retrospective study conducted at Asan Medical Center, Seoul, Korea, between 1990 and 2015 among patients diagnosed with borderline tumors histopathologically.

**Results:** Of the total 678 patients, patients with sBOT and mBOT were 200 and 478, mean ages were 44.1 and 40.9 years (P = 0.016), and averages of the largest tumor diameter were 9.4 cm and 16.4 cm (P < 0.001), respectively. Of patients who underwent open surgery, 61.5% was for sBOT and 73.4% for mBOT. The rate of staging procedure was 33.5% in sBOT and 5.2% in mBOT. We found that the rate of stages IB, IC, or II–IV was higher in sBOT than in mBOT. In sBOT, the recurrent rate was lower in the staging procedure group compared with the nonstaging group, while the recurrence rate in the incomplete staging surgery group of mBOT was lower than that of sBOT. Furthermore, there was also no difference in DFS between sBOT and mBOT (P = 0.176).

**Conclusion:** During surgery, sBOT was diagnosed at a more advanced stage than mBOT. Also, the recurrent rate was lower in the staging procedure group compared with the nonstaging group in sBOT. Our study has shown that the staging procedure can be omitted in mBOT; however, it should be considered carefully when stage is more than IA in sBOT. Also, since there is no difference in DFS, more research is needed to confirm whether the staging procedure is meaningful.

The efficacy of secondary debulking surgery for recurrent ovarian, tubal and peritoneal cancer in low risk scores in the Tian model

**Objective:** In recurrent ovarian, tubal, and peritoneal cancer (ovarian cancer), it is not revealed which contributes to longer OS, secondary debulking surgery (SDS) plus chemotherapy or chemotherapy alone (CT). The aim of this study is to investigate the efficacy of SDS for recurrent ovarian cancer patients with low-risk scores (equal to or less than 4.7) of the Tian model, which can estimate higher rates of complete resection (more than 50%) at SDS.

**Method:** Of 118 patients of ovarian cancer at the first recurrence who underwent treatment in our hospital between 2004 and 2016, we selected patients who satisfy low-risk scores in the Tian model and more than 6 months of disease-free interval, resulting in 52 patients. Using the propensity score matching method to reduce the bias of variables in this retrospective study, we analyzed 44 cases (22 in the SDS group, 22 in the CT group).

**Results:** The rates of complete resection in SDS for patients with a single site and multiple sites of recurrence were 83% (5/6) and 69% (11/16), respectively. OS after initial recurrence was significantly longer in the SDS group than in the CT group (median 7.5 years vs 2.9 years, P = 0.002). In the cases with multiple sites recurrence, the SDS group (n = 16) had also significantly longer OS than the CT group (n = 16) (median 7.5 years vs 2.4 years, P = 0.027). In the cases with a single-site recurrence, all cases were alive (6/6) at the cutoff date. There was no fatal complication in either the SDS or CT group.

**Conclusion:** Although this is a retrospective matching analysis, we suggest that SDS should be taken into consideration for patients with low-risk Tian scores, even in cases with multiple sites recurrence.
**2452 - Poster Session**

**Effect of platinum sensitivity on the efficacy of hyperthermic intraperitoneal chemotherapy (HIPEC) in epithelial ovarian cancer**

A.B. Costales\(^a\), L. Moulton Chambers\(^b\), A.M. Chichura\(^a\), P.G. Rose\(^b\), H. Mahdi\(^a\), C.M. Michener\(^a\), M. Yao\(^a\) and R. DeBernardo\(^a\).

*\(^a\)Cleveland Clinic, Cleveland, OH, USA, \(^b\)The Cleveland Clinic Foundation, Cleveland, OH, USA*

**Objective:** Previously published data have suggested that survival is not different between patients with platinum-resistant disease versus platinum-sensitive. The aim of this study was to examine whether PFS and OS were similar in these cohorts.

**Method:** A retrospective, single-institution study of 37 women with recurrent epithelial ovarian cancer who were treated with debulking and HIPEC between the years 2010 and 2018 was performed. PFS and OS were calculated using the Kaplan-Meier method. Survival was calculated from the date that HIPEC was performed until recurrence for PFS and death/last follow-up for OS.

**Results:** In this cohort, 26 patients (70.3%) were platinum-sensitive and 11 (29.7%) were platinum-resistant. There were no significant differences between the groups in age, histology, ASA score, Charlson comorbidity index, BRCA mutational status, number of prior debulkings, or disease location preoperatively. Seventy eight percent of patients had serous histology. Median follow-up following HIPEC for platinum-sensitive versus platinum-resistant patients was 14.5 months (7.3–40.0 months) and 10.6 months (5.5–21.9 months), respectively. The number of prior lines was >3 in 7.7% in the platinum-sensitive cohort and 18.2% in the platinum-resistant cohort. The median PFS for the platinum-sensitive group was 36.3 months compared to 9.4 months in the platinum-resistant group (\(P = 0.097, HR = 0.44, 95\% CI 0.16–1.19\)). The 1-year recurrence free survival was 66.8% compared to 25.5% in the platinum-sensitive and -resistant cohorts, respectively. Recurrences have occurred in 20% versus 42% with median 1-year overall survival of 92.1% versus 70.7% in the platinum-sensitive and -resistant cohorts, respectively. There was no difference in 3-year OS in the platinum-sensitive versus platinum-resistant cohorts (59.2% vs 38.9%, \(P = 0.28\), HR (0.14–1.80).

**Conclusion:** Combining cytoreduction and HIPEC may be an option in select patients with recurrent epithelial ovarian cancer, including in those with platinum-resistant disease.

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**2453 - Poster Session**

**Exploratory analysis of somatic BRCA mutations in endometrial cancer and its clinical implications**

W.C. Burkett Jr\(^a\), K.N. Moore\(^a\), L.L. Holman\(^a\), G.E. Koncny\(^b\), J.G. Cohena\(^b\), E.N. Prendergast\(^b\), K. Odunsic and K. Ding\(^d\).

*\(^a\)The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, \(^b\)University of California, Los Angeles, Los Angeles, CA, USA, \(^c\)Roswell Park Cancer Institute, Buffalo, NY, USA, \(^d\)The University of Oklahoma, Oklahoma City, OK, USA*

**Objective:** Germline BRCA mutations in ovarian cancer patients are associated with improved response to chemotherapy and survival. With the increased use of molecular profiling, many women with endometrial cancer (EC) have been found to harbor somatic BRCA mutations, the significance of which is unknown. The goal of this study is to evaluate the prognostic and predictive features of somatic BRCA mutations (BRCA+) in EC.

**Method:** An Institutional Review Board-approved, retrospective review of patients with molecularly profiled EC from 4 academic institutions between 2010 and 2018 was performed. Summary statistics were used to describe demographic and clinical characteristics. Analysis included a comparison of response and survival following treatment with platinum-based chemotherapy among BRCA+ and somatic BRCA wild-type (BRCAwt) patients.

**Results:** Of the 209 patients included, 15.8% were BRCA+. Of these, the median age was 62.5 years, and 63% were endometrioid. This was not statistically different from the 176 BRCAwt patients, of which the median age was 61.9 years and 56% were endometrioid (all \(P > 0.05\)). BRCA+ patients were more likely to have a higher level of tumor mutation burden (TMB) than BRCAwt (40% vs 15%, \(P = 0.015\)). After adjusting for TMB, BRCA+ is associated with a shorter PFS for platinum therapy (12 vs 13 months, \(P = 0.046, \text{Figure 1}\)), but not with OS (19 vs 13 months, \(P = 0.73\)).

**Conclusion:** Among EC patients, somatic BRCA mutations are relatively uncommon. BRCA+ patients are more likely to have a higher level of TMB tumors, but no other clinical factors were associated with these mutations. BRCA+ appears to be a negative predictive biomarker for PFS in EC, but has no impact on OS. These findings suggest that BRCA+ may not be predictive of...
therapeutic response to platinum therapy in EC. Data collection continues with obtaining allelic frequency of the somatic BRCA mutation to identify those mutations that are more likely to be germline.

![Survival Probability vs. PFS for Platinum Therapy](image)

**Fig. 1.** Product-Limit Survival Estimates.

**2454 - Poster Session**

**Tumor proximity to serosal surface as an independent prognostic factor in stage I endometrial cancer**

L.M. Harbin, L.K. Berry, E. Green, A. Wahlquist and W.A. Graybill. *Medical University of South Carolina, Charleston, SC, USA*

**Objective:** The purpose of this study is to determine whether tumor distance from serosal surface is an independent prognostic factor for survival and disease recurrence in stage I endometrial cancer.

**Method:** Eligible patients diagnosed with stage I endometrial cancer between 1988 and 2015 were identified from a database at our institution. A retrospective chart review was performed of 738 patients to assess differences in tumor distance from serosal surface, histologic subtype, histologic grade, use of adjuvant treatment, recurrence rates, and OS. Wilcoxon rank sum tests and Cox proportional hazard models were used to determine whether the variables of interest were related to recurrence and overall survival.

**Results:** Of the 738 patients, 643 patients (87%) had stage IA disease and 95 patients (12.9%) had stage IB disease based on the 2009 FIGO classification. Final pathology demonstrated type 1 disease in 540 (73%) patients with the remaining 190 (27%) patients having type 2 disease. Tumor distance from serosal surface ranged from 0 cm to 14 cm. At time of analysis, 76 (10%) patients had experienced recurrence. The risk of recurrence is 2.80 times higher for those with type 2 disease than that for patients with type 1 disease ($P < 0.0001$). Similarly, tumors classified as grade 2 and grade 3 had nearly two-fold and four-fold increased risk of recurrence, respectively, when compared to grade 1 malignancies ($P = 0.06$ and $P < 0.0001$). For survival, similar trends were evident. Risk of death was increased two-fold for patients with type 2 disease compared to type 1 ($P = 0.0002$). Risk of death due to any cause was also increased in patients with higher grade disease. There appears to be evidence that tumors with closer proximity to the serosal surface (<5 mm) have a higher incidence of recurrence and mortality based on preliminary analysis; however, final results are still in process.

**Conclusion:** Our study demonstrates that type 2 histology and higher grade disease are strongly associated with risk of recurrence and risk of death from any cause in stage I endometrial cancer. Final results are still pending; however, there appears to be an association between recurrence risk for tumors in close proximity to the serosal surface. Through this study we hope to demonstrate that tumors with close proximity (<5 mm) to the serosal surface are associated with poorer patient...
2455 - Poster Session
Is gonadotropin-releasing hormone analogue effective to preserve ovarian function in women undergoing chemotherapy for gynecologic malignancies?
K.B. Leea, S. Lima, M.C. Chob and J.M. Leec. aGachon University Gil Medical Center, Incheon, South Korea, bCHA Bundang Medical Center, CHA University, Gyeonggi-do, South Korea, cKGOG (Korean Gynecologic Oncology Group), Seoul, South Korea

Objective: To determine whether GnRHa before chemotherapy and during chemotherapy for gynecologic malignancies could preserve post-treatment ovarian function in young women.

Method: Twenty-nine premenopausal patients of three institutes with gynecological malignancies who had undergone ovarian-conserving surgery were retrospectively evaluated. Patients received combined GnRHa and chemotherapy. A hormone profile (FSH) was measured after completion of chemotherapy.

Results: The median age was 31 years. Thirteen patients (44.9%) underwent hysterectomy. Most patients (26/29, 89.7%) received 4–6 cycles of chemotherapy. Most commonly used chemotherapeutic regimens were BEP (27.6%) and taxane/CBDCA combination (27.6%). Mean number of GnRHa cycles was 4.9 ± 1.4. The mean FSH level after completion of chemotherapy was 21.6 ± 25.8 IU/L. Two (12.5%) of 16 patients who preserved their uterus became pregnant during the follow-up period. Nine (56.3%) of 16 patients restored their menstrual cycles after completion of treatment. See Table 1.

Conclusion: GnRHa before and during chemotherapy for gynecologic malignancies in young women could be effective for protecting ovarian function. Long term follow-up and large-scale controlled prospective trials are required.

2456 - Poster Session
The ability of whole-body suvmax in f-FDG PET/CT to predict suboptimal cytoreduction during primary debulking surgery for advanced ovarian cancer
G.O. Chonga, Y.H. Leea, H.J. Leea, D.G. Honga, Y.S. Leea and C.M. Parkb. aKyungpook National University Medical Center, Daegu, South Korea, bJeju National University Hospital, Jeju, South Korea

Objective: The aim of this study was to (1) evaluate the ability of the whole-body standardized uptake value (SUVmax) in F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) to predict suboptimal cytoreduction and (2) to create a risk model using metabolic parameters for predicting suboptimal cytoreduction in advanced ovarian cancer.

Method: From 2011 to 2015, 51 patients underwent primary cytoreductive surgery for advanced ovarian cancer (FIGO stage III–IV). Residual disease with maximal diameter >1 cm was considered a suboptimal surgical result. The SUVmax values for 9 abdominal regions (central, right upper, epigastrium, left upper, left flank, left lower, pelvis, right lower, right flank) and as the sum of 9 regional SUVmax (WB1SUVmax) were used for PET parameter. Whole-body 2 SUVmax (WB2SUVmax) was the sum of the SUVmax values for 3 regional lymph nodes (pelvis, paraaortic, and extra-abdominal) and the WB1SUVmax. Multiple logistic regression analysis was used to determine the predictive value of PET and clinical parameters for the risk model. In addition, assessments of disease-free survival (DFS) and OS were performed using the risk model.

Results: Seventeen of the 51 patients (33.3%) underwent suboptimal cytoreduction. According to univariate analysis, among the clinical parameters, only ECOG status was associated with suboptimal cytoreduction with marginal significance (OR = 4.091, 95% CI 0.97–17.29, P = 0.0520). Among the PET metabolic parameters, PET 0 (central, OR = 5.250, 95% CI 1.41–19.59, P = 0.0136), PET 1 (right upper, OR = 4.148, 95% CI 1.13–15.19, P = 0.0317), and PET 3 (left upper, OR = 5.921, 95% CI 1.17–30.02, P = 0.0318) were significantly associated with suboptimal cytoreduction. Moreover, WB2SUVmax was significantly associated with suboptimal cytoreduction (OR = 4.148, 95% CI 1.13–15.19, P = 0.0317). Kaplan-Meier survival plots showed that the DFS and OS in the high-risk group were significantly worse than those in the low-risk group (P = 0.0379 for DFS; P = 0.0211 for OS).

Conclusion: The presence of hypermetabolic lesions in the central, right upper, and left upper regions showed predictive value for suboptimal cytoreduction. WB2SUVmax was significantly associated with suboptimal cytoreduction. Furthermore, we suggest a simple risk model to predict suboptimal cytoreduction using PET and clinical parameters.
2457 - Poster Session

Is there a benefit to the lowest possible CA-125: The relationship between biomarkers and survival in epithelial ovarian cancer

M. Clarka, L. Al houssanb, Z. Liuc and M.Q. Bernardinic. aUniversity of Toronto, Toronto, ON, Canada, bRoyal College of Surgeons in Ireland, Dublin, Ireland, cUniversity Health Network, Princess Margaret Hospital, Toronto, ON, Canada

Objective: The aim of this study was to investigate the relationship between CA-125 levels at diagnosis, after surgery, and at the completion of upfront treatment in epithelial ovarian cancer as it relates to PFS and to understand whether achieving the lowest possible value within the normal range is associated with a survival advantage.

Method: This was a retrospective cohort study at the University Health Network of all women with epithelial ovarian cancer between January 2008 and December 2015. During upfront treatment, all CA-125 levels were collected, as well as important clinical and pathologic variables including age, stage, histology, number of cycles, toxicities, and recurrences. Survival analysis was completed by Cox proportional hazard models and Kaplan-Meier methods. CA-125 levels within the normal range were divided into <5, 6–10, and 11–35 IU. PFS is defined as time from completion of primary treatment to date of first recurrence.

Results: A total of 349 patients met eligibility criteria. Among patients treated with primary cytoreductive surgery (PCS), CA-125 at completion of treatment is significantly associated with PFS (HR = 1.3, P = 0.013); however, CA-125 at completion of treatment is not significantly associated with PFS in a neoadjuvant chemotherapy (NACT) treatment model (P = 0.053). In PCS, the difference between preoperative and postoperative CA-125 is significantly associated with PFS (HR = 1.25, P < 0.001) but not in NACT (P = 0.397). There is no statistically significant difference in PFS between women who have a CA-125 of <5 IU, 6–10 IU, or 11–35 IU at the completion of primary treatment (P = 0.218). In PCS, women who receive more than 6 cycles of chemotherapy have a worse PFS (10.6 months) than those who receive 6 (35.8 months, P = 0.018) and experience more grade 3 hematologic and gastrointestinal toxicities. In NACT, there is no PFS advantage to >3 cycles of either preoperative (P = 0.078) or postoperative (P = 0.87) chemotherapy.

Conclusion: The differences in CA-125 before and after treatment are an important factor in assessing a woman’s risk for progression after PCS and adjuvant chemotherapy but not in NACT. Achieving the lowest possible CA-125 within the normal range was not associated with a survival advantage. Additional chemotherapy beyond the standard regimen does not improve survival and may lead to further toxicity. Three cycles before and after interval surgery appears to be sufficient in terms of PFS in NACT.

2458 - Poster Session

Diagnostic accuracy of risk of ovarian malignancy algorithm (ROMA) experienced in the clinical practice

H.N. Lee, K.H. Lee and H. Park. The Catholic University of Korea, Seoul, South Korea

Objective: We investigated whether the clinically acceptable minimal sensitivity of >0.800 of the risk of ovarian malignancy algorithm (ROMA) could be obtained with the suggested cutoff of 7.4%/25.3% for pre- and postmenopausal women, and with different cutoffs set to a specificity of ≥0.750, in a hospital with a lower epithelial ovarian cancer (EOC) prevalence than has been reported.

Method: ROMA scores were calculated from measurements of HE4 and CA-125 in blood samples drawn from 443 patients with a pelvic mass. The risk group was compared against the results of biopsy (n = 309) or clinical follow-up with imaging studies (n = 134). The ROMA sensitivity and specificity for predicting EOC were calculated for the suggested and adjusted cutoff values.

Results: When EOC prevalence was 0.041, the sensitivity and specificity at the suggested cutoff were 0.778 and 0.894, respectively. Meanwhile, the sensitivity was 0.889 at the 4.78%/14.35% cutoff set to a specificity of 0.750.

Conclusion: In a hospital serving a patient population with a low EOC prevalence, the sensitivity of ROMA in clinical practice could be less than expected when using the suggested cutoff.
Survival outcomes between minimal invasive surgery and open surgery for consecutive patients with early stage cervical cancer
L.Y. Li, S.W. Kim, J.Y. Lee, E.J. Nam, S. Kim and J.W. Kim. Yonsei University College of Medicine, Seoul, South Korea

Objective: The aim of this study is to compare the 3-year PFS and OS in cervical cancer patients (stage 1A1–2B) treated with open radical hysterectomy (ORH), laparoscopic radical hysterectomy (LRH), and robotic radical hysterectomy (RRH).

Method: Patients who underwent ORH, LRH, or RRH between 2000 and 2015 were retrospectively reviewed. Survival curves were analyzed using the Kaplan-Meier method and log rank test according to the operation modality (ORH vs LRH vs RRH) and periods (first-half vs second-half phase). Patients who received neoadjuvant treatment were excluded. The learning curve was evaluated using the cumulative summation method.

Results: Of the 438 patients, 258 patients underwent ORH, 72 patients underwent LRH, and 108 patients underwent RRH. Median follow-up time was 109.2 months. We found that the RRH group had significantly lower 3-year PFS than the ORH or LRH group (P = 0.012). In the multivariate analysis of 3-year PFS, the RRH group had higher risk of recurrence than the ORH group after adjusted for invasion depth, lymphovascular invasion, and stage (HR = 2.803, 95% CI 1.433–5.483). In the first-half consecutive patients, the RRH group was still highly associated with worse 3-year PFS than the ORH group, but there were no significant differences between the three groups in the second-half consecutive patients. Learning curve showed that the 3-year recurrence rate was significantly decreased in single-surgeon RRH groups after the first 50 cases (from 35% to 5%). OS of the three groups did not vary significantly both in the first- and second-half patients.

Conclusion: Robot-assisted surgery requires a learning curve of 50 cases, which will reduce the 3-year recurrence rate to a similar level comparable to open or laparoscopic surgery. OS was similar regardless of operative method.

Fig. 1. Kaplan-Meier estimates of PFS (a) for cervical cancer patients treated with ORH, LRH, or RRH. Each group was further divided into two groups: the first half (F) and the second half (S). Cumulative sum (CUSUM) for 3-year recurrence number of every 10 cases was plotted. Decreased recurrence number was observed after 50 cases in RRH group (b).

Conservative management of adenocarcinoma in situ in pregnancy
D.B. Chau, C.J. VandenBussche and K.L. Levinson. Johns Hopkins School of Medicine, Baltimore, MD, USA, Johns Hopkins Hospital, Baltimore, MD, USA

Objective: There is currently no defined standard management of adenocarcinoma in situ (AIS) in pregnant women, and literature to guide management is limited. The objective of this study was to perform a case control analysis of gravid women with AIS who did not have an antepartum excision and to compare outcomes of patients with AIS who did undergo immediate excision for AIS.

Method: Patients with AIS diagnosed during pregnancy between 1998 and 2018 were identified, and control patients were selected, matched by age, race, and smoking status. Retrospective chart review was conducted to determine management and
Outcomes, including disease persistence or progression, need for additional procedures, and time elapsed from biopsy to excision were compared using *t* tests.

**Results:** Of 344 individual pathology specimens with AIS, 10 gravid women with a median age of 32 years were identified, and 20 nongravid controls were selected. Women were white or Hispanic and 60% nonsmoking. All 10 women were conservatively managed, with excisional procedure performed postpartum. Elapsed time from cervical biopsy to excision was significantly different (*P* < 0.05) between gravid and nongravid groups, 32.4 weeks versus 6.6 weeks, respectively. Of the 10 gravid women, 6 underwent excision with negative margins, 1 underwent excision with margins positive for AIS, 2 underwent excision that showed invasive carcinoma, and 1 underwent hysterectomy that showed invasive carcinoma. There was no significant difference in invasive cancer diagnosed at time of excision (OR = 1.71, 95% CI 0.30–9.77) or likelihood of completion hysterectomy (OR = 1.17, 95% CI 0.09–15.46) between gravid and nongravid groups. Pregnant women were 9 times more likely to have imaging recommended to them as part of their initial evaluation compared to their nongravid controls (OR = 9.00, 95% CI 1.33–61.14).

**Conclusion:** Standard management of AIS during pregnancy has not been well defined; however, these preliminary data suggest that conservative management with excisional procedure postpartum may be reasonable. Despite longer time from biopsy to excision for gravid versus nongravid patients, no difference in likelihood of progression was detected in this initial limited analysis. Further multiinstitutional investigation is therefore ongoing.

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**2501 - Poster Session**

**The effect of third line or more chemotherapy in recurrent ovarian cancer patients**

S. Pyeon¹, K.B. Lee² and J.M. Lee³. ¹Kyung-Hee University Hospital at Gangdong, Seoul, South Korea, ²Gachon University Gil Medical Center, Incheon, South Korea

**Objective:** Many patients with recurrent ovarian cancer receive palliative chemotherapy. However, there are sparse data on the optimal extent of palliative chemotherapy. The purpose of this study was to identify the difference in the survival rate and toxicity of palliative chemotherapy in recurrent ovarian cancer between patients (ET) who started chemotherapy immediately after diagnosis of recurrence and patients (DT) who received delayed chemotherapy.

**Method:** A retrospective review of patients with recurrent ovarian cancer who had undergone primary surgical treatment at 2 centers in Korea from 2006 to 2016 was performed. All of these patients were followed up and had received palliative chemotherapy at the same institutions of diagnosis. The patients who had partial response or progression after second-line chemotherapy were analyzed. The time of initiation of palliative chemotherapy was calculated from the second recurrence or progression based on radiologic findings. Patients were divided into two groups. The ET group included patients who started chemotherapy less than 3 weeks after recurrence or progression, and the DT group included patients who received delayed chemotherapy more than after 3 weeks. The variables were analyzed using *χ²* test or Fisher exact test and *t* test. Analysis of the survival was carried out using Kaplan-Meier analysis.

**Results:** A total of 74 women were included in this study. The ET group included 44 patients, and the DT group included 30 patients. There was no difference in the initial characteristics of the 2 groups. The median values for the number of regimens applied from the third-line chemotherapy were 2 and 1, respectively. And the median value of the chemotherapy cycles from the third-line was 8 and 6, respectively. The median values of the sum of the intervals between the diagnosis of further progression and change of regimen were 1.7 weeks and...
13.9 weeks, respectively. There was no difference in toxicity between the groups. There was no significant difference in overall survival between the 2 groups ($P = 0.369$, Figure 1).

**Conclusion:** In patients with recurrent ovarian cancer receiving third-line or more palliative chemotherapy, there seems to be no survival benefit of early initiation of regimens compared to that of delayed palliative chemotherapy.

**Fig. 1.** 1, the first group (ET) who started chemotherapy immediately after diagnosis of recurrence; 2, the second group (DT) who received delayed chemotherapy.

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**2502 - Poster Session**

**Feasibility of the use of an articulating bipolar vessel sealer in robotic-assisted transperitoneal pelvic and infrarenal paraaortic lymphadenectomy for gynecologic malignancies**

H.J. Lee, Y.H. Lee, G.O. Chong, D.G. Hong and Y.S. Lee. Kyungpook National University Medical Center, Daegu, South Korea

**Objective:** The objective of this study was to evaluate the feasibility and safety of a bipolar energy device, the Endowrist® Vessel Sealer (VS), in robotic-assisted transperitoneal pelvic and infrarenal paraaortic lymphadenectomy.

**Method:** From April 2013 to April 2018, we analyzed retrospectively 69 patients undergoing robotic-assisted pelvic and infrarenal paraaortic lymphadenectomy using VS ($n = 35$) or conventional bipolar ($n = 34$) for gynecologic malignancies. Perioperative data including operation time and retrieved lymph node number, estimated blood loss, serum C-reactive protein, albumin, total protein level, and postoperative complications were compared.

**Results:** The operation time for infrarenal paraaortic (42.24 vs 23.69 minutes, $P < 0.01$) and pelvic (23.50 vs 19.97 minutes, $P = 0.04$) lymphadenectomy was significantly shorter in the VS group. The retrieved number of pelvic and infrarenal paraaortic lymph nodes, estimated blood loss, differences of serum albumin, and C-reactive protein levels between preoperative and second postoperative day were not different. The perioperative complications related to lymphadenectomy were lower in the VS group; only 1 chylous ascite occurred in the VS group, while there were 5 cases in the conventional group.

**Conclusion:** Our study showed that use of the VS in robotic-assisted pelvic and transperitoneal infrarenal paraaortic lymphadenectomy could be feasible and safe.

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**2503 - Poster Session**

**Age-related risk of postoperative mortality after cytoreductive surgery for advanced ovarian cancer**

A. Bercowa,b, A. Melameda,b, E.L. Eisenhauera,b, J.A. Rauh-Hain,c, J.D. Wrightd, L.W. Ricee and M.G. del Carmenab, aMassachusetts General Hospital, Boston, MA, USA, bHarvard Medical School, Boston, MA, USA, cThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, dColumbia University, New York, NY, USA, eUniversity of Wisconsin School of Medicine and Public Health, Madison, WI, USA

**Objective:** Surgical cytoreduction is a critical component of primary therapy for advanced ovarian cancer. However, patients who die within 90 days of cytoreductive surgery do not benefit from the operation and may experience significant harm. We investigate the association between age and 90-day postoperative mortality after cytoreductive surgery, and how neoadjuvant chemotherapy (NACT) modulates this association.

**Method:** Using the National Cancer Data Base, we conducted an analysis of age-related trends in 90-day postoperative mortality after cytoreductive surgery among women with stage IIIIC or IV epithelial ovarian cancer, treated in Commission on Cancer-accredited hospitals in the United States between 2004 and 2013. We fit logistic joinpoint models to quantify the probability of 90-day postoperative mortality as a function of age for women undergoing primary (PCS) and interval (ICS) cytoreductive surgery. We fit separate models to estimate crude and adjusted age-specific relative odds of postoperative death after PCS relative to ICS.

**Results:** We identified 47,117 of whom 37,024 (78.5%) underwent PCS and 10,153 (21.5%) underwent ICS. Overall, 90-day mortality was more common after PCS (7.2%, 2,658 deaths) than ICS (3.1%, 312 deaths). Age-related trends in 90-day mortality differed between PCS and ICS ($P_{interaction}< 0.001$, see Figure 1). Women age 47 years and younger experienced no age-related increase in risk of 90-day mortality after ICS ($P = 0.36$) or PCS ($P = 0.75$). Among women who underwent PCS, the
odds of 90-day postoperative mortality began rising at age 47 years, increasing by 5.7% per year (95% CI 5.0–6.5, P < 0.001) until age 71, and by 9.9% per year (95% CI 8.8–10.9, P < 0.001) thereafter. In contrast, odds of 90-day mortality after ICS began to increase at age 62 years and increased steadily by 5.7% per year (95% CI 3.9–7.5, P < 0.001). By age 75 years the probability of 90-day postoperative mortality after ICS was 4.2% (95% CI 3.6–4.9) compared with 12.3% after PCS (95% CI 11.4–12.7). By age 85 years these probabilities increased to 7.2% (95% CI 5.5–9.2) and 26.0% (95% CI 24.1–27.9), respectively.

**Conclusion:** Women undergoing PCS incurred an age-related risk of postoperative mortality at a younger age, and to a greater magnitude, than those undergoing ICS. Among older women, NACT may reduce the frequency on unbeneficial cytoreductive surgery.

**Fig. 1.** Observed age-specific probabilities of 90-day mortality after primary cytoreductive surgery (blue dots) and interval cytoreductive surgery (red dots) are plotted along with predicted probabilities (solid lines) and 95% confidence intervals (shaded areas) from piecewise logistic regression models. The number operations, as well as crude and adjusted odds ratios for 90-day mortality after primary cytoreductive surgery, relative to interval debulking surgery, are tabulated by age group. Adjusted odds ratios are adjusted for year of diagnosis, histologic type, grade, stage, comorbidity index, geographic region, insurance type, hospital volume, and cancer program.

PCS: primary cytoreductive surgery. ICS: interval cytoreductive surgery, CI: confidence interval.

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**2504 - Poster Session**

**Anti-cancer effect of PARP inhibitor (olaparib) with DNA-demethylating agent (5-Azacytidine) in ovarian cancer**

S.Y. Jeong, M.S. Kim, J.H. Kim, E.S. Paik, Y.Y. Lee, C.H. Choi, T.J. Kim, B.G. Kim, D.S. Bae and J.W. Lee. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

**Objective:** Olaparib, one of the first poly(ADP-ribose) polymerase (PARP) inhibitors, has been used for maintenance therapy in ovarian cancer. In one AML and breast cancer cell line experiment, DNA-demethylating agents, inhibitors of DNA methylation and DNA methyltransferases, increase PARPi tightly bound into chromatin. The purpose of this study is to investigate the anticancer effect of combination therapy, olaparib with DNA-demethylating agents (5-azacytidine), in ovarian cancer cell models including in vitro and in vivo experiments.
Method: In in vitro experiments, we treated ovarian cancer cell lines (A2780, SKOV3ip1, HeyA8) with olaparib only, 5-azacytidine only, and combination with olaparib and 5-azacytidine to evaluate the effect on cell proliferation using MTT assay. To check the human active caspase3, MMP2, and MMP9 level and apoptosis, we performed Western blot, ELISA, and apoptosis assays in ovarian cancer cell lines. With wound-healing assay and migration assay, invasive ability of cancer cell was evaluated and compared after a few hours of treatment with inhibitors. In addition, in vivo therapy experiments for this cotreatment in established cell line xenografts and PDX models of epithelial ovarian cancer were done. For cell line xenografts, A2780 was injected into the peritoneal cavity of mice. For the PDX model, surgical patient tumor specimens (less than 2–3 mm) were implanted into the subrenal capsule of left kidney and propagated by serial transplantation. We recorded body weight, tumor weight, and number of tumor nodules.

Results: Both olaparib and 5-azacytidine inhibited the cell survival and increased apoptosis in ovarian cancer cells. In this study, combination treatment with olaparib and 5-azacytidine significantly inhibited cell growth and increased apoptosis compared to the single-agent treatment in ovarian cancer cells. In in vivo experiments, combination treatment with olaparib and 5-azacytidine significantly decreased weight and nodule numbers of tumor in cell-line xenograft models with A2780 cells and PDX model compared with other groups.

Conclusion: We found that combination treatment with olaparib and 5-azacytidine has a synergistic effect to attack ovarian cancer cells compared with control or single-agent treatment through in vitro and in vivo tests.

2505 - Poster Session
Risks and patterns of paraaortic node metastasis after chemoradiotherapy for pelvic node-positive paraaortic node negative cervical cancer in the era of metabolic imaging
K. Haines, A. Hochreiter, M. Young, S. Damast, and B. Litkouhi. Yale University School of Medicine, New Haven, CT, USA, Charite Universitätsmedizin Berlin, Berlin, Germany, Universitätsklinikum Charite, Berlin, Germany

Objective: Evaluation and treatment of the paraaortic lymph nodes (PAN) in locally advanced cervical cancer (LACC) remains an active area of investigation. Pelvic lymph node involvement at the time of diagnosis is an important prognostic factor. The purpose of this study was to determine the risks of PAN failures after chemoradiotherapy for patients with pelvic node-positive PAN-negative LACC receiving pelvic radiotherapy (RT) without extended field.

Method: We performed a retrospective chart review of all patients with LACC and pelvic lymph node metastasis who were treated with pelvic RT and concurrent chemotherapy, followed by brachytherapy, at a single institution between 2005 and 2016. Patients were included based on pretreatment imaging (PET scan) revealing positive pelvic lymph nodes, with concurrent negative PAN. None of the patients underwent pretreatment surgical nodal staging. Patient demographics, pretreatment tumor burden, treatment fields, and sites of anatomic recurrence were collected.

Results: Of the 103 patients with LACC treated with definitive chemoradiotherapy in the study period, 24 (23.3%) met inclusion criteria. Nine (38%) experienced recurrence. Four patients (17%) had recurrence in the PAN with simultaneous sites of distant failure, whereas only 1 patient (4%) experienced isolated PAN failure. There were no unifying factors identified to predict PAN recurrence. Evaluation of the primary locations of pelvic lymph node involvement (obturator, external/external iliac, common iliac) did not reveal any difference in likelihood or location of recurrence. In addition, comparison of initial tumor volume, stage, and dosage of pelvic/nodal RT or brachytherapy failed to reveal any patterns of recurrence.

Conclusion: In the era of PET imaging and pelvic chemoradiation, isolated PAN failure for pelvic node-positive, PAN-negative patients with LACC is rare. This study did not identify unifying characteristics to predict risks or patterns of PAN recurrence in these patients, suggesting that chemoradiation therapy without prophylactic extended field RT or surgical nodal staging may be adequate treatment, and that PAN metastasis may be a reflection of systemic disease rather than local recurrence after therapy failure.

2506 - Poster Session
Withdrawn at author’s request

2507 - Poster Session
Preoperative strategy to assess parametrial involvement in early-stage cervical cancer: Impact of conization and
sentinel lymph node biopsy


aHôpital Européen Georges-Pompidou, Paris, France, bCHU Vaudois, Lausanne, Switzerland, cHospices Civils de Lyon, Bron, France

Objective: The purpose of this study was to identify patients with low risk of parametrial involvement (PI) in early-stage cervical cancer based on preoperative conization and sentinel lymph node (SLN) status.

Methods: We performed an ancillary analysis of data from two prospective trials on sentinel node biopsy for cervical cancer (SENTICOL I and II). Patients with FIGO IA–IIA cervical cancer treated with radical surgery between 2005 and 2012 were identified from 25 French oncologic centers. Patients with a prior conization and a SLN biopsy were included for analysis.

Results: Of 160 patients who fulfilled the inclusion criteria, 7 patients (4.4%) had a pathological PI. There were no significant differences between both groups in BMI, clinical FIGO stage, histologic type, and preoperative brachytherapy. In univariate analysis, patients with PI were more likely to be older (50.3 ± 16 vs 41.9 ± 10.6 years, P = 0.049) and to have lymphovascular space invasion (LVSI) in the biopsy (71.4% vs 26.8%, P = 0.01), tumor size larger than 20 mm in conization specimen (71.4% vs 31.6%, P = 0.02), and positive SLN (42.9% vs 10%, P = 0.003). In multivariate analysis, PI was significantly associated only with positive SLN (aOR = 6.83, 95% CI 1.13–41.43, P = 0.02). Among the 74 patients (46.2%) with tumor size smaller than 20 mm in conization specimen, negative LVSI, and negative SLN, none had PI. See Table 1.

Conclusion: Patients with tumor size smaller than 20 mm in conization specimen, no LVSI, and negative SLN had low risk of PI and may be eligible for less radical surgery.

Table 1: Probability of Parametrial involvement according to preoperative variables.

<table>
<thead>
<tr>
<th>Risk of PI (%)</th>
<th>IC 95%</th>
<th>Age</th>
<th>Presence of LVSI</th>
<th>Conization size</th>
<th>Positive SLN</th>
<th>No. total patients</th>
<th>%</th>
<th>No. patients with PI</th>
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<tbody>
<tr>
<td>0.6</td>
<td>0.1 – 3.9</td>
<td>&lt; 70</td>
<td>No</td>
<td>&lt; 20 mm</td>
<td>No</td>
<td>73</td>
<td>45.6</td>
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<td>1.4</td>
<td>0.02 – 45.4</td>
<td>&gt; 70</td>
<td>No</td>
<td>≥ 20 mm</td>
<td>No</td>
<td>1</td>
<td>0.6</td>
<td>0</td>
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<tr>
<td>2.7</td>
<td>0.5 – 13</td>
<td>&lt; 70</td>
<td>Yes</td>
<td>&lt; 20 mm</td>
<td>No</td>
<td>30</td>
<td>18.8</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>0.6 – 14.4</td>
<td>&lt; 70</td>
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<td>&lt; 20 mm</td>
<td>Yes</td>
<td>26</td>
<td>16.3</td>
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<td>3.8</td>
<td>0.5 – 14.8</td>
<td>&lt; 70</td>
<td>Yes</td>
<td>&lt; 20 mm</td>
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<td>13.1</td>
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<td>&gt; 70</td>
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<td>≥ 20 mm</td>
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<td>16.1</td>
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<td>≥ 20 mm</td>
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<td>17.4</td>
<td>2.9 – 60.2</td>
<td>&gt; 70</td>
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<td>≥ 20 mm</td>
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<td>27</td>
<td>1.5 – 89.8</td>
<td>&gt; 70</td>
<td>Yes</td>
<td>&gt; 20 mm</td>
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<td>1.3</td>
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<td>50.7</td>
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<td>&gt; 70</td>
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<td>≥ 20 mm</td>
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<td>71.6</td>
<td>9.5 – 96.4</td>
<td>&gt; 70</td>
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</table>

2508 - Poster Session

Up-regulation of STAT3 signaling promotes invasion and metastasis of BRCA2-mutated epithelial ovarian cancer

Z.P. Lin, Y.L. Zhu, Y.C. Lo, P.H. Huang and E.S. Ratner. Yale University School of Medicine, New Haven, CT, USA

Objective: BRCA mutations lead to defective homologous recombination (HR) repair that underpins the development and progression of epithelial ovarian cancer (EOC) and renders hypersensitivity to poly(ADP-ribose) polymerase (PARP) inhibitor and platinum therapy. The objective of this study was to investigate the mechanism by which defective HR repair perpetuated invasion and metastasis of EOC in vitro and in vivo, as well as its therapeutic implications.

Method: BRCA2-mutated PEO1 and BRCA2 wildtype PEO4 cell lines derived from the same patient were used in the studies. Cancer stem cell markers were examined by Western blot and flow cytometric analyses. Tumor spheroid formation and scratch-wound healing assays were conducted. Napabucasin (BBI-608), a STAT3 and cancer stem cell inhibitor, was used to
induce caspase activation. Peritoneal progression of PEO1 and PEO4 xenografts was investigated in SCID mice treated with napabucasin alone and in combination with the PARP inhibitor olaparib. The survival time of tumor-bearing mice was determined by the Kaplan-Meier curves, and histological analysis of tumor invasion/metastasis were performed.

**Results:** BRCA2-mutated PEO1 cells exhibited an increase in STAT3/cancer stem cell markers, scratch-wound healing, and tumor spheroid formation compared with BRCA2-wild type PEO4 cells. Treatment of PEO1 cells with napabucasin caused a significant increase in apoptosis compared with PEO4 cells. In SCID mice, PEO1 xenografts caused widespread metastasis and organ destruction in the peritoneum. In contrast, PEO4 cells resulted in prominent ascites development and abdominal distension with minimal organ invasion. Treatment of mice with napabucasin blocked invasion and metastases of PEO1 xenografts. Napabucasin had no effects on the progression of PEO4 xenografts in mice. Napabucasin and olaparib combination abrogated peritoneal metastases and significantly prolonged the survival time of PEO1-bearing mice.

**Conclusion:** Defective HR repair upregulates cancer stem cell markers and STAT3 signaling in EO C. These traits strongly correlate with an increase in invasive and metastatic phenotypes in vitro and in vivo. Pharmacologic inhibition of STAT3 signaling reduces the metastatic potential of BRCA2-mutated EOC and holds promise in combination therapy with PARP inhibitors to improve treatment outcomes in patients.

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**2509 - Poster Session**

**Characterization of endometrial cancer in young patients diagnosed under the age of 40 years**

J. Sona, C.E. Carra, M. Yao, M. Radeva, A. Priyadarshini, J. Marquard and M.M. AlHill

**Objective:** We sought to investigate clinical and pathologic features of endometrial cancer (EC) in patients 40 years and younger and their impact on survival.

**Method:** Patients with EC treated between 2004 and 2017 were retrospectively reviewed. Age at diagnosis was used to classify patients into two groups: 40 years and younger and 41–60 years. Patients older than 60 years and those receiving neoadjuvant chemotherapy or primary radiation were excluded. Clinical and pathologic variables were compared between the 2 age groups. Mismatch repair (MMR) expression of MLH1, MSH2, PMS2, and MSH6 was assessed by immunohistochemistry. MLH1 methylation status was determined for MLH1/PMS2-deficient tumors. PFS and OS were evaluated using Cox proportional hazards regression right-censored univariate models.

**Results:** A total of 551 patients were evaluated, of which 103 (18.7%) were 40 years and younger and 448 (81.3%) were 41–60 years. Age 40 years and younger was associated with higher BMI (38.8 vs 35.8 kg/m², \( P = 0.008 \)), noninvasive tumors (54.2% vs 32.6%, \( P < 0.001 \)), lower uterine segment involvement (29.5 vs 22.7%, \( P = 0.001 \)), and lower rate of LVSI (16.8% vs 29.1%, \( P = 0.015 \)). Synchronous ovarian cancers were identified in 9.2% of patients 40 years and younger (\( n = 12 \)) versus 0.7% of those aged 41–60 years (\( P < 0.001 \)). The 5-year PFS in ages 40 years and younger was 74.9% versus 80.7% in ages 41–60 years (\( P = 0.017 \)), and the 5-year OS was 95.8% versus 87.1% (\( P = 0.11 \)), respectively. Factors associated with worse PFS and OS included myometrial invasion >50%, nonendometrioid histology, stage II/III, MLH1 methylation, grade 3, and LVSI (\( P < 0.05 \)). On multivariate analysis, grade 3 (HR 4.29, \( P < 0.001 \)) and LVSI (HR = 2.69, \( P = 0.004 \)) were associated with poorer PFS. After adjusting for these factors, age 40 years and younger was an independent predictor of worse PFS (HR = 3.96, \( P < 0.001 \)). OS was not significantly different between the 2 groups.

**Conclusion:** In this large cohort of patients 40 years and younger, favorable prognostic clinical and pathologic factors prevailed compared to patients ages 41–60 years. The incidence of synchronous ovarian cancer was 9.2% in patients 40 years and younger in this study. This possibly contributed to the detriment in PFS seen in this age group despite controlling for adverse prognostic factors (including grade 3 and LVSI). Importantly, 5-year OS was 95.8% in this age group.

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**2510 - Poster Session**

**Pathologic upstaging due to tumor size is associated with worse oncologic outcomes in patients with stage IB1 cervical cancer**

S. Smrza, M.H. Vetter and K. Bixel

**Objective:** We sought to investigate clinical and pathologic features of endometrial cancer (EC) in patients 40 years and younger and their impact on survival.
**Objective:** Clinical and pathologic staging of cervical cancer are discrepant in approximately 30% of patients with stage IB1 cervical cancer. We aim to estimate the rate of discordance between clinical and pathologic tumor size and to determine the impact on oncologic outcomes.

**Method:** This is a retrospective review of patients with stage IB1 cervical cancer undergoing radical hysterectomy between 2010 and 2017 at a large academic institution. Demographics, clinical characteristics, pathologic findings, and oncologic outcomes were extracted from the medical record. Patients with incomplete data were excluded. The primary outcome was the rate of pathologic upstaging with respect to tumor size (clinical exam <4 cm, pathologic tumor size >4 cm). Secondary outcomes included rate of recurrence, PFS, and OS.

**Results:** A total of 128 patients were included; 36 patients (28.1%) had a pathologic tumor size ≥50% larger than what was noted on clinical examination. Pathologic upstaging was seen in 22.7% (n = 29) of patients. Upstaged patients were more likely to have adenosquamous histology (13.8% vs 2.1%), poorly differentiated tumors (37.9% vs 19.2%), presence of LVSI (55.2% vs 44.9%), and positive pelvic lymph nodes (27.6% vs 11.1%) than patients with tumors <4 cm on final pathology. Upstaged patients were more likely to have preoperative imaging (51.7% vs 30.3%) with over 85% of imaging being performed with CT or PET/CT. Factors associated with pathologic upstaging included adenosquamous histology (P = 0.029), use of preoperative imaging (P = 0.034), moderately or poorly differentiated tumors (P = 0.035), positive pelvic lymph nodes (P = 0.028), and receipt of adjuvant therapy (P < 0.0001). Recurrence rates were higher in upstaged patients (20.7% vs 6.1%, P = 0.017). Median PFS was shorter in upstaged patients than in those with pathologically confirmed stage IB1 disease (84.3 vs 97.7 months, P = 0.019). There was a trend towards poorer OS in upstaged patients (P = 0.082).

**Conclusion:** Accurate evaluation of tumor size on clinical examination is challenging in patients with stage IB1 cervical cancer. Pathological tumor sizes >4 cm are associated with poor prognostic features and worse outcomes compared to patients with pathologically confirmed stage IB1 cervical cancer. Further research on how to improve clinical staging should be undertaken.

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**2511 - Poster Session**

Salvage re-irradiation with single modality interstitial brachytherapy for the treatment of recurrent gynecological tumours in the pelvis: A multi-institutional study

H. Razieea, D. D'Souzaa, V. Velkerb and E. Leungc,d. aBC Cancer Agency - Fraser Valley Centre, Surrey, BC, Canada, bLondon Health Sciences Centre, London, ON, Canada, cToronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada, dUniversity of Toronto, Toronto, ON, Canada

**Objective:** Recurrent gynecological tumors can cause significant morbidities for patients, with limited options of salvage therapy. Patients who are not candidates for salvage surgery are often managed with a palliative approach. This study investigates the strategy of high-dose salvage radiation with single-modality interstitial brachytherapy (SM-ISBT) for the management of recurrent gynecologic pelvic disease at two specialized interstitial brachytherapy centers.

**Method:** Patients with gynecologic malignancies who had received SM-ISBT for salvage treatment from September 2008 to January 2017 were included. All patients had recurrent gynecologic tumors confined to the pelvis with no distant metastasis at the time of recurrence. Locoregional control, distant metastasis, and long-term toxicities were evaluated.

**Results:** A total of 26 patients with a median follow-up of 24 months after SM-ISBT were included. The primary cancer sites were endometrium (20), cervix (4), vulva (1), and vagina (1). All patients had prior pelvic external-beam RT, and 16 had previous brachytherapy. Median disease-free survival prior to SMISBT was 20.3 months. SM-ISBT was delivered with a fraction dose of 500 to 700 cGy in 3 to 6. Median HRCTV volume was 34.6 cc (range 4.8–96.0 cc). SMISBT HRCTV was located in the upper, middle, and lower vagina in 15, 1, and 3 patients, respectively. Four patients had treatment to the entire vagina, and 3 to suburethral recurrence. Complete and partial overlap with previous radiation volume was detected in 14 and 12 patients (54% and 46%), respectively. After SM-ISBT, complete and partial response were achieved in 17 (64%) and 5 (19%) patients, respectively. Two (7.4%) patients had grade 3 toxicities (both vaginal stenosis), with no patients experiencing grade 4 complications. Eighteen patients (69%) had recurrence, including local, regional, and metastatic in 14 (54%), 8 (30%), and 5 (19%) patients, respectively. Two-year relapse-free survival and 3-year OS were 40% and 38%, respectively.

**Conclusion:** Salvage radiation with SM-ISBT for recurrent gynecologic malignancies in the pelvis is feasible and safe, and is associated with acceptable rates of toxicities with reasonable local control rates. With limited treatment options available for recurrent gynecologic tumors in the pelvis, developing strategies to address this morbid local disease is a priority. Prospective multiinstitutional studies are warranted to further investigate SM-ISBT as a standard option for salvage GYN treatment.
**2512 - Poster Session**

**Phase I trial of autologous NK cell immunotherapy combined with chemotherapy in patients with recurrent epithelial ovarian cancer**

W.D. Joo. CHA University, Seongnam, South Korea

**Objective:** NK cell plays an important role in innate immunity against cancer cells. Adopted immunotherapy with NK cell has been applied in various malignancies. This trial evaluated safety and efficacy of autologous NK cell immunotherapy combined with chemotherapy in patients with recurrent epithelial ovarian cancer.

**Method:** Patients with platinum-sensitive recurrent epithelial ovarian cancer were included. Three cycles of carboplatin AUC 5 and paclitaxel 175 mg/m² were administered every 3 weeks. Blood of the patients was withdrawn at least 1 week before the first cycle of chemotherapy. Peripheral blood monocytes were separated and cultured for 2 weeks to enrich the population of NK cells, and then were administered on day 7 of each cycle of chemotherapy. Response was judged by RECIST criteria ver. 1.1. Adverse events were recorded according to CTCAE ver. 4.03. The EORTC QLQ-C30 Korean questionnaire was used to assess quality of life of the patients.

**Results:** Four patients were enrolled, and three patients received the therapy. All patients were serous carcinoma, stage IIIc, and second recurrence. Three patients showed partial response. Two recurrences were observed. Hepatic mass increased and chemotherapy started again. Peritoneal mass size increased after 7 months, and it was resected. Serious adverse events were observed: grade 4 neutropenia, grade 3 upper respiratory infection with positive influenza A virus, and grade 3 cellulitis. Adverse events were observed: grade 3 neutropenia without febrile event and anemia; grade 2 nausea, peripheral sensory neuropathy, pain in extremity, urine output decrease, stomach pain, maculopapular rash, and dyspnea; and grade 1 ucticiaria, pruritus, fatigue, abdominal pain, lymphedema, noncardiac chest pain, fever, and allergic reaction. Most of the adverse events were related to chemotherapy, not related directly to NK cell immunotherapy. The severity was mild to moderate and not life-threatening.

**Conclusion:** Autologous NK cell immunotherapy combined with chemotherapy is considered to be tolerable for recurrent ovarian cancer. Three more patients will be enrolled for the second step, in which NK cell is administered on day 7 of each cycle of chemotherapy.

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**2513 - Poster Session**

**Novel site-specific detection of ovarian cancer using cell-free DNA (cfDNA) modeling**

B. Reva, J. Martignetti, M.A. Finan, L. Madeira da Silva and R.P. Rocconi. aIcahn School of Medicine at Mount Sinai, New York, NY, USA, bMitchell Cancer Institute, University of South Alabama, Mobile, AL, USA

**Objective:** Despite advancements in ovarian cancer (OC) therapy, the largest impact for improving OC mortality lies within the discovery of screening tests that detect early-stage disease or identify patients at risk for developing OC. The objective of this study was to develop a cell-free DNA (cfDNA) molecular signature to detect OC utilizing site-specific collection of cervicovaginal fluids (CVF).

**Method:** After Institutional Review Board approval, we prospectively collected CVF via Pap methodologies from postmenopausal patients during their initial visit to gynecologic oncology prior to surgical evaluation of a pelvic mass. Specimens were stored in preservative liquid and then analyzed using next-generation sequencing. Specimens were grouped and analyzed by final pathology of (a) benign/borderline, (b) early-stage OC, or (c) late-stage OC.

**Results:** Samples from 30 patients were analyzed, and groups were similar in age, BMI, and race. The cfDNA from site-specific Pap samples revealed a significant number of mutations in all samples. Significantly higher driver mutations were seen in 86% of cancer patients compared to 38% of benign patient samples \( (P = 0.002) \). The most common germline benign samples were enriched with non-uniform missense and/or truncating mutations compared to malignant samples \( (P < 0.01) \) and that hypermutated samples were only malignant. Using a threshold of allele frequency of 0.4%, cfDNA mutations were able to differentiate cancer versus benign/borderline \( (P = 0.0018) \).

**Conclusion:** Cell-free DNA found in site-specific collected CVF demonstrated the ability to differentiate OC from benign pelvic masses. Although these methods hold promise, larger studies are needed to develop effective modeling of both diagnostic and
Efficacy of combined metformin and progestin therapy for complex atypical hyperplasia and well-differentiated endometrial cancer in patients desiring fertility


Johns Hopkins School of Medicine, Baltimore, MD, USA, Johns Hopkins Hospital, Baltimore, MD, USA

Objective: Our study objectives were to (1) determine the efficacy of single-agent progestin versus combined therapy with metformin as primary treatment in patients with complex atypical hyperplasia (CAH) or grade 1 endometrioid adenocarcinoma (EC) desiring fertility-preserving management and (2) determine pregnancy rate following hormonal therapy.

Method: From 1999 to 2018, reproductively aged patients with CAH and/or well-differentiated EC who were treated with progestin therapy with or without metformin at an urban academic center were retrospectively reviewed. Treatment response was assessed on subsequent biopsy. Kaplan-Meier analysis was used to calculate time to complete response with comparison of potential predictors of response by the Cox proportional hazards method.

Results: Sixty-three patients met criteria. Median age at diagnosis was 32.6 years, and median BMI was 36.4 kg/m². The median follow-up time was 28 months. Twenty-three (36%) patients received metformin along with progestin therapy. The remainder received single-agent progestin therapy with either a levonorgestrel-releasing intrauterine (LNG-IUD), megestrol acetate, or medroxyprogesterone. Of the 60 patients who had follow-up, 48 (80%) had a complete response on initial therapy with a median time to complete response of 7.0 months (range 4–10 months). There was a trend toward improved complete response rate with metformin ($P = 0.10$). However, the addition of metformin to progestin therapy was not associated with improvement in the overall response rate ($P = 0.35$) nor with a shorter interval to response (5 versus 9 months, $P = 0.47$). There were 10 (17%) pregnancies resulting in live births during the study period, 7 (70%) of which required assisted reproductive technologies (ART).

Conclusion: Combined progestin-metformin therapy may be associated with improved complete response rates compared to progestin monotherapy. Larger prospective studies are needed to evaluate the impact of adding metformin to hormonal regimens in this setting. Less than 20% of patients desiring fertility-preserving management achieved pregnancy, with the majority requiring ART. It is important to counsel this patient population regarding pregnancy feasibility and likelihood of requiring ART in those who respond to progestin therapy.

Phase I trial of nelfinavir added to cisplatin chemotherapy with concurrent pelvic radiation for locally advanced cervical cancer


University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA, University of Miami Miller School of Medicine, Miami, FL, USA, University of Pennsylvania, Philadelphia, PA, USA

Objective: Despite platinum-based chemoradiation (C-XRT), 40%–50% of women with locally advanced cervical cancer will die from their disease. Nelfinavir (NFV), a protease inhibitor, has been shown to target the Akt pathway sensitizing cancer cells to chemoradiation. The objective of this phase I trial was to evaluate the safety and tolerability and identify the recommended phase II dose (RP2D) of NFV in combination with standard concurrent C-XRT in locally advanced cervical cancer.

Method: Untreated patients with FIGO stage IIA to IVA cervical cancer were included. Cohort dose level 1 (DL 1) was NFV 875 mg PO BID and cohort dose level 2 (DL 2) was NFV at 1,250 mg PO BID. Both cohorts had a 7-day run-in prior to initiating standard C-XRT. NFV was continued with weekly cisplatin 40 mg/m² and pelvic radiation. Patients received a total dose of at least 80 Gy to the primary tumor. DLT were evaluated in the first 8 weeks. Toxicity was evaluated during treatment and every 3 months for 1 year. Responses were evaluated (RECIST 1.1). Biopsies were obtained at baseline, after 1 week of NFV, after 4 and 6 weeks of NFV plus C-XRT, and at 3-month follow-up for IHC, nanostring, and RPPA analysis.

Results: A total of 11 patients with squamous cell carcinoma of the cervix were enrolled; 6 were accrued to DL 1 and 5 to DL 2. Seven patients were stage IIB, and 4 were stage IIB. Median follow-up of all patients is 3.75 years (range 2–5 years). In DL 1,
expansion to 6 patients was required after a patient developed a DLT (grade 3 diarrhea, which was thought secondary to noncompliance). Two patients had grade 3 leukopenia, which did not require dose modifications and resolved after chemoRT. In DL 2, there were no grade 3/4 toxicities. All patients completed the trial regimen. Ten of 11 patients had no evidence of tumor on biopsies at week 6 with only inflammatory cell infiltration noted. Two recurrences were observed, one at DL 1 and the other at DL 2. The first patient recurred outside of the XRT field (paraaortic) and was salvaged with chemo-XRT and is NED at 3.5 years post-salvage treatment. The second recurrence was noted after trial completion with disease outside the XRT field (paraaortic and lung). The patient progressed on chemotherapy and died of disease. Ten of 11 patients are without evidence of disease.

**Conclusion:** NFV with chemoradiation was well tolerated, and a RP2D was identified. The overall response rates and local regional control are promising compared to historical rates and warrant further investigation.

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**2516 - Poster Session**

*Mode of lymphadenectomy may be responsible for inferior oncologic outcome of laparoscopic radical hysterectomy compared to abdominal radical hysterectomy in cervical cancer*

T.H. Kim\(^a\), T.S. Lee\(^b\), B.J. Kim\(^c\), M.H. Kim\(^d\) and S.Y. Ryu\(^e\).  
\(^a\)SMG-SNU Boramae Medical Center, Seoul, Korea, Republic of (South),  
\(^b\)Seoul National University Hospital, Seoul, South Korea,  
\(^c\)Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences (KIRAMS), Seoul, South Korea

**Objective:** The aim of this study was to compare laparoscopic radical hysterectomy (LRH) and abdominal radical hysterectomy (ARH) in the view of the oncologic outcome stratified by risk factors and adjuvant radiotherapy (RT).

**Method:** We retrospectively identified 247 patients with FIGO stage IB1 and IIA2 invasive cervical cancer treated with LRH or ARH between 2008 and 2016. Exclusion criteria were neoadjuvant chemotherapy, not receiving adjuvant RT for any high-risk factor, and microinvasive cancer on hysterectomy specimen. Survival analyses were performed separately in surgery only and adjuvant RT cohorts.

**Result:** Among 233 patients who met the eligible criteria, ARH and LRH were performed in 133 and 100 patients, respectively. The ARH group had a more advanced stage, larger tumor size, and less frequent margin involvement. Adjuvant RT was delivered in 156 patients according to risk stratification system. Among 77 patients in the surgery-only cohort, 32 and 45 patients received ARH and LRH, respectively. Age, stage, all intermediate-risk factors, and the number of removed lymph nodes were not different between the LRH and ARH groups in the surgery-only cohort. Multivariate analysis revealed that LRH (HR = 6.2, 95% CI 1.2–33.3), tumor size (HR = 17.4, 95% CI 1.4–220.2), lymphovascular space invasion (HR = 9.0, 95% CI 1.4–58.9), and stage (HR = 8.2, 95% CI 1.2–54.7) were independent poor prognostic factors for recurrence in the surgery-only cohort. A larger number of resected pelvic lymph node (>19) was associated with poor PFS in the LRH group in the surgery-only cohort. PFS and OS were not different between ARH and LRH in the adjuvant RT cohort.

**Conclusion:** The inferior oncologic outcome of LRH compared to ARH was identified in the surgery-only cohort. Exposure of cancer cells to nodal basin under CO\(_2\) pneumoperitoneum might be responsible for the high recurrence rate in the LRH group.

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**2517 - Poster Session**

*Clinical calculator predictive of chemotherapy benefit in early-stage uterine papillary serous cancers*

D.P. Mysona\(^a\), J.X. She\(^b\), L. Tran\(^c\), P. Tran\(^d\), L. Van Le\(^e\), S. Ghamande\(^e\), B.J. Rungruang\(^f\), A.K. Mann\(^g\) and J.K. Chang.  
\(^a\)University of North Carolina at Chapel Hill, Chapel Hill, NC, USA,  
\(^b\)Georgia Regents University, Augusta, GA, USA,  
\(^c\)Medical College of Georgia, Augusta, GA, USA,  
\(^d\)University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA,  
\(^e\)Georgia Regents University, Augusta, GA, USA,  
\(^f\)Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA,  
\(^g\)California Pacific & Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA

**Objective:** We sought to determine the utility of a clinical calculator to identify subsets of stage I uterine papillary serous cancer that will or will not benefit from chemotherapy.

**Method:** Predictive factors included demographic, surgical, tumor-specific, and treatment factors. Each patient had a cumulative score generated by multiplying each variable by its impact factor and then summing all components. Based on a patient’s total score, they were assigned to a low-risk group, score <50, or high-risk group, score >50. Fifty percent of the
dataset was used to train the model; 50% was used for validation. The groups were assessed for benefit of chemotherapy using Cox proportional hazards.

**Results:** Of 1,364 total patients, 682 were included in the training set and 682 in the validation set. Older age (HR = 1.04), increasing number of comorbid conditions (HR = 1.21), large tumor size (HR = 1.09), positive margins (HR = 1.28), lymphovascular invasion (HR = 2.09), lack of paraaortic node dissection (HR = 1.65), no omentectomy (HR = 1.41), and no chemotherapy (HR = 1.69) were all associated with poor prognosis. Using the clinical calculator, those in the low-risk group had a 5-year OS of 94.1% versus 80.2% for the high-risk group. On subgroup analysis, the low-risk group did not benefit from chemotherapy (HR = 0.582, 95% CI 0.046–7.42, P = 0.7), while the high-risk group did benefit from chemotherapy (HR = 0.612, 95% CI 0.458–0.818, P < 0.001).

**Conclusion:** Our data suggest that a clinical calculator may have utility towards personalizing chemotherapy treatment for this heterogeneous group of patients with stage I uterine papillary serous cancer. Clinical trials are warranted to validate these findings.

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**2518 - Poster Session**  
**Combining radical surgery with at least five cycles of adjuvant cisplatin and etoposide chemotherapy improved treatment outcomes in patients with FIGO stage I-II small cell neuroendocrine carcinoma of the cervix**  
X. Pei, H. Yang and L. Xiang. Fudan University Shanghai Cancer Center, Shanghai, China

**Objective:** This study sought to explore the outcomes and prognostic factors of patients with small cell neuroendocrine carcinoma of the cervix (SCNEC) with FIGO stage I–II and to determine the effects of primary and adjuvant treatment after radical surgery on patient survival.

**Method:** A total of 92 patients from Fudan University Shanghai Cancer Center (FUSCC) (2006–2016) who underwent radical surgery were recruited. To further determine the optimal primary treatment modality, 165 patients with FIGO stage I–II retrieved from the Surveillance, Epidemiology End Result (SEER) database between 2004 and 2013 were included. Retrospectively, all clinical-pathologic variables and treatment strategies were reviewed. Kaplan-Meier and Cox regression methods were used for survival analyses.

**Results:** For patients included in FUSCC, during a median follow-up period of 38 months, 43 (46.7%) patients experienced disease recurrence, and distant metastases were documented in 35 (81.4%) patients. The 3-year recurrence-free survival (RFS) rate was 50.1%. Multivariate analysis confirmed that lymph node metastasis, positive parametrial extension (PME), and cycles of etoposide plus platinum (EP) were independent prognostic factors for disease recurrence. Adjuvant chemotherapy after radical surgery for at least 5 cycles of EP (EP 5+, n = 39) was associated with improved 5-year RFS compared with other treatments (n = 46) (67.6% vs 20.9%, P < 0.001). Additional radiotherapy or concurrent chemoradiation failed to validate further improved RFS in patients with EP 5+, and this finding was consistent in the subset of patients with high-risk factors (positive lymph nodes or positive parametrium). Further investigation of 165 patients from the SEER database demonstrated that the primary treatment imposed significant influence on survival in univariate analysis; patients undergoing radical surgery had a trend of better outcomes compared with those receiving radiotherapy (5-year cancer-specific survival, 48% vs 35.6%, P = 0.049).

**Conclusion:** FIGO stage, lymph node involvement, and PME are important prognostic factors for FIGO stage I–II SCNEC. Primary radical surgery seems to have survival benefits over primary radiotherapy. Half of stage I–II SCNEC patients experienced disease failure within 3 years, and distant metastasis was an outstanding issue. EP regimen for at least 5 cycles improved long-term RFS after radical surgery. Additional radiation might be unnecessary, even in patients with high-risk factors.

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**2520 - Poster Session**  
**Further use of liposomal doxorubicin regimen after initial dose hypersensitivity**  
J.P. Geisler, K. Webb, C. Moore, K. King and K.J. Manahan. Cancer Treatment Centers of America, Newnan, GA, USA

**Objective:** Initial dose hypersensitivity reactions (HSR) to liposomal doxorubicin appear to be a complement-activated pseudo-allergy (CARPA). The objective of this study was to report on use of a rapid desensitivity regimen in patients reacting to initial dose of liposomal doxorubicin.
**Method:** Medical records were reviewed to determine number of patients being initiated on liposomal doxorubicin over a 24-month period and the number having initial infusion reactions. All patients with initial reactions were treated with subsequent infusions with a standardized rapid desensitization protocol parallel to platinum rapid desensitization.

**Results:** One hundred twenty three patients had new liposomal doxorubicin initiations in 24 months. Seven patients (5.7%) had initial HSR/CARPA reactions. All seven were able to receive further liposomal doxorubicin without reaction by following a rapid desensitization regimen.

**Conclusion:** Although CARPA can be life-threatening, using a rapid desensitization protocol allowed the continued use of liposomal doxorubicin without further HSR/CARPA.

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**2521 - Poster Session**  
**Neutrophil-to-lymphocyte ratio as a prognostic factor in advanced stage ovarian carcinoma treated with neoadjuvant chemotherapy**  
R. Eitan, L. Salman, G. Sabah, A. Jakobson-Setton, O. Raban, E. Yeoshoua and D. Tsore. Rabin Medical Center, Petach-Tikvah, Israel

**Objective:** We aimed to evaluate the prognostic significance of neutrophil-to-lymphocyte ratio (NLR) upon diagnosis and its impact on surgical outcome in patients with advanced-stage ovarian carcinoma treated with neoadjuvant chemotherapy (NACT).

**Method:** This was a retrospective cohort study of all patients with stage IIIC and IV ovarian carcinoma receiving NACT in one university-affiliated medical center (2005–2006, 2017). The study group was defined as NLR at diagnosis ≥6.0, and the control group included patients with NLR <6.0 at diagnosis. Demographics and treatment outcome were compared between groups. Primary outcome was defined as surgical outcome including optimal debulking (<1 cm largest residual disease) and optimal debulking with no macroscopic disease. Progression-free survival (PFS) and overall survival (OS) were compared between groups using Kaplan-Meier survival analysis.

**Results:** Overall, 111 patients met inclusion criteria: 33 (29.7%) had NLR ≥6.0 at diagnosis, and 78 (70.3%) had NLR <6.0. Patients with NLR ≥6.0 were significantly older than the NLR <6.0 group (67.0 ± 11.1 vs 61.85 ± 11.2 years, \( P = 0.02 \)) and had higher level of CA-125 at diagnosis (2,306 ± 3,596 vs 1,871 ± 3,540 u/mL, \( P = 0.03 \)). There were no differences between groups in histology or stage of disease (\( P > 0.05 \)). Rates of NLR at the end of NACT were similar between the NLR ≥6.0 and NLR <6.0 group (4.10 ± 3.9 vs 3.28 ± 2.3, \( P = 0.33 \)). In addition, post-NACT complete imaging response was comparable between groups (15.2% vs 24.4%, \( P = 0.78 \)). Among patients who underwent interval cytoreduction, no differences were found in rates of optimal debulking between the group with NLR ≥6.0 and NLR <6.0 (78.9% vs 84.7%, OR = 0.67, 95% CI 0.18–2.5, \( P = 0.55 \)), and rates of optimal debulking with no macroscopic disease (47.4% vs 62.7%, OR = 0.53, 95% CI 0.18–1.52, \( P = 0.23 \)). Using Kaplan-Meier survival analysis, NLR ≥6.0 was associated with significantly worse overall survival (OS) (Figure 1). However, no difference in PFS was noted between groups (\( P = 0.08 \)). In a Cox proportional hazard model, elevated NLR at diagnosis was found to be associated with poor OS (HR = 1.065, 95% CI 1.01–1.13, \( P = 0.04 \)).

**Conclusion:** In advanced-stage ovarian carcinoma, elevated NLR at diagnosis does not predict surgical outcome; however, it is a predictive factor for poor OS.
**Objective**: Somatic TP53 mutation (TP53mut) is a characteristic finding in high-grade serous ovarian cancer (HGSOC). The aim of this study was to assess the clinical efficacy and utility of TP53mut circulating tumor DNA (ctDNA) monitoring as a biomarker for managing HGSOC.

**Method**: TP53 mutations were evaluated in patients who received primary treatment for suspected ovarian cancer at Asan Medical Center. In patients diagnosed with HGSOC and with TP53mut, ctDNA, CA-125, and computed tomography were followed up according to the treatment course.

**Results**: Direct sequencing analysis of 103 tumor tissues from 61 HGSOC patients confirmed TP53 mutations in 41 patients (67.2%). All these patient-specific somatic mutations were detected in plasma cfDNA. The mean value of preoperative TP53 mutant allele count (TP53MAC) in stage III patients was 12.2 copies/µL and in stage IV patients was 45.3 copies/µL. TP53MAC was significantly reduced by treatment, and there was no significant difference in the rate of decrease compared to CA-125 by the generalized linear mixed model. When patients were divided into a low-TP53MAC group (<0.2 copies/µL) and a high-TP53MAC group (≥0.2 copies/µL) based on the TP53MAC value at 3 months after the end of chemotherapy, there was a significant difference in TTP between the two groups ($P = 0.038$).

**Conclusion**: TP53mut ctDNA shows potential as a tumor-specific biomarker for treatment response monitoring in HGSOC. Further large-scale studies are required to compare the efficacy of ctDNA with CA 125 as a biomarker for early detection of recurrence.

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**2523 - Poster Session**

**High expression of TRPV-1 is associated with poor prognosis in cervical cancer**

D.B. Chaya,b, G.H. Hanac, H. Choac, S. Kimc and J.H. Kimac. aYonsei University College of Medicine, Seoul, South Korea, bYonsei
Objective: The Transient Receptor Potential Vanilloid type 1 (TRPV-1) is one of the well-investigated transient receptor potential (TRP) channels, nonselective membranous ion channels associated with calcium and sodium ion exchange. Its role has been pronounced in malignancies. However, the role of TRPV-1 in cervical cancer has not yet been elucidated. Here, we investigated the expression and clinical significance of TRPV-1 in cervical cancer.

Method: Immunohistochemical analyses TRPV-1 and PTEN were performed using tissue microarray analysis of 150 cervical cancer and 230 cervical intraepithelial neoplasia (CIN) patients, and the data were compared with clinicopathologic variables, including the survival of cervix cancer patients.

Results: TRPV-1 expression increased during tumor progression from normal to cancer (P < 0.001). Also, it was significantly associated with tumor stage (P < 0.001), grade (P < 0.012), and chemoradiation response (P < 0.013). Furthermore, the correlation between the expressions of TRPV-1 and PTEN was assessed in cervical neoplasia specimens. TRPV-1 and PTEN were negatively correlated (Spearman ρ = −0.121, P = 0.009). The Kaplan-Meier plots demonstrated that patients with TRPV-1 over-expression were associated with shortened DFS and OS (P < 0.001 and P < 0.001, respectively). In case of PTEN, the low expression group was significantly associated with poor DFS (P = 0.031). The DFS and OS rates with expression of high TRPV-1/low PTEN were compared with patients with low TRPV-1/high PTEN by Kaplan-Meier plot. It revealed a significant difference in DFS and OS (P < 0.001 and P < 0.001, respectively). The Cox proportional hazards model revealed that a combination of high TRPV-1 and low PTEN expression was an independent prognostic factor with respect to OS (HR = 8.48, 95% CI 3.36–21.37, P < 0.01).

Conclusion: High expression of TRPV-1 or combined with PTEN is an indicator of poor prognosis in cervical cancer, suggesting their potential utility as prognostic tests in clinical assessment.

2524 - Poster Session
Evaluation of a novel classification of cervical adenocarcinoma to predict pelvic lymph node status in patients with early-stage cervical cancer
G. Salvoa, P.T. Ramirezb, N.R. Abu-Rustumb, A. Fagottic, G. Scambiac, M. Frumovitzd, R.A. Soslowsb, G.F. Zannonic, B.N. Pitcherab and E.G. Silvaa. aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, bMemorial Sloan Kettering Cancer Center, New York, NY, USA, cCatholic University of the Sacred Heart, Rome, Italy

Objective: A three-pattern classification of cervical adenocarcinoma may be a predictor of prognostic risk factors. The aim of this study is to evaluate the accuracy and reproducibility of this novel pathologic classification in predicting pelvic lymph node status in a multicenter setting.

Method: A multiinstitutional evaluation of cervical adenocarcinoma using a novel three-pattern classification was analyzed. Pathologic patterns were defined as (A) well-demarcated glands frequently forming clusters or groups with relative lobular architecture and lacking destructive stromal invasion or lymphovascular space invasion (LVI), (B) localized destructive stromal invasion, and (C) diffuse glandular infiltration. Descriptive statistics were used to summarize demographic and clinical characteristics. Recurrence-free survival (RFS) was measured as time from surgery to recurrence or death. Kaplan-Meier was used to estimate RFS stratified by tumor classification and the log rank test to compare the classifications for this outcome.

Results: Of the 235 patients, 37 (15.7%) were pattern A, 51 (21.7%) pattern B, and 147 (62.6%) pattern C. The median age was 41 years (19–83 years), and most patients (83.7%) had stage IB1. There was no difference in age, BMI, or stage among the three patterns. Overall rate of lymph node metastases was 6.6%. There was a difference in lymph node positivity among the three groups: A, 0%; B, 2%; and C, 10% (P < 0.03). The rate of lymphvascular invasion increased with the type of pattern: A, 5.6%; B, 28.6%; and C, 44.1% (P < 0.001). See Table 1. There was no difference in the rate of adjuvant therapy among the groups (P = 0.41). Median follow-up was 44.4 months (0.1–279 months). The RFS was similar among the three tumor classifications (P = 0.13).

Conclusion: The three-pattern classification of cervical adenocarcinoma may serve as a predictive indicator of lymph node status in patients with early cervical cancer. Pelvic lymphadenectomy in patients with patterns A or B may be associated with low yield of metastasis.
Table 1: Patient Characteristics by Classification

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median</td>
<td>(Min, Max)</td>
<td>Median</td>
<td>(Min, Max)</td>
</tr>
<tr>
<td></td>
<td>42.0 (20.0, 68.0)</td>
<td>42.0 (24.0, 74.0)</td>
<td>41.0 (19.0, 83.0)</td>
<td>41.0 (19.0, 83.0)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>26.7 (19.1, 43.2)</td>
<td>23.8 (16.8, 47.8)</td>
<td>24.5 (17.7, 47.7)</td>
<td>24.6 (16.6, 47.8)</td>
</tr>
<tr>
<td>FIGO Stage</td>
<td>IA1-LVSI</td>
<td>IA2</td>
<td>IB1</td>
<td>IIA1</td>
</tr>
<tr>
<td>Grade I</td>
<td>12 (38.7%)</td>
<td>1 (2.0%)</td>
<td>1 (0.7%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Grade II</td>
<td>18 (58.1%)</td>
<td>10 (20.4%)</td>
<td>10 (6.8%)</td>
<td>26 (11.2%)</td>
</tr>
<tr>
<td>Grade III</td>
<td>30 (91.1%)</td>
<td>37 (75.5%)</td>
<td>128 (87.1%)</td>
<td>195 (63.7%)</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td>No</td>
<td>37 (100.0%)</td>
<td>48 (98.0%)</td>
<td>127 (90.1%)</td>
</tr>
<tr>
<td>Positive Nodes</td>
<td>Yes</td>
<td>1 (2.0%)</td>
<td>1 (2.0%)</td>
<td>8 (5.4%)</td>
</tr>
<tr>
<td>LVSI</td>
<td>No</td>
<td>26 (72.2%)</td>
<td>30 (61.2%)</td>
<td>75 (52.4%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2 (5.6%)</td>
<td>14 (28.6%)</td>
<td>63 (44.1%)</td>
</tr>
</tbody>
</table>

2525 - Poster Session
Effects of PARP inhibitors therapy on the PFS and OS in platinum-sensitive recurrent ovarian cancer: A meta-analysis of randomized controlled trials
B.H. Min*, S.H. Yoon* and S.H. Shim*. aSanggye Paik Hospital, Inje University, School of Medicine, Seoul, South Korea, bKonkuk University School of Medicine, Seoul, South Korea

Objective: We sought to quantify the effect of PARP inhibitors in platinum-sensitive recurrent ovarian cancer through a meta-analysis of randomized controlled trials (RCTs).

Method: A systematic literature review was conducted through July 2018. To be included in the meta-analysis, RCTs had to compare PARP inhibitor with placebo in the treatment for only relapsed platinum-sensitive ovarian cancer, regardless of sample size, type of PARP inhibitor, dosage used, or duration of treatment. Uncontrolled and open-label trials were reviewed but excluded from the meta-analysis. PFS and OS were used as primary outcome measures. A subgroup analysis was conducted for the type of BRCA mutation. Adverse events were also investigated.

Results: A total of 5 randomized controlled trials were included in our analysis with a total of 1,839 patients (PARP n = 1, 160). The meta-analysis based on the fixed effects model indicates significant better PFS using PARP inhibitor relative to the placebo group (HR = 0.359, 95% CI 0.314–0.410, P < 0.0001, I² = 48.159). This pattern was also observed in the subgroup analysis for the type of BRCA. PFS was significantly better in the PARP group in BRCA-positive patients (HR = 0.272, 95% CI 0.220–0.337, P < 0.00001). PFS was significantly better in the PARP group in BRCA-negative patients (HR = 0.450, 95% CI 0.358–0.569, P < 0.00001). The meta-analysis based on the fixed effects model indicates OS was not significantly better using PARP inhibitor relative to the placebo group (HR = 0.844, 95% CI 0.688–1.038, P < 0.105, I² = 46.814). However, we found a significant difference in OS between the two groups in BRCA-positive patients (HR = 0.693, 95% CI 0.508-0.946, P = 0.021). The risk of any symptom clustering was significantly higher in the treatment group than in the controls (anemia, RR = 6.098, 95% CI 2.349–15.831, P < 0.0001; diarrhea, RR = 1.461, 95% CI 1.141–1.870, P < 0.003; fatigue, RR = 2.363, 95% CI 1.908–2.926, P < 0.0001; nausea, RR = 5.401, 95% CI 4.254–6.858, P < 0.0001; neutropenia, RR = 3.580, 95% CI 1.836–6.982; P < 0.0001; vomiting, RR = 2.560, 95% CI 1.973–3.324, P < 0.0001).
Conclusion: PARP inhibitor significantly improves PFS and OS in BRCA mutation women with platinum-sensitive recurrent ovarian cancer with acceptable side effects. More studies are needed to elucidate useful details regarding the PARP inhibitor regimen and how to control adverse events.

2526 - Poster Session
Is adjuvant therapy beneficial for stage I uterine leiomyosarcoma?
aUniversity of Pennsylvania Health System, Philadelphia, PA, USA, bThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, cUniversity of Pennsylvania, Philadelphia, PA, USA

Objective: We sought to determine the effect of adjuvant therapy on overall survival in patients with stage I uterine leiomyosarcoma.

Method: The Medicare and Surveillance, Epidemiology, and End Results (SEER) database was queried to identify women 65 years or older who underwent hysterectomy as primary treatment for stage I uterine leiomyosarcoma from 2000 to 2013. Exclusion criteria included more than 1 primary cancer, history of end-stage renal disease/dialysis, and lack of activity in Medicare 1 year pre- and postdiagnosis. Demographics, comorbidity data, adjuvant therapy, and survival outcomes were collected. Descriptive statistics, Kaplan-Meier curves, and Cox models were used for analyses. Treatment groups required at least 10 patients to be included for analysis.

Results: We identified 84 women diagnosed with stage I uterine leiomyosarcoma in the Medicare-SEER database. The majority, 70.2% (59/84), of patients received no adjuvant treatment. Adjuvant therapy included radiation alone, radiation with concurrent chemotherapy, chemotherapy alone, and radiation and chemotherapy in 13.1% (11/84), 1.2% (1/84), 13.1% (11/84), and 2.4% (2/84) of patients, respectively. In univariate analysis neither radiation alone (HR = 1.64, 95% CI 0.79–3.42) nor chemotherapy alone (HR = 0.61, 95% CI 0.21–1.72) was associated with a significant difference in OS compared with no adjuvant treatment. Age, race, Charlson comorbidity score, marital status, and income were not associated with receiving adjuvant therapy. Radiation therapy was more commonly given from 2000 to 2008, and chemotherapy was more commonly utilized from 2009 to 2013 (P = 0.03). Neither radiation therapy nor chemotherapy was associated with a significant difference in OS in multivariate analysis.

Conclusion: In the Medicare SEER database, the majority of women 65 years and older with stage I uterine leiomyosarcoma did not receive adjuvant therapy. Patients who do receive adjuvant therapy do not appear to have improvement in outcome. Based on available data, observation is reasonable for women with stage I uterine leiomyosarcoma.

2527 - Poster Session
The somatic and germline mutation pattern of 21 hereditary ovarian cancer genes in 62 Chinese ovarian cancers
L. Li, X. Meng, C. Lin, D. Shao Sr., Y. Xiong and M. Wu.
PeKing Union Medical College Hospital, Beijing, China, BGI Shenzhen, Shenzhen, China

Objective: This study aims to evaluate the specific genetic alterations of hereditary ovarian cancer genes including both somatic and germline mutations in Chinese patients with epithelial ovarian cancer (EOC).

Method: Patients were enrolled consecutively and unselectively at Peking Union Medical College Hospital (PUMCH) without age or family history consideration. To assess the genetic profile of ovarian carcinomas in the Chinese population, a 21-gene panel covering BRCA1, BRCA2, and 19 other tumor suppressor genes related to hereditary ovarian cancer (including homologous recombination and mismatch repair genes) was detected by targeted region capture and next-generation sequencing (NGS) technology across the whole coding exons and exon-intron (±20 base pairs) boundaries.

Results: A total of 62 unselective patients with ovarian cancer were enrolled in our study. All patients received the 21-gene panel testing including BRCA1, BRCA2, CHEK2, PALB2, BRIIP, TP53, PTEN, STK11, CDH1, ATM, BARD1, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PMS1, PMS2, RAD50, and RAD51C. In total, we discovered 64 genetic alterations, including 19 germline and 45 somatic deleterious mutations, and 12 individuals with both germline and somatic mutations. BRCA1/2 mutants were found in 17 of 62 (27.4%) patients, including 14 germline mutations and 3 somatic ones. Except for BRCA1/2, germline mutations in PALB2, CHEK2, RAD51C, and STK11 were also found. In the somatic mutation analysis, TP53 showed the most frequent pathogenic or likely pathogenic mutations, which were screened out in 56.5% (35/62) of enrolled cases with EOC.
Other 10 somatic mutations in the panel were also found, including **BRCA1**, **BRCA2**, **PTEN**, and **ATM**. However, in our 62-patient cohort, we did not observe a secondary hit mutation in the tumor cells of the germline-mutated genes accordingly. **Figure 1** describes the germline and somatic pathogenic mutations in **BRCA1** (A), **BRCA2** (B), and **PTEN** (C) detected in 62 paired blood and tumor tissue samples.

**Conclusion:** In both germline and somatic aspects, the genetic mutation spectrum of ovarian cancer-related genes in Chinese ovarian cancer patients has its own peculiarity. We need more large-scale studies to verify and supplement our description.

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Fig. 1.
2528 - Poster Session
Evaluation of the constructed the device along with the software for digital archiving, sending the data and supporting the diagnosis of cervical cancer

Objective: The incidence and mortality of cervical cancer are high in Poland. There are effective methods of prevention and early diagnosis; however, they require well-trained medical professionals including cytologists. In this project we built a prototype of a new device together with implemented software to convert the currently used optical microscopes to fully independent scanning systems for cytological samples. The use of the device is intended to improve the effectiveness of cytological screening and registration of cytological test results. The features of the software include digital backup as well as transmission and telediagnosis evaluation.

Method: The software uses the artificial neural network (U-NET architecture), which is designed to be able to recognize suspicious regions, and an enhanced CNN neural network, which allows determination of the type of disorder such as ASCUS, ASC-H, HIS, AGC, and cancer. A total of 7,128 liquid-based cytology (LBC) samples were evaluated by trained cyto-screeners. Cytological abnormalities such as ASCUS, ASC-H, HIS, AGC, and cancer were found in 254 (3.6%) cases. All samples were scanned and archived. Selected samples with diagnosed abnormality were used as a model to teach the artificial neural networks.

Results: Preliminary results obtained with use of U-NET and CNN networks so far indicate 71%–94% compliance with results obtained using standard methods.

Conclusion: Further refinement of neural networks is necessary to reduce the number of false positives and false negatives. A study with a larger sample size is required to evaluate the software. Therefore in the next stages of the study the whole population of 7,128 samples will be included into the neural network learning and assessment process. Afterward the sample will be extended by 3,800 additional samples. In the final stage of the study, the learning and assessment process will be accomplished by including additional conventional Pap smear samples.

2529 - Poster Session
Therapeutic efficacy of local ablation for cervical precancer in HIV-positive women – preliminary results of a randomized control trial in Zambia

Objective: A randomized control trial of the safety, acceptability, and efficacy of a novel thermocoagulator for the treatment of preneoplastic cervical lesions is ongoing in Lusaka, Zambia. We describe the preliminary results of treatment efficacy in HIV-positive women.

Method: VIA screen-positive women eligible for ablative treatment are randomized to receive thermal ablation (TA), cryotherapy, or LLETZ. Demographic information is collected, including HIV status. Samples for HPV DNA are collected at baseline and follow-up. Treatment efficacy is based on VIA and HPV status at 6-month follow-up. Side effects, pain, and client satisfaction are scored and recorded; however, these data are not included in this analysis.

Results: Seven hundred and fourteen (95%) of the targeted 750 women have been randomized to treatment, of which 376 (53%) are HIV-positive, with the vast majority (93%) on antiretroviral therapy (ART). There were no differences in the number of HIV-positive women or those receiving ART among the treatment arms (P = 0.270). Six-month follow-up data are available on 339 women (47%), 139 of which are HIV-positive. Based on VIA results alone, HIV-positive women had lower overall cure rates than HIV-negative women (74% vs 86%, respectively, P = 0.0088), regardless of treatment type. Women positive for HPV 16 at baseline had significantly lower cure rates (HPV 16 clearance and VIA negative) across all study arms,
compared to HIV-negative women (67% vs 86%, respectively, \(P = 0.0002\)). When all HPV types are considered, overall cure rates (clearance of baseline type-specific HPV and VIA negative) in HIV-positive women decreased to 42%.

**Conclusion:** This subanalysis of preliminary data of a randomized control treatment trial of ablative methods for cervical precancer highlights the challenge in eradicating this disease in women living with HIV. Investigations are underway to determine the underlying causes of these findings.

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**2530 - Poster Session**

**Nomograms based on HPV load for predicting survival in cervical squamous cell carcinoma: An observational study with a long-term follow-up**

L. Zuo\(^a\), Y. Huang\(^b\) and L.Y. Wu\(^c,d\). \(^a\)Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China, \(^b\)Women's Health Integrated Research Center, Annadale, VA, USA, \(^c\)Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China, \(^d\)Cancer Institute & Hospital, Chinese Academy of Medical Sciences, Beijing 100021, PR, China

**Objective:** The aim of this study was to define the prognostic value of pretreatment human papillomavirus (HPV) viral load for cervical cancer, as well as to develop nomograms based on HPV load and other clinicopathological factors for long-term survival.

**Method:** We conducted a prospective study on cervical squamous cell carcinoma (SCC) patients diagnosed between January 2003 and December 2008. Cervical samples were tested for HPV viral load by the hybrid capture II (HCII) assay before treatment and 6 months after treatment. Clinical characteristics and follow-up information were also collected. A multivariate Cox proportional hazards model was used to adjust for covariates in both the radical hysterectomy treatment group (RH) and concurrent chemoradiotherapy treatment group (CCRT) to identify relevant covariates; then nomograms were constructed and used for internal validation.

**Results:** A total of 520 SCC patients were enrolled in this study with a median follow-up of 127 months; 360 patients received RH, whereas 160 patients received CCRT. The median HPV viral load in the RH and CCRT groups was 356.10 and 294.29, respectively. Tumor size was positively correlated with high pretreatment HPV load in both groups. In the CCRT group, the advanced FIGO stage and enlarged retroperitoneal lymph node status determined by computed tomography (LNSCT) were related in the low HPV load group. Initial HPV viral load, FIGO stage, and lymph node metastasis were prognostic factors for the RH group, whereas HPV viral load, squamous cell carcinoma antigen (SCC-Ag) level, and LNSCT were identified as prognostic factors for the CCRT group. Nomograms incorporating these predictors for 10-year PFS were constructed (concordance index 0.756, 0.749).

**Conclusion:** A low pretreatment HPV viral load is an independent prognostic factor for poor prognosis of cervical SCC and is related to other clinicopathological factors. The survival nomogram based on HPV viral load could predict recurrence.

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**2531 - Poster Session**

Withdrawn at author’s request

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**2532 - Poster Session**

**Predictors for pathological parametrial invasion in clinical stage IIB cervical cancer: A nation-wide cohort study**

H. Tokunaga\(^a\), M. Shimada\(^a\), K. Matsuoka\(^a\), K. Nakamura\(^a\), Y. Takei\(^b\), K. Ushijima\(^a\), T. Sumi\(^c\), T. Ohara\(^b\), H. Yahata\(^b\), M. Mikami\(^b\) and T. Sugiyama\(^a\). \(^a\)Tohoku University School of Medicine, Miyagi Prefecture, Japan, \(^b\)Keck School of Medicine of USC, Los Angeles, CA, USA, \(^c\)Okayama University Graduate School of Medicine, Okayama, Japan, \(^d\)Jichi Medical University, Shimotsuke, Japan, \(^e\)Kurume University School of Medicine, Fukuoka, Japan, \(^f\)Osaka City University Graduate School of Medicine, Osaka, Japan, \(^g\)St. Marianna University School of Medicine, Kanagawa, Japan, \(^h\)Kyushu University, Fukuoka, Japan, \(^i\)Tokai University School of Medicine, Isehara, Japan, \(^j\)Iwate Medical University, Morioka, Japan

**Objective:** To examine predictors of pathological parametrial invasion in clinical stage IIB cervical cancer, and to examine prognostic factors in pathological stage IIB disease.

**Method:** This study is an ancillary analysis of a nationwide retrospective cohort examining 6,003 clinical stage IB-IIB cervical cancers. Women with clinical stage IIB disease who underwent primary radical hysterectomy with lymphadenectomy were
examined \( (n = 723) \). Multivariate analysis was performed to identify independent clinicopathological factors for pathological parametrial invasion and to identify independent prognostic factors in pathological stage IIB disease.

**Results:** Parametrial invasion was identified on the surgical specimen in 401 cases (55.5%, 95% CI 51.9–59.2). On multivariate analysis, age ≥50 years (aOR = 1.59), deep stromal invasion (DSI, aOR = 4.28), lymphovascular space invasion (aOR = 2.41), and multiple pelvic nodal metastases (aOR = 3.00) remained independent predictors for pathological parametrial invasion. In regression-tree models, tumors with DSI and multiple pelvic nodal metastases had the highest incidence of pathological parametrial invasion (78.8%); in contrast, tumors without DSI had the lowest incidence (21.2%). Among patients with pathological stage IIB disease, the absolute difference in 5-year disease-free survival rates was 57.2%, ranging from 80.9% in those with squamous histology with none/single pelvic nodal metastasis to 23.7% in those with nonsquamous histology with multiple pelvic nodal metastases.

**Conclusion:** In clinical stage IIB cervical cancer, accuracy for pathological parametrial invasion is low to modest. With absence of DSI, only one in five clinical stage IIB diseases has pathological stage IIB disease. Survival of pathological stage IIB varies widely and is largely dependent on nodal factors.

**2533 - Poster Session**

**Feasibility of intraoperative intraperitoneal chemotherapy with paclitaxel in patients with epithelial ovarian cancer.**

W.M. Lee\(^a\), J.S. Choib, J. Bae\(^b\), J.M. Eom\(^a\) and U.S. Jung\(^a\).

\(^a\)Hanyang University College of Medicine, Seoul, Korea, Republic of (South),

\(^b\)Hanyang University College of Medicine, Seoul, Korea, Republic of (South)

**Objective:** The most common cause of treatment failure in patients with ovarian cancer is recurrence and dissemination in the peritoneal cavity, and treatment results of patients with disseminated disease are disappointed with a 5-year survival rate of only 30%. For this reason intraperitoneal (IP) delivery of chemotherapy is introduced as a new treatment option; however, the results of IP chemotherapy are still debatable because of catheter-related and IP infusion-related complications. We sought to determine whether intraoperative intraperitoneal (IP) chemotherapy with paclitaxel improves PFS and OS among patients with epithelial ovarian cancer.

**Method:** Between January 2000 and December 2008, we reviewed the medical records of patients who underwent surgery for epithelial ovarian cancer except stage I. Staging operations were performed as recommended by FIGO, and paclitaxel was instilled at a dose of 60 mg/m\(^2\) diluted in 1 L of warmed Hartmann’s solution after all surgical procedures. Drain tubes were clamped for 24 hours after surgery. Treatments were administered 6 times at 3-week intervals, and chemotherapies were added 3–6 times in cases of recognition from public insurance. Univariate and multivariate analyses were executed to evaluate the potential variables for survival analysis.

**Results:** Of a total of 51 patients, 33 patients (64.7%) were intraoperative IP group and 18 patients (35.3%) were non-intraoperative IP group. Univariate analysis revealed that stage IV (HR = 6.7, 95% CI 2.0–21.9, \( P = 0.002 \), and HR = 6.2, 95% CI 2.0–19.1, \( P = 0.001 \), respectively) and level of postoperative CA-125 (HR = 1.5, 95% CI 1.1–1.9, \( P = 0.004 \), and HR = 1.4, 95% CI 1.1–1.8, \( P = 0.017 \), respectively) were significantly associated with OS and PFS. On multivariate analysis, parity ≥3 (HR = 4.4, 95% CI 1.1–18.6, \( P = 0.041 \)), stage IV (HR = 12.0, 95% CI 2.2–65.5, \( P = 0.004 \)), intraoperative IP chemotherapy (HR = 0.3, 95% CI 0.08–0.8, \( P = 0.021 \)), and number of chemotherapies (9–12) (HR = 0.2, 95% CI 0.5–0.9, \( P = 0.039 \)) were significantly associated with OS. Stage IV (HR = 16.7, 95% CI 3.2–86.7, \( P = 0.001 \)), intraoperative IP chemotherapy (HR = 0.5, 95% CI 0.07–0.6, \( P = 0.05 \)), and number of chemotherapies (9–12) (HR = 0, 95% CI 0.03–0.6, \( P = 0.01 \)) were significantly associated with PFS.

**Conclusion:** Adding IP chemotherapy with paclitaxel during operation decreases the risk of recurrence and death without significant adverse events. Therefore this modality is feasible for a new treatment option in patients with epithelial ovarian cancer.

**2534 - Poster Session**

**Efficacy and safety of peritoneal mesometrial resection for endometrial cancer: A prospective cohort study with historical comparison**

N. Lee\(^a\), H.S. Kim\(^b\) and N.H. Park\(^c\).

\(^a\)Seoul National University Hospital, Seoul, South Korea, \(^b\)Seoul National University, Seoul, Korea, Republic of (South)

**Objective:** The aim of this study was to evaluate the clinical efficacy and safety of peritoneal mesometrial resection for endometrial cancer in comparison with historical data.

**Method:** We enrolled 115 patients who underwent peritoneal mesometrial resection for endometrial cancer from January 2010 to December 2014. The characteristics of patients, surgical outcomes, and postoperative oncological outcomes were compared with those of a historical cohort of 115 patients who underwent a hysterectomy and bilateral salpingo-oophorectomy for endometrial cancer from January 2005 to December 2009.

**Results:** There were no significant differences in the distribution of clinicopathological factors between the two groups. The operating time was significantly shorter in the peritoneal mesometrial resection group compared with the historical group (174 vs. 206 minutes, \( P = 0.001 \)). The rate of postoperative complications was also significantly lower in the peritoneal mesometrial resection group (11% vs. 31%, \( P = 0.001 \)). The recurrence rate was not significantly different between the two groups (10% vs. 14%, \( P = 0.26 \)).

**Conclusion:** Peritoneal mesometrial resection for endometrial cancer is a feasible and safe surgical procedure with similar oncological outcomes compared with hysterectomy and bilateral salpingo-oophorectomy.
**Objective:** Peritoneal mesometrial resection (PMMR) is the compartmental surgery based on embryonic development for endometrial cancer, which consists of mesometrial resection including hysterectomy and adnexectomy, and therapeutic pelvic and paraaortic lymphadenectomy without adjuvant radiotherapy. Thus, we investigated the efficacy and safety of PMMR in a prospective cohort study with historical comparison (NCT02986568).

**Method:** Twenty patients with endometrial cancer were consecutively treated with PMMR by 1 gynecologic oncologist from January 2015 to December 2016 (group A). They received adjuvant chemotherapy without radiotherapy if 2 or more lymph node metastasis and positive resection margin were shown in pathologic examination. Their clinical-pathologic characteristics and clinical outcomes were compared with 168 patients with endometrial cancer who received conventional treatment.

**Results:** Laparotomic approach, large tumor size, lymphovascular space invasion, and transfusion during surgery were more common, and operation time and hospitalization were longer in group A despite no differences in other clinical-pathologic characteristics between the 2 groups. Although recurrence was more frequent in group A (25% vs 8.3 %, $P = 0.04$), there was no difference in risk of recurrence between in intermediate- or high-risk patients (45.5% vs 20%, $P = 0.12$). In all patients, group A showed shorter PFS than group B, whereas there was no difference in PFS between the 2 groups for intermediate- or high-risk disease. Moreover, PMMR was not a prognostic factor for PFS in multivariate analysis (adjusted HR = 1.46, 95% CI 0.46–4.62).

**Conclusion:** PMMR may be feasible and safe compared with conventional treatment especially for intermediate- or high-risk endometrial cancer. More trials are required for proving the evidence.

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**2535 - Poster Session**

**Long-term oncological outcomes after laparoscopic versus open radical hysterectomy in stage IB1 cervical cancer patients with tumor size ≤2cm and without lymph-node metastasis**

X. Yan$^a$, N. Zhao$^a$, X. Chen$^a$, P. Ye$^a$, L. Xu$^a$, X. Nan$^a$, H. Shang$^b$ and H. Zhao$^{a,c}$. $^a$the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, $^b$The First People’s Hospital of Foshan, Foshan, China, $^c$Wenzhou Medical University, Wenzhou, China

**Objective:** The aim of our study is to retrospectively evaluate the long-term oncological outcomes—disease free survival (DFS)—of laparoscopic radical hysterectomy (LRH) and open radical hysterectomy (ORH) for treatment of stage IB1 cervical cancer patients with tumor size ≤2 cm and without lymph-node metastasis (non-LNM).

**Method:** Stage IB1 cervical cancer patients with tumor size ≤2 cm and non-LNM performed radical hysterectomy (RH) between 2010 and 2018 were retrospectively reviewed in this study. Follow-up data were available for all patients.

**Results:** Of a total of 155 patients, 65 patients underwent ORH and 90 patients underwent LRH. The median follow-up time was 38 months (range 8–90 months) for ORH and 39 months (range 5–96 months) for LRH. There was no significant difference between the 2 groups in age, rate of histologic types, lymphovascular space invasion, depth of cervical stromal invasion, or parametrial invasion. However, the patients who underwent LRH were more likely to be lower grade tumors ($P < 0.05$) and lower cervical canal involvement rate ($P < 0.05$). None of the patients in the ORH group was recurrent, but a total of 7 patients in the LRH group suffered recurrence. The 5-year DFS rate was 100% with ORH and 89% with LRH ($P = 0.017$). In the subgroup analyses, for patients with low-intermediate grade (G1 + G2), the 5-year DFS rate was 100% with ORH and 90% with LRH ($P = 0.067$); for patients with low-intermediate grade (G1 + G2) and squamous cell type, the 5-year DFS rate was 100% with ORH and 89% with LRH in ($P = 0.082$).

**Conclusion:** Our data demonstrate that LRH in stage IB1 cervical cancer patients with tumor size ≤2 cm and without lymph node metastasis is associated with worse prognosis than ORH in terms of DFS. And there was no significant difference in the 5-year DFS rate of ORH and LRH for patients with low-intermediate grade (G1 + G2) or low-intermediate grade (G1 + G2) and squamous cell type subgroup. However, it did not mean it was safe to perform the LRH in these subgroup patients, as our study was not powered to assess the safety of LRH in that subgroup. The feasibility and safety of LRH for stage IB1 cervical cancer, non-LNM patients with tumor size ≤2 cm and with G1 + G2 or with G1 + G2 and squamous cell type need further investigation.

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**2536 - Poster Session**

**Clinicopathological features and prognostic factors for patients with recurrent cervical cancer treated with secondary**
**surgical resection plus radiotherapy**

T. Zhu and Z. Shao. Zhejiang Cancer Hospital, Zhejiang, China

**Objective:** Standard treatment for recurrent cervical cancer has not been established. To help improve management of the disease, this study presented clinico-pathological features and identified prognostic factors in patients treated with secondary surgical resection and radiotherapy.

**Method:** We retrospectively reviewed medical records of patients with recurrent cervical cancer confined to the pelvis during 2012 to 2017. This study selected only patients whose primary tumors were diagnosed at stage IIA2 or earlier and received surgical resection for both primary and recurrent tumors. Their clinico-pathological data were collected and analyzed. Cox regression models were applied to identify risk factors associated with post-recurrence survival.

**Results:** A total of 54 patients with recurrent cervical cancer were included. Thirty seven (68.5%) recurrences occurred with 2 years after the initial treatment and 17 (31.5%) of them had tumor size >4 cm. Recurrences were treated with radical surgery plus pelvic radiotherapy. In addition, some patients received vaginal radiotherapy (31.5%), concurrent chemotherapy (76.0%), and consolidated chemotherapy (37.0%). Chemoradiotherapy was administrated to 44.4% of patients <4 weeks after secondary surgery. The 1-, 3-, and 5-year post-recurrence survival rates were 88.5%, 72.0%, and 62.3%, respectively. Interval between secondary surgery and chemoradiotherapy and size of recurrent tumors were significantly associated with post-recurrence survival.

**Conclusion:** After surgical resection plus radiotherapy, patients with recurrent cervical cancer confined to the pelvis have relatively high post-recurrence survival. Earlier start of chemoradiotherapy after secondary surgery and smaller recurrent tumors are associated with better post-recurrence survival.
Objective: The aim of this study was to examine the association between surgical volume and survival of women with early-stage cervical cancer who underwent radical hysterectomy.

Method: This is a nationwide multicenter retrospective study examining consecutive women with clinical stage IB1 – IIB cervical cancer who underwent radical hysterectomy from 2004 to 2008 (n = 5,964). Extent of surgical volume per site over the 5-year period was defined by a minimum P value method for recurrence risk: low volume (<32 cases, n = 649, 10.9%), mid-volume (32–104 cases, n = 3,662, 61.4%), and high volume (≥105 cases, n = 1,653, 27.7%). Surgical volume-specific survival was examined with multivariate analysis and propensity score matching.

Results: The median number of surgeries per site was 44 (IQR 17–65). On multivariate analysis, women in high-volume centers had a decreased risk of recurrence (aHR = 0.689, 95% CI 0.581–0.817, P < 0.001) and all-cause mortality (aHR = 0.725, 95% CI 0.586–0.897, P = 0.003) compared to those in mid-volume centers. Specifically, women in high-volume centers had a decreased risk of local recurrence (aHR = 0.620, 95% CI 0.494–0.777, P < 0.001) but not distant recurrence (aHR = 0.845, 95% CI 0.674–1.058, P = 0.142) compared to those in mid-volume centers. Among 1,700 women with clinical stage IB1 disease who received radical hysterectomy alone, surgery at high-volume centers was associated with a decreased risk of recurrence (aHR = 0.446, 95% CI 0.251–0.791, P = 0.006) and all-cause mortality (aHR = 0.285, 95% CI 0.107–0.764, P = 0.013) compared to surgery at mid-volume centers on multivariate analysis. After propensity score matching, surgery at high-volume centers remained an independent prognostic factor for decreased recurrence (aHR = 0.693, 95% CI 0.570–0.843, P < 0.001) and all-cause mortality (aHR = 0.747, 95% CI 0.589–0.946, P = 0.016) compared to surgery at mid- and low-volume centers on multivariate analysis. See Figure 1.

Conclusion: Our results suggest that surgical volume for radical hysterectomy may be a prognostic factor for stage IB1–IIB cervical cancer, and surgery at high-volume centers is associated with decreased local-recurrence risk resulting in improved survival.
**Objective:** In general, a combination of histological types and cytological grade is used to select patients of poor prognosis for clinical studies. Based on our long-term follow-up study we thought that these criteria could be further refined to make uniformly tighter iso-prognostic groups. The aim of this analysis was to fashion iso-prognostic groups in endometrial cancer patients using traditional histological features.

**Method:** Consecutive intermediate- and high-risk endometrial cancer patients treated with hysterectomy, lymphadenectomy, and adjuvant radiotherapy between 1996 and 2012 were retrieved from a prospective database. Prognostic factors considered were histological type, tumor grade, myometrial invasion, lymphovascular space invasion (LVSI), and lymph node metastases. The analysis was carried out using univariate and multivariate Cox proportional hazards regression models for OS and failure-free survival.

**Results:** Of 1,207 patients, there were 80% endometrioid/mucinous, 7% clear cell, and 13% serous histology. In multivariate analysis for relapse, only LVSI was found to be significant, which resulted in an HR = 4.9 ($P = 0.000$). HR in patients with LVSI
and positive nodes rose to 8.8 ($P = 0.004$). Prognostic significance of tumor diameter, grade, myometrial invasion, as well as the type of adjuvant radiotherapy was also studied in patients ($n = 495$) who did not have LVSI or lymph node metastasis. For OS, tumor grade HR = 1.55 ($P = 0.33$), myometrial invasion HR = 1.27 ($P = 0.31$), tumor diameter (cm) HR = 0.916 ($P = 0.19$), and vagina vault brachytherapy HR = 0.725 ($P = 0.20$). Based on these observations, out of intermediate- and high-risk patients 3 groups emerged, as shown in Table 1. These were low risk consisting of LVSI and node negative, intermediate risk with LVSI positive but node negative, and patients with positive nodes.

**Conclusion:** A simple combination of grade, LVSI, and nodal status can provide much tighter iso-prognostic groups among endometrial cancer patients.

**Table 1:** Iso-prognostic groups in endometrial cancer

<table>
<thead>
<tr>
<th>N=1207</th>
<th>Infiltration</th>
<th>Metastasis</th>
<th>Relapse/Total</th>
<th>% Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endmtrd, G1&amp;2</strong></td>
<td>LVSI -</td>
<td>Node -</td>
<td>28/344</td>
<td>8%</td>
</tr>
<tr>
<td><strong>Endmtrd, G3</strong></td>
<td>LVSI -</td>
<td>Node -</td>
<td>6/93</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Clear Cell</strong></td>
<td>LVSI -</td>
<td>Node -</td>
<td>4/36</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Serous</strong></td>
<td>LVSI -</td>
<td>Node -</td>
<td>8/55</td>
<td>14%</td>
</tr>
<tr>
<td><strong>Endmtrd, G1&amp;2</strong></td>
<td>LVSI +</td>
<td>Node -</td>
<td>46/253</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Endmtrd, G3</strong></td>
<td>LVSI +</td>
<td>Node -</td>
<td>26/117</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Clear Cell</strong></td>
<td>LVSI +</td>
<td>Node -</td>
<td>9/36</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Serous</strong></td>
<td>LVSI +</td>
<td>Node -</td>
<td>19/57</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Endmtrd, G1&amp;2</strong></td>
<td>LVSI -/+</td>
<td>Node +</td>
<td>25/112</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Endmtrd, G3</strong></td>
<td>LVSI -/+</td>
<td>Node +</td>
<td>28/52</td>
<td>54%</td>
</tr>
<tr>
<td><strong>Clear cell</strong></td>
<td>LVSI -/+</td>
<td>Node +</td>
<td>9/16</td>
<td>56%</td>
</tr>
<tr>
<td><strong>Serous</strong></td>
<td>LVSI -/+</td>
<td>Node +</td>
<td>23/36</td>
<td>64%</td>
</tr>
</tbody>
</table>

**2540 - Poster Session**  
Pregnancy and oncologic outcomes after fertility-sparing management for early stage endometrioid endometrial cancer  
S.H. Shim, S.H. Chae, A. Lee, S. Suh and S.B. Kang. *Konkuk University School of Medicine, Seoul, South Korea*

**Objective:** Hormonal management is an alternative treatment for preserving fertility in patients with presumed early-stage endometrioid endometrial cancer (EC). This study aimed to define the pregnancy and oncologic outcomes and factors of successful conception after hormone therapy for endometrioid EC.

**Method:** We retrospectively analyzed patients presumed to have stage IA, grade 1–2 endometrioid EC who underwent fertility-sparing treatment. Concurrent medroxyprogesterone (MPA) and levonorgestrel-release intrauterine devices were used for treatment. The pregnancy outcomes and oncologic outcomes were compared between the pregnant and nonpregnant groups.

**Results:** Seventy-one patients presumed to have stage IA grade 1–2 endometrioid EC had complete remission, and 49 of them tried to conceive. Twenty-two (44.9%) patients became pregnant; the total number of pregnancies was 30. These pregnancies resulted in 7 abortions (23.3%), 1 preterm birth (3.3%), and 20 full-term births (66.6%). The total live birth rate was 66.6% (20/30). The median duration of hormonal treatment was 11.9 months (range 4–49 months) and 12.0 months (range 3–35...
months) in the pregnant and nonpregnant groups, respectively. On multivariate analysis, age, BMI, treatment duration, MPA dose, and number of dilatation and curettage biopsies were not significantly associated with pregnancy failure, but the association with grade (OR = 6.2, 95% CI 0.98–38.9, P = 0.05) was statistically significant. The median disease-free survival duration was 26 months (range 20–38 months) and 12 months (range 4–48 months) in the pregnant and nonpregnant groups, respectively (P < 0.05, log rank test).

**Conclusion:** A lower grade might be a positive factor for future pregnancy. Moreover, successful pregnancy might be a factor in preventing recurrence.

2541 - Poster Session

**The influence of depression on health utility value in patients with gynecologic cancer: A comparison with physical symptoms and performance status**

Y.L. Yu, H. Yeo and S. Kang. aNational Cancer Center Korea, Goyang-si, South Korea, bGachon University, Seongnam, Korea, Republic of (South)

**Objective:** The impact of depression on health utility value has not been studied sufficiently in gynecologic cancer patients. We hypothesized that depression may adversely influence the health-related quality of life (HRQoL) to the extent similar to that caused by performance status or symptoms such as fatigue or pain.

**Method:** Patient-reported outcome data of 304 gynecologic cancer patients were retrospectively reviewed. Health utility value was measured using EuroQoL-5 (EQ-5D) and EuroQol Visual Analog Scale (EQ-VAS). Patient Health Questionnaire 9 (PHQ-9) was used to measure the severity of depression. Impact of depression on health utility value was analyzed using the generalized linear model.

**Results:** In multivariate analysis, moderate to severe depression was significantly associated with decrease of health utility value (P < 0.0001 in EQ-5D). The decrease of health utility value was associated with moderate to severe depression (β = −0.115) and was comparable to that associated with severe fatigue or severe pain in EQ-5D (β = −0.089 and β = −0.163, respectively). Moreover, not only gynecologic cancer patients with moderate to severe depression but also patients with mild depression showed significantly lower health utility value than those without depressive symptoms (both P < 0.0001). Even mild depression resulted in a decrease of health utility value to an extent similar to that from physical symptoms such as mild fatigue or mild pain (P < 0.0001 in EQ-5D).

**Conclusion:** Depressive symptoms, even when mild, were major factors compromising health utility value in gynecologic cancer patients. It is important to develop simple and accurate tools for verifying the level of depression in order to make efficient psychiatric referrals. Also, gynecologic oncologists should put more effort into preventing, detecting, and managing depression properly.

2542 - Poster Session

**Surgical lymph node staging by retroperitoneal approach for endometrial cancers**

F. Guyon. Comprehensive Cancer Center Bordeaux-Aquitaine, Bordeaux, France

**Objective:** The treatment of endometrial cancers with a surgical and minimally invasive approach is recommended. If a lymphadenectomy is to be performed, it is a pelvic and paraaortic dissection to the left renal vein. It allows a tailoring adaptation of adjuvant treatments. The risk of lymph node involvement is <5% for low risk and about 15% for intermediate risk. Performing lymph node staging by detection of sentinel lymph node remains in the process of being validated. The retroperitoneal laparoscopic paraaortic lymphadenectomies are, in our experience, easier to perform, especially in obese patients. We present an original surgical approach for the detection of sentinel lymph nodes for endometrial cancer and summarize our results.

**Method:** These are the results of a constitutive and ongoing series concerning the management of 45 patients managed for intermediate- to high-risk endometrial cancer (according to ESMO-ESTRO-ESGO criteria). Concerning the SND, we have studied detection and false negative rates. We also analyze conversion rates and complications related to this surgical approach.
Results: The different surgical steps are described: transperitoneal staging with transperitoneal exploration of node areas with immunofluorescence (ICG) and exploration of the node areas by retroperitoneal route with the removal of all mapped sentinel lymph nodes. All suspicious nodes must be resected regardless. Extemporaneous examination of GS and a custom-made lymphadenectomy were performed systematically. The results were as follows: failure of the technique for 2 patients (4%); bilateral detection rate of SND of 89% (40/45 patients); false negative rate of 0%; rate of conversion to laparotomy of 0%; and to transperitoneal lymphadenectomy 4.5%. No grade III and IV surgical complications using the Clavien-Dindo classification lymphatic drainage channels and sentinel lymph node detection sites are listed.

Conclusion: This is from our point of view a promising surgical approach. Prospective complementary studies are needed.

2543 - Poster Session
Sequential chemoradiotherapy (SCRT) compared to radiotherapy (RT) in endometrial carcinoma
O.E. Ali, S. Abdulkhalek, D. Abdelmoety and A. Zeeneldin. King Abdullah Medical City, Makkah, Saudi Arabia

Objective: The role of combined modality in the adjuvant treatment of endometrial cancer has not been established. However, patients with high-risk disease features are at increased risk of recurrence. This study was initiated to investigate the benefits of adjuvant chemotherapy followed by radiotherapy (chemoradiotherapy, SCRT) compared to radiotherapy alone (RT) for women with endometrial cancer.

Method: We performed a retrospective analysis of patients with endometrial cancer stage I to stage IIIC at King Abdullah Medical City, Makkah, Saudi Arabia. We compared cases treated with SCRT with cases treated with RT. Women were assigned to receive RT alone (external pelvic RT, 45 Gy/5 fractions/25 fractions), brachytherapy (1,200 cGy/25 fractions), or combination. SCRT consisted of 6 cycles of carboplatin (AUC 5) and paclitaxel 175 mg/m² followed by radiotherapy. The primary endpoint was disease-free survival (DFS), and the secondary endpoint was OS.

Results: In July 2011 and July 2018, 56 women were evaluated (26 received SCRT and 30 received RT). The age ranged between 34 and 84 years with a median of 58 years. There were no statistically significant differences between the RT versus SCRT groups regarding patient characteristics. Patients who received SCRT had poorer prognostic tumor characteristics. They had more advanced-stage, higher grade tumors, deeper myometrium invasion, and more non-endometrioid histology (P < 0.05 for all). Median follow-up was 29.6 months (95% CI 19.6–39.5 months). All deaths (n = 5) were due to endometrial cancer and exclusively in the RT arm. The 2- and 4-year OS rates were 100% and 100% in SCRT arm versus 87.3% and 64.9% in RT arm, respectively (HR = 0.018, 95% CI 0.01–24.4, P = 0.038). The 2- and 4-year DFS were 100% and 100% in SCRT arm versus 78.1% and 43.9% in RT arm, respectively (HR = 0.102, 95% CI 0.10–0.80, P = 0.008). Febrile neutropenia occurred in 4 (15%) who received SCRT. Neuropathy (grade 2 or worse) was significantly more often after SCRT than after RT (8 women, 30%, vs none). See Figure 1.

Conclusion: Adjuvant chemotherapy given before radiotherapy for high-risk endometrial cancer may alleviate the effect of high-risk features on the DFS and OS, and getting systemic therapy into patients earlier has important deliverables in terms of addressing distant metastases rates. This needs validation from large randomized trials.

![Figure 1](image-url)

2544 - Poster Session
Withdrawn at author’s request
Addressing pain along the continuum of cervical cancer care among women ultimately presenting at Mulago national referral hospital and the Uganda cancer institute

Objective: We sought to report the proportion of women with cervical cancer who were screened for pain and the proportion of women reporting pain who received pain medication at initial presentation for care and at the time of consultation with a specialist at government-funded tertiary care centers in Kampala, Uganda.

Method: We recruited women with cervical cancer at Mulago or the Uganda Cancer Institute (UCI). Interviews occurred after a gynecologic cancer specialist had assessed biopsy results, performed a staging examination, and recommended treatment. This observational study is part of a larger study evaluating predictors of delay. Univariate and multivariate analyses investigated associations between predictors and outcomes.

Results: Between April and November 2017, 138 participants consented for participation; 90% (124/138) originally sought care for symptoms. Most (83%, 103/124) reported pain when initially seeking care for cervical cancer. At first visit to a health center, 77% (96/124) were specifically asked about pain. Among the women with pain at this initial presentation, 57% (59/103) were given medication (tramadol or acetaminophen). No single clinical or demographic factor was independently associated with being screened for pain or receiving pain medication in adjusted analysis. At the time of consultation, 64% (88/138) disclosed having pain in their interviews. During the consultation, most women (77%, 107/138) were asked about pain. Of the women who had pain, 72% (63/88) were given pain medication by the specialist (morphine or acetaminophen). Again, in adjusted analysis, no single or demographic factor was independently associated with being screened for pain or receiving pain medication.

Conclusion: Most women experienced pain while seeking care for cervical cancer. While about three-quarters of women were screened for pain at each visit, a greater proportion of women received medication during specialist consultation, compared to first visit at any health center. These data reveal a missed opportunity to treat pain early in the continuum of care for cervical cancer. Reasons underlying the lack of provision of pain medication should be explored. Palliative care, including pain management, should be initiated early and concurrently with cancer treatment.

Vulvar cancer and HIV at a teaching hospital in Ethiopia

Objective: In 2017, there was an estimated 350,000 women living with human immunodeficiency virus (HIV) in Ethiopia. Primary cancers including vulvar cancer are increased among HIV women, which is associated with the numbers of years of HIV infection and compliance with antiretroviral therapy (ART). In 2013, the Addis Ababa city cancer registry reported a vulvar cancer incidence of 1.4 per 100,000 women. In 2016, a gynecologic oncology clinical service was initiated with the start of the gynecologic oncology fellowship training program in Addis Ababa at St. Paul’s Hospital Millennium Medical College (SPHMMC). Surgical and chemotherapy can be delivered at SPHMMC, but lack of radiation therapy, an average delay greater than 6 months, limits access to definitive radiation treatment for women with vulvar cancer. The aim of this study is to report early data on the trend of vulvar cancer.

Method: A hospital-based retrospective cross-sectional study was conducted to evaluated the clinical characteristics and management of women with vulvar cancer treated at SPHMMC in Ethiopia. Women with histologically confirmed vulvar
cancer treated from October 2016 to September 2018 were identified for this study. Clinical data were extracted from medical charts, and descriptive analysis was performed to identify trends.

**Results:** From October 2016 to September 2018, 21 cases of vulvar cancer were referred to SPHMMC. Data on 17 cases could be retrieved. The mean age was 42.9 years (range 18–80 years). Seven (41%) patients were HIV positive. There was a difference in mean age between HIV positives (33 years) and HIV negatives (49.4 years) \((P < 0.05)\). The mean duration from first symptom to hospital appearance was 18.3 months, while the average time to initiation of treatment after initial evaluation was 2.6 months. Seven (41%) presented in advanced stages (III and IV).

**Conclusion:** Our experience with vulvar cancer has identified challenges including late-stage presentation, increased number of women with HIV status, and limited access to radiation therapy. Opportunities exist to develop resource-specific management protocols for vulvar cancer.

**2550 - Poster Session**
**Evaluation of early removal of indwelling urinary catheter (IDUC) after radical surgery in cervical cancer**

**Faculdade de Ciências da Saúde de Barretos Dr. Paulo Prata, Barretos, Brazil, Barretos Cancer Hospital, Barretos, Brazil, Hospital Erasto Gaertner, Curitiba, Brazil**

**Objective:** To evaluate whether early removal of indwelling urinary catheter (IDUC) differs from delayed removal after open or minimally invasive radical surgery for cervical cancer.

**Method:** Cervical cancer patients submitted to radical hysterectomy or trachelectomy were divided into two groups. An ambispective study was conducted. In the retrospective group, all patients treated from January 2012 to November 2013 with IDUC removal at least on the seventh postoperative day (delayed removal) were analyzed. In the prospective group, IDUC removal was performed on the first postoperative day (early removal) in all patients treated from May 2014 to June 2017. At the time of IDUC removal after surgery, a post-void residual (PVR) urine test (test 1) was performed, and in the prospective group, it was repeated on the seventh postoperative day (test 2). In patients with PVR volume >100 ml or who did not present spontaneous voiding, IDUC was reinserted and additional PVR urine tests were performed on next removals. \(\chi^2\) and Mann-Whitney tests were used to analyze prospective and retrospective groups, and \(P < 0.05\) was significant.

**Results:** We included 47 patients in the retrospective group and 48 in the prospective group. After the first PVR test (test 1), IDUC reinsertion was necessary in 16 (34%) patients from the retrospective group and in 12 (25%) patients from the prospective group \((P = 0.374)\). In test 1, the median PVR volume was 82.5 ml in the retrospective group and 45 ml in the prospective group \((P = 0.055)\). On the seventh postoperative day, the median PVR volume was 82.5 ml in the retrospective group (test 1) and 60 ml in the prospective group (test 2) \((P = 0.055)\). Urinary tract infection (UTI) within 30 days after surgery occurred in 7 (14.9%) patients from the retrospective group and in 2 (4.2%) patients from the prospective group \((P = 0.091)\). In the retrospective group, of all patients who needed IDUC reinsertion, 5 (31.3%) presented urinary tract infection (UTI), while it occurred in only 2 (6.5%) patients of those who did not need IDUC reinsertion \((P = 0.036)\). In the prospective group, UTI occurred in 1 (2.9%) patient with IDUC reinsertion in 1 (7.1%) patient without IDUC reinsertion \((P = 0.503)\).

**Conclusion:** IDUC removal on the first postoperative day does not differ from delayed removal (≥7 days), in terms of necessity of IDUC reinsertion, PVR volume, and 30-day UTI rate. In the delayed removal group, the UTI rate was significantly higher in the group that needed IDUC reinsertion.

**Team Oriented Care**

**2551 - Poster Session**
**Phase III randomized trial of comparing chemoradiotherapy vs. radiotherapy alone in lymph node negative patients with early-stage cervical cancer following radical hysterectomy**
H. Zhao and C. Xie. Wenzhou Medical University, Wenzhou, China

**Objective:** Chemotherapy concurrent with radiotherapy has become the standard treatment for cervical cancer patients with high-risk factors. However, the treatment modality in patients with low risk is still disputable. The purpose of this study is to
determine whether concurrent paclitaxel/cisplatin chemoradiotherapy is more effective than radiotherapy alone in treating early-stage cervical cancer patients with negative lymph nodes after radical hysterectomy.

**Method:** Between January 2011 and November 2014, 165 eligible cervical cancer patients with stage IA2–IIB and negative lymph nodes were enrolled, randomized to chemoradiotherapy (CRT) (80 patients) and radiotherapy (RT) (85 patients), respectively. An RT dose of 46–50 Gy was administered in 23–25 fractions with 2- or 4-field box technique. Chemotherapy consisted of paclitaxel 135 mg/m² day 1 and cisplatin 25 mg/m² days 1–3 intravenously every 4 weeks with radiation.

**Results:** The HR for disease-free survival (DFS) and OS in the CRT arm versus the RT alone arm were 0.84 (95% CI 0.36–1.93, \(P = 0.67\)) and 0.61 (95% CI 0.20–1.86, \(P = 0.38\)), respectively. The 5-year DFS and OS for CRT and RT alone groups were 85.9% versus 83.5% and 92.6% versus 88.4%, respectively. For subgroup analysis, CRT significantly increased the 5-year DFS and OS for patients tumor sizes ≥3 cc (HR = 0.23, 95% CI 0.05–1.0, and HR = 0.21, 95% CI 0.04–0.99, for DFS and OS, respectively). For patients with negative lymphovascular invasion, CRT increased 5-year DFS (HR = 0.21, 95% CI 0.04–0.99). Multivariate analysis indicated that tumor size was a significant prognostic factor associated with both DFS and OS, and age was significantly associated with OS. Grade 2–4 gastrointestinal disorders, radiation enteritis, radiation cystitis, and myelosuppression were more frequent side effects observed in the CRT arm. Grade 3 and 4 toxicities were rare and manageable overall.

**Conclusion:** CRT with cisplatin and paclitaxel achieved better DFS and OS in early-stage cervical cancer patients after radical hysterectomy with negative lymph nodes compared with RT alone, along with a higher rates of acute grade 2–4 complications. Concurrent chemotherapy might enhance radio-sensitizing effect to improve survival outcome for patients with large tumor size. Grade 3 and 4 toxicities were infrequent and tolerable overall.

**2552 - Poster Session**

**Cascade genetic testing for cancer-associated germline mutations: Patient-reported anxiety and uncertainty regarding communication with family members**

M.K. Freya, R.M. Kahnb, K. Lipkinb, E. Chapman-Davisb, B. Jordanb, F. Tubitob, M. Piresb, S. Ram-Junnarkarb, T.A. Caputoa and K.M. Holcombb. aWeill Cornell Medicine, New York, NY, USA, bWeill Cornell Medical College, New York, NY, USA

**Objective:** For patients diagnosed with a germline cancer-associated mutation, informing at-risk relatives (ARR) is a critical but challenging task. As part of a prospective facilitated cascade genetic testing strategy, we assessed patients’ attitudes toward cascade testing.

**Method:** Patients with a new diagnosis of a germline cancer-associated mutation at our institution were offered enrollment. The patient worked with a genetics team to identify ARR who would be contacted by the team, provided genetic counseling, and offered cascade testing. Patients were given three quality-of-life questionnaires after meeting with the genetics team: Hospital Anxiety and Depression Scale (HADS), Satisfaction with Decision Scale (SDS), and the Multidimensional Impact of Cancer Risk Assessment (MICRA).

**Results:** Between September 2017 and March 2018, 30 patients were enrolled and 22 completed questionnaires. Ninety-six percent (21) reported that they were adequately informed about genetic testing and that the decision for testing was consistent with their personal values. Seventy-seven percent (17) reported the maximum score for satisfaction with their decision to participate in cascade testing. Sixty-three percent (15) of patients reported uncertainty regarding interpretation of cancer risk for themselves and their family members. Twenty-one percent (5) reported understanding their choices for cancer prevention or early detection. Twenty-five percent (6) reported difficulty talking about test results with family members. Thirteen percent (3) reported never feeling satisfied with family communication about genetic testing results (Figure 1).

**Conclusion:** Although patients feel adequately informed and satisfied with decisions about genetic and cascade testing, many are uncertain about cancer risk and available risk reduction strategies. Our findings illustrate the complexities patients face when attempting to communicate and encourage cascade testing among family members and highlight the need to identify strategies for cascade testing that limit the burden placed on the newly diagnosed patient.

**Table 1.** The Multidimensional Impact of Cancer Risk Assessment (MICRA) Questionnaire
Objective: Precision medicine has the potential to transform our health care system and improve the treatment of cancer. At our institution, we have implemented a multidisciplinary precision medicine program to make major advancements in the ability to individualize treatments and improve the lives of women diagnosed with ovarian cancer.

Method: We have integrated multiple, comprehensive genomic platforms with clinical and pharmacologic data of women diagnosed with ovarian cancer. We have initiated single-cell transcriptome RNA and exome DNA sequencing, bulk tumor transcriptome RNA and exome DNA sequencing, germline medical exome sequencing, and NanoString-based TCGA molecular subtyping on newly diagnosed patients. In addition, we establish patient-derived xenograft (PDX) for each to study resistance mechanisms. We have created bioinformatic pipelines and predictive models to integrate and analyze molecular and clinical data. We have instituted a local version of the cbioPortal platform to organize primary and derivative data for utilization by the entire research community. Our goal is to develop a systematic, evidence-based method for individualizing treatment for women with ovarian cancer based on molecular and clinical findings.

Results: We have enrolled 58 patients into the program over 12 months; 35 single-cell RNA-seq datasets and 5 single-cell exome DNA-seq datasets have been completed. In addition, bulk RNA-seq and DNA-seq have been completed on the first 35 patients, and germline medical exome data are complete on 16 of those patients, with the remainder pending genetic counseling and sequencing. All patients are undergoing NanoString subtyping. We have successfully generated 19 PDX models, with 7 pending and 10 failures. We are currently correlating results of single-cell and bulk tumor genomic analyses with patients’ primary response to adjuvant therapy. Pharmacogenomics germline research is identifying actionable variants to design clinical integration strategies. Molecular phenotypes will be integrated with clinical data to create improved patient stratification models and drive future research hypotheses.

Conclusion: Ovarian cancer comprises a heterogenous group of tumors, with distinctive molecular signatures and disease trajectories. We are pioneering a precision medicine project to accelerate research, improve the understanding of ovarian cancer, and translate the work into new treatments and strategies to improve patient outcomes.
2554 - Poster Session
Prospective feasibility trial of a novel strategy of facilitated cascade genetic testing using telephone counseling and mailed saliva kit genetic testing
M.K. Freya, R.M. Kahn, K. Lipkin, E. Chapman-Davis, B. Jordan, F. Tubito, M. Pires, S.V. Blank, T.A. Caputo, S.R. Anderson and K.M. Holcomb. aWeill Cornell Medical College, New York, NY, USA, bIcahn School of Medicine at Mount Sinai, New York, NY, USA, cWeill Cornell Medicine, New York, NY, USA

Objective: A powerful consequence of detecting cancer-associated mutations is the ability to inform and test at-risk relatives (ARR), termed cascade testing. However, studies suggest that cascade testing uptake is less than 50% in large part because of difficulties with family information sharing. We sought to evaluate the feasibility of a novel method of cascade genetic testing whereby the process is facilitated by a genetics team using telephone genetic counseling and mailed saliva kit genetic testing.

Method: Patients with newly diagnosed cancer-associated germline mutations were offered enrollment between September 1, 2017, and March 1, 2018. The genetics team identified ARR and contacted ARR by telephone, with the patient’s permission, to disclose the familial mutation and offer genetic assessment via mailed saliva kits. Post-testing results, and guideline-based clinical recommendations were reviewed with ARR by telephone with a certified genetic counselor and shared with the AAR’s primary care physician. All ARR were asked to complete anxiety/depression/satisfaction questionnaires following genetic assessment.

Results: Thirty patients were enrolled. After discussion with the genetics team, 5 elected not to proceed with ARR contact. The median number of ARR designated per patient was 2 (range 1–15). A total of 98 ARR were called, and contact was established with 84 (86%). Median age of ARR was 51 years (range 20–85). Seventy-seven (92%) of those contacted agreed to testing, and 58 (69%) completed testing. Twenty-three ARR were found to carry pathogenic mutations, or 40% of those tested. None of the demographic/clinical variables were associated with uptake of cascade testing (age, gender, education, parity, personal/family cancer history). Thirty-six ARR (67%) completed questionnaires demonstrating low levels of stress/anxiety and overall satisfaction with cascade testing (Table 1). At 6-month follow-up, 3 risk-reducing surgeries were performed (bilateral salpingo-oophorectomy 2, mastectomy 1), and 6 ARR underwent breast or colon cancer surveillance interventions.

Conclusion: Facilitated cascade genetic testing with telephone genetic counseling and mailed saliva kits resulted in high uptake of testing among ARR with minimal stress/anxiety and high levels of participant satisfaction.

Table 1. Post-testing questionnaires (Hospital Anxiety and Depression Scale, Satisfaction with Decision Scale, The Multidimensional Impact of Cancer Risk Assessment Questionnaire).

<table>
<thead>
<tr>
<th>Hospital anxiety and depression score - Anxiety (median, range)</th>
<th>Normal 0-7</th>
<th>Abnormal 8-21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital anxiety and depression score - Depression (median, range)</td>
<td>Strongly Disagree</td>
<td>Disagree</td>
</tr>
<tr>
<td>I was adequately informed about the option for genetic testing</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>The decision I made was the best decision possible for me personally</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>My decision was consistent with my personal values</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>I expect to successfully carry out (or continue to carry out) the decision I made</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>I had as much input as I wanted in the choice about genetic testing</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>I am satisfied with the decision that was made about genetic testing</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Feeling regret about getting my genetic testing results</td>
<td>Never</td>
<td>Rarely</td>
</tr>
<tr>
<td>Worrying that the genetic counseling and testing process has brought about conflict with my family</td>
<td>28 (90%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

2555 - Poster Session
Prognostic significance of supraclavicular lymphadenopathy in patients with high-grade serous ovarian cancer

Objective: To assess outcomes and patterns of recurrence in patients with high-grade serous ovarian cancer (HGSOC) with radiographic supraclavicular lymphadenopathy at diagnosis.
**Method:** We evaluated all patients with newly diagnosed HGSOC treated at our center between January 1, 2008, and May 1, 2013 who had supraclavicular lymphadenopathy (defined as >1 cm in short axis) on radiographic imaging (either CT or PET) at the time of diagnosis.

**Results:** Of 586 patients with HGSOC, 16 (2.7%) had supraclavicular lymphadenopathy diagnosed on pretreatment imaging. Five patients (31%) had clinically palpable nodes on physical examination. Because of stage IVB disease, all underwent neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS). The median age at diagnosis was 50.5 years (range 38–72 years). Five patients (31.3%) had a known BRCA mutation. Patients received a median of 4 cycles of neoadjuvant intravenous (IV) chemotherapy (range 3–7). At IDS, complete gross resection was achieved in 12 (75%) patients, and optimal resection (0.1–1 cm) in 4 (25%). One patient (6%) had surgical excision of supradiaphragmatic lymph nodes. Thirteen patients (81%) recurred; however, only 2 patients (12.5%) recurred in the supraclavicular lymph nodes. Median follow-up time was 45.2 months (range 22.4–95.4 months). Median PFS was 12.2 months (95% CI 9.2–15.2). Median OS was 78.1 months (95% CI 28.8–127.4). See Figure 1.

**Conclusion:** Radiographic supraclavicular lymphadenopathy at diagnosis of HGSOC does not portend an unfavorable prognosis. Perhaps classification as stage IVB disease should be reconsidered, and these patients should be offered primary debulking surgery.

![Figure 1](image-url)

**Fig. 1.** Overall Survival

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**2556 - Poster Session**

**NCCN distress thermometer underscores unmet psychological needs**


**Objective:** To identify etiologies and describe risk factors for psychological distress among gynecologic oncology patients and assess patient adherence to follow-up recommendations.
Method: We performed a cross-sectional study of 922 women screened for distress using the National Comprehensive Cancer Network (NCCN) Distress Thermometer (scale 0–10) throughout gynecologic oncology outpatient clinics at a high-volume academic cancer center between June 2017 and September 2017. Self-reported scores were dichotomized as low (<5) versus high (≥5). Multivariate logistic regression was used to identify independent risk factors for distress, adjusting for insurance type, race, marital status, employment status, BMI, cancer site, stage, and appointment type.

Results: Of 922 gynecologic oncology patients surveyed, 796 (87%) reported some distress, and of these, 167 (18%) met criteria for high distress. Etiologies of distress were underreported (192/796, 24%), but included physical (44%), emotional (18%), family (8%), and financial, work/school, or other problems (28%). Risk factors for high distress included no insurance or Medicaid primary (P < 0.0001), unemployment (P < 0.0001), BMI <30 (P = 0.008), cancer site (P = 0.0002), advanced stage (P = 0.007), treatment type (chemotherapy, surgery, radiation, palliative treatment, or no treatment, P = 0.007), concurrent pain medication and antidepressant/anxiolytic use (P < 0.0001), and number of office visits (P = 0.03). In our multivariate analysis, factors associated with high distress included no insurance or Medicaid primary (aOR = 3.1, 95% CI 1.69–5.74), and unemployment (aOR = 1.6, 95% CI 1.11–2.36). Referral to psycho-oncology counseling was recommended the most of all available support services at our cancer center (Table 1). Among 34 referrals to psycho-oncology counseling, adherence was disproportionately worse among patients with high distress 99/14, 5%, vs 5/14, 0.7%, P < 0.0001).

Conclusion: Despite a high prevalence of distress among gynecologic oncology patients, etiologies of distress are underreported and psycho-oncology services are poorly accessed by patients. Future studies should evaluate the role of NCCN distress score screening and integrated psychological care into gynecologic oncology outpatient visits to better identify and reduce patients’ distress.

Table 1. Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Total N=922</th>
<th>Distress score ≤ 5 N=757</th>
<th>Distress score ≥ 5 N=467</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician discussed with patient</td>
<td>123(13.81)</td>
<td>49(6.47)</td>
<td>74(44.31)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Nurse discussed with patient</td>
<td>32(3.46)</td>
<td>13(1.72)</td>
<td>19(11.38)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Physical symptoms addressed</td>
<td>9(0.97)</td>
<td>5(0.66)</td>
<td>4(2.40)</td>
<td>0.0514</td>
</tr>
<tr>
<td>Education provided</td>
<td>5(0.54)</td>
<td>2(0.26)</td>
<td>3(1.80)</td>
<td>0.0437</td>
</tr>
<tr>
<td>Medication prescribed/adjusted</td>
<td>12(1.30)</td>
<td>5(0.79)</td>
<td>6(3.59)</td>
<td>0.0113</td>
</tr>
<tr>
<td>Referral to counseling</td>
<td>34(3.68)</td>
<td>11(1.45)</td>
<td>23(13.77)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Referral to dietician</td>
<td>0</td>
<td>0(0.00)</td>
<td>0(0.00)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Referral to physical therapy</td>
<td>1(0.11)</td>
<td>1(0.13)</td>
<td>0(0.00)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Referral to primary care</td>
<td>0</td>
<td>0(0.00)</td>
<td>0(0.00)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Referral to social work</td>
<td>8(0.87)</td>
<td>2(0.26)</td>
<td>5(3.59)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Referral to Siteman financial specialist</td>
<td>2(0.22)</td>
<td>0(0.00)</td>
<td>2(1.20)</td>
<td>0.0325</td>
</tr>
<tr>
<td>Referral to spiritual care</td>
<td>0</td>
<td>0(0.00)</td>
<td>0(0.00)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Referral to Barnard Health &amp; Cancer Info Center</td>
<td>2(0.22)</td>
<td>1(0.13)</td>
<td>1(0.60)</td>
<td>0.3290</td>
</tr>
</tbody>
</table>

2557 - Poster Session
Genetic counselor involvement with abnormal immunohistochemistry results improves genetic testing in patients with endometrial cancer
A.L. Brodsky, J. Leeb, S. Asgari, J. Fehnigec, D.A. Levine and B. Pothuri. aNew York University School of Medicine, New York, NY, USA, bThe University of Texas Southwestern Medical Center, Dallas, TX, USA, cNYU Langone Health, New York, NY, USA

Objective: Lynch syndrome (LS) accounts for 3%–5% of endometrial cancers. Screening high-risk (HR) patients with endometrial cancer (EC) for LS can result in prevention of other cancers and cascade testing for family members. We implemented universal mismatch repair (MMR) immunohistochemistry (IHC) in patients undergoing hysterectomy for EC in July 2015. In April 2017, we implemented the practice of genetic counselors (GC) accessing IHC data from pathology reports and contacting physicians to approve genetic counseling for patients with a loss of MMR protein expression. By involving genetic counselors, we sought to increase rates of genetic counseling referrals (GCRs) and genetic testing (GT) in EC patients with abnormal MMR IHC.
**Method:** All women diagnosed with EC who underwent hysterectomy between July 2015 and July 2018 at a single institution were retrospectively identified. Demographic data, IHC results, rates of GCR, and GT rates were abstracted before and after implementation of GC involvement in MMR IHC review and GCR.

**Results:** Of 356 patients with EC who underwent hysterectomy, 321 (90%) had MMR IHC testing. Abnormal MMR IHC was found in 86 (27%) patients with the following distribution: MLH1 and PMS2, 68; MLH1, 2; PMS2, 3; MSH6, 8; and MSH2 and MSH6, 5. In 63 (73%) of the 86 patients, MLH1 promoter methylation was identified as the cause of the abnormal MMR IHC. Of the remaining 23 patients with abnormal MMR IHC, 18 (78%) received GCR, and 16 (70%) had GT. Comparing the time frame from July 2015 to April 2017 (prior to GC involvement) to April 2017 to July 2018 (after GC involvement), there was an increase in GCR from 10/15 (67.7%) to 8/8 (100%). GT rates for the MMR abnormal cohort were 8/15 (53%) compared to 8/8 (100%), respectively. Of the 16 patients with an abnormal MMR IHC result who underwent GT for LS, 9 (56%) were identified to have LS, 7 with MSH6 mutations and 2 with MSH2 mutations. See Table 1.

**Conclusion:** GC access to abnormal MMR IHC results in EC patients' improved rates of GCRs and GT to capture all patients with LS. GC involvement in the review of IHC results and GCR is a feasible and effective strategy to ensure both GCR and GT. Proper follow-up and GT of at-risk patients is critical to increase screening and prevention of other LS-related cancers in the proband, as well as for cascade testing of family members.

**Table 1. GCR and Genetic Testing Rates for Abnormal MMR IHC**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>GCR</th>
<th>GT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 4/2017 – before GC involvement</td>
<td>10/15 (67%)</td>
<td>8/15 (53%)</td>
</tr>
<tr>
<td>After 4/2017 – after GC involvement</td>
<td>8/8 (100%)</td>
<td>8/8 (100%)</td>
</tr>
</tbody>
</table>

---

**Integrated psychological care in gynecologic oncology outpatient clinics: A feasibility study**


**Objective:** To determine patient acceptability and need for integrated psychological care by a trained psychologist in gynecologic cancer outpatient clinics.

**Method:** From May to August 2018, we surveyed women who presented to care at 3 outpatient gynecologic oncology clinics at a single academic institution affiliated with a cancer center. Integrated psychological care was randomly provided based on 1 psychologist's availability of 8 hours per week. Four surveys were administered prior to being seen by a provider: National Comprehensive Cancer Network Distress Thermometer, PROMIS Depression & Anxiety, quality of life short form-12, and a patient awareness & satisfaction survey. Primary outcome was patient enrollment.

**Results:** Of 156 women approached, 100 (64%) women were enrolled. Reasons for nonparticipation included lack of interest (36%), time commitment (27%), feeling tired (9%), perception of no personal benefit (9%), and no explanation (9%). Two patients specifically declined because of concerns regarding "counseling." Mean age was 54 years, and the majority were diagnosed with either ovarian/fallopian tube/primary peritoneal carcinoma (30%) or endometrial (28%). Twenty-four women (25%) had a history of depression, and 19 were currently taking an antidepressant. Overall 46% met criteria for high distress, and the majority of women reported poor quality of life (Figure 1). Of 74 respondents who completed the satisfaction survey, 54 (73%) expressed that it was important to discuss areas of distress at their gynecologic oncology office visit. Sixty-one (82%) endorsed support for having integrated psychological services available, but 20 (27%) expressed unwillingness or indifference (19, 26%) to make a separate appointment for counseling. Overall awareness of psychological support services at our cancer center was 71%.

**Conclusion:** There is a high patient need and desire for integrated psychological care in gynecologic oncology outpatient clinics. This multidisciplinary model of care has potential to improve patient satisfaction and quality of life and efficiency of health care delivery, and to reduce barriers to access free psychological support services.
Fig. 1. High Distress and Poor Quality of Life Among Gynecologic Oncology Patients. A) National Comprehensive Cancer Network (NCCN) Distress Thermometer. Scale 0-10; scores ≥5 indicate high distress. Median score was 3, interquartile range 6, and 46% met criteria for high distress; B) Quality of life short form-12 (SF-12) scores. A linear T score transformation was used so that both the SF-12 physical and mental component summary (PCS and MCS, respectively) were standardized based on average value of 50 and a standard deviation of 10 in the general U.S. population.

2559 - Poster Session
Mind over matter: Depression and anxiety are common in endometrial cancer survivors but not associated with poorer weight loss outcomes in a prospective observational cohort
E.V. Conner, K. Maurer, K.R. Cooper, P.R. Schauer, P.G. Rose, C.M. Michener and A.M. Jernigan. The Cleveland Clinic Foundation, Cleveland, OH, USA; University of Utah, Salt Lake City, UT, USA; Cleveland Clinic, Cleveland, OH, USA; Louisiana State University Health Science Center, New Orleans, LA, USA

Objective: To assess the prevalence of symptoms of depression and anxiety in obese endometrial cancer survivors and to prospectively correlate with weight loss after medical and surgical weight management referral.

Method: From December 2013 to May 2015, women aged 18–65 years with complex atypical hyperplasia or stage I–II endometrioid adenocarcinoma and a BMI ≥30 kg/m² were prospectively enrolled at 3 hospitals in an academic health system. Exclusion criteria included nonendometrioid histology, poorly controlled medical conditions precluding weight loss intervention, or a second active malignancy. Women with BMI ≥30 kg/m² were offered referral for medical management, and women with obesity-related comorbid conditions or BMI ≥40 kg/m² were also offered surgical consultation. At enrollment and each clinic visit up to 2 years, participants completed EORTC QLQ-C30 questionnaires about quality of life and symptoms. BMI was tracked concurrently.

Results: Of 153 women enrolled, 120 participated in the survey. Mean initial age was 55 years (SD 9); mean initial BMI was 43 kg/m² (SD 9). Median follow-up time was 15 months (IQR 10–18). Overall, 56 women (47%) endorsed depressed mood, and 77 (64%) endorsed anxiety. Difficulty sleeping (56%), poor appetite (26%), fatigue (84%), and difficulty concentrating (23%) were common. Women with a higher index of depressive symptoms reported significantly poorer quality of health (4.3 vs 5.4, P < 0.0001), and significantly poorer quality of life (4.6 vs 5.6, P < 0.0001) despite no differences in age or medical comorbid conditions. Women with higher index of depressive symptoms had higher mean BMI at enrollment (48 kg/m² vs 40 kg/m², P < 0.0001), but were not more likely to gain weight during the study period (42% vs 42%, P = 1.00). Women reporting anxiety also had higher BMI at enrollment (45 kg/m² vs 39 kg/m², P = 0.001), but similarly were not any more likely to gain weight during the study period (42% vs 41%, P = 0.992).

Conclusion: Depression and anxiety are prevalent among women with obesity and endometrial cancer, and these women should be screened. Depression is associated with poorer quality of life, but is not associated with a difference in weight loss after referral to weight management.
To admit or not admit: An evaluation of avoidable and potentially avoidable admissions on a gynecologic oncology service
H.A. Moss, C. Watson, B.A. Davidson, K.C. Nolte, T. Truong, J.M. Weber and L.J. Havrilesky. aDuke University Medical Center, Durham, NC, USA; bDuke University School of Medicine, Durham, NC, USA

Objective: To examine reasons for hospitalization to a gynecologic oncology service and to identify factors associated with avoidable and potentially avoidable hospital admissions.

Method: This was a retrospective study of sequential hospital admissions in patients admitted to a gynecologic oncology service at a tertiary care center between January and December 2017. A team of gynecologic oncologists and mid-level practitioners used a consensus-driven medical record review to identify reasons for admission and categorize each hospitalization as “not avoidable,” “potentially avoidable,” or “avoidable.” A series of univariate models were fitted to identify factors associated with avoidable admission.

Results: We evaluated 144 hospitalizations in 96 unique patients. We identified 29 (20.1%) avoidable, 26 (18.1%) potentially avoidable, and 89 (61.8%) not avoidable admissions. Among avoidable admissions, the most common malignancy was ovarian cancer (41.4%), and the majority of admissions (64.3%) had occurred after another hospitalization within the past 12 months. Poorly controlled pain (34.5%) was the most common reason for an avoidable hospitalization. Younger age (OR = 0.96, 95% CI 0.93–0.99, P = 0.03) and Medicaid insurance (OR = 6.14, 95% CI 1.66–22.7, P = 0.01) relative to Medicare were associated with avoidable admissions, with a trend among African Americans (OR = 2.47, 95% CI 0.90–6.74, P = 0.08) compared to whites to have an avoidable admission. Among the avoidable and potentially avoidable admissions, 58.2% could have been managed in an outpatient setting if patient navigation, an oncology extended care clinic, or a home-based hospital program existed at the care facility.

Conclusion: Avoidable hospitalizations are common in patients with a gynecologic malignancy. Investment in interventions, including targeted patient navigation, oncology extended care clinics, and home-based hospital programs, could reduce unnecessary hospitalizations in this population.

Referral to a weight loss specialist is associated with long-term weight control in endometrial cancer survivors: Long-term follow-up of a prospective cohort study
E.V. Connor, K. Maurer, K.R. Cooper, P.R. Schauer, P.G. Rose, C.M. Michener and A.M. Jernigan. aThe Cleveland Clinic Foundation, Cleveland, OH, USA; bUniversity of Utah, Salt Lake City, UT, USA; cCleveland Clinic, Cleveland, OH, USA; dLouisiana State University Health Science Center, New Orleans, LA, USA

Objective: To prospectively evaluate the long-term effects of medical and surgical weight loss referral of obese endometrial cancer survivors.

Method: From December 2013 to May 2015, women 18–65 years with complex atypical hyperplasia or stage I–II endometrioid adenocarcinoma and a BMI ≥30 kg/m² were prospectively enrolled at 3 hospitals in an academic health system. Exclusion criteria included poorly controlled medical or psychiatric conditions or a second active malignancy. Women with BMI ≥30 kg/m² were offered referral for medical management, and women with obesity-related comorbid conditions or BMI ≥40 kg/m² were also offered surgical consultation. A historic control group was identified during the enrollment period. All patients were followed for up to 2 years.

Results: One hundred and fifty-three women were enrolled in the intervention group and compared to a control group of 104 women. Mean initial age was 55 years (SD 8), and mean initial BMI was 42 kg/m² (SD 9), with no significant differences between groups. Median follow-up time was 18 months (IQR 12–24). One hundred forty-five women (95%) were offered referral for medical management, and 63 (43%) accepted, of which 23 (37%) attended the appointment and 18 (29%) initiated a weight loss plan. One hundred and two women (67%) met criteria for surgical management, and 45 (44%) accepted, of which 6 (13%) attended the appointment and 4 (9%) underwent bariatric surgery. Initial BMI was higher for women accepting versus declining referral (44.4 vs 41.4 kg/m², P = 0.048). Of all 257 women, 74 demonstrated BMI loss >1 kg/m² (29%); 107 (42%) remained stable within 1 kg/m²; and 76 (30%) demonstrated BMI gain >1 kg/m². Both women who accepted or declined the referral in the intervention cohort demonstrated BMI loss compared to the control group, which demonstrated BMI gain (−0.82 vs −0.50 vs +0.50 kg/m², P = 0.041). Women in the intervention group were more likely to lose...
weight (54 vs 39%, $P = 0.016$). Women in the control group were more likely to experience weight gain (59% vs 41%, $P = 0.005$) and were almost twice as likely to gain >1 kg/m² (40% vs 22%, $P = 0.001$).

**Conclusion:** Obese endometrial cancer survivors should be referred to medical and surgical obesity management programs, as referral is associated with better long-term weight control.

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2602 - Poster Session
Implementation and evaluation of a novel subspecialty society fellows robotic surgical course: The SGO minimally invasive academy surgical curriculum

**Objective:** To evaluate the utility of a society-based robotic surgery training program for fellows in gynecologic oncology (GO).

**Method:** All participants underwent a two-day robotic surgery training course between 2015 and 2017. Based on instructional theory, the course was designed with interactive didactic sessions with video, dry labs, and robotic cadaver labs. The educational sessions and videos reviewed a variety of surgical practices and complications of robotic surgery. The labs encompassed a wide range of subject matter including troubleshooting, instrument variation, radical hysterectomies, lymph node dissections, among other procedures. Fellows were encouraged to attend the course with a supervising attending. Participants were asked to complete a pre- and post-course survey rating their confidence levels. A five-point Likert scale that ranged from “not confident” to “extremely confident” was used to measure confidence levels in participants. Statistical analysis including a paired t test was performed using SPSS Statistics v. 24.

**Results:** The response rate was high with 86% of the 70 participants completing the survey. Sixteen (26.7%) of these individuals were attending physicians, and 44 (73.3%) were fellows. On average, participants had performed 35.7 robotic hysterectomies (range 4–100) and 3.3 radical hysterectomies (range 0–16) in the preceding year. In general, there was a significant increase in confidence in more complex procedures and concepts such as radical hysterectomy ($P = 0.01$), lymph node dissection ($P = 0.01$), troubleshooting ($P = 0.001$), and managing complications ($P = 0.004$) (Table 1). Furthermore, there was an overall trend of increased confidence in most areas with 15 of 21 being significant. Faculty comfort and practice patterns were cited as the primary reason (58.9%) for limitations during robotic procedures followed secondarily by surgical resources (34.0%).

**Conclusion:** In both GO fellows and attendings, this educational theory-based curriculum led to significantly improved confidence levels in the majority of procedures and concepts taught. The study emphasizes the value of hands-on skills labs. Robotic surgery courses can augment traditional surgical education to ensure surgeons are kept up-to-date on procedures, troubleshooting, and society standards.
Table 1. Confidence Level Questions and Results

<table>
<thead>
<tr>
<th>CONCEPT AND PROCEDURES</th>
<th>AVERAGE CL* BEFORE</th>
<th>AVERAGE CL* AFTER</th>
<th>P-VALUE</th>
<th>95% CONFIDENCE INTERVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PORT PLACEMENT &amp; PATIENT POSITIONING</td>
<td>3.36</td>
<td>4.15</td>
<td>.079</td>
<td>[-1.81, 0.23]</td>
</tr>
<tr>
<td>INSTRUMENT SELECTION &amp; 3RD PARTY PRODUCTS</td>
<td>2.92</td>
<td>3.95</td>
<td>.053</td>
<td>[-2.09, 0.03]</td>
</tr>
<tr>
<td>DOCKING AND PORT PLACEMENT</td>
<td>3.28</td>
<td>4.20</td>
<td>.016</td>
<td>[-1.43, -0.42]</td>
</tr>
<tr>
<td>ROBOTIC HYSTERECTOMY</td>
<td>3.53</td>
<td>4.17</td>
<td>.086</td>
<td>[-1.51, -0.42]</td>
</tr>
<tr>
<td>RADICAL HYSTERECTOMY</td>
<td>2.26</td>
<td>3.34</td>
<td>.011</td>
<td>[-1.57, -0.60]</td>
</tr>
<tr>
<td>LYMPH NODE DISSECTION</td>
<td>2.70</td>
<td>3.59</td>
<td>.011</td>
<td>[-1.28, -0.48]</td>
</tr>
<tr>
<td>ROBOTIC OMENTECTOMY</td>
<td>2.16</td>
<td>3.02</td>
<td>.051</td>
<td>[-1.73, 0.01]</td>
</tr>
<tr>
<td>UTERINE MANIPULATORS</td>
<td>3.78</td>
<td>4.19</td>
<td>.068</td>
<td>[-0.90, 0.07]</td>
</tr>
<tr>
<td>PORT PLACEMENT IN OBESE PATIENTS</td>
<td>3.08</td>
<td>4.11</td>
<td>.014</td>
<td>[-1.56, -0.50]</td>
</tr>
<tr>
<td>PORT PLACEMENT IN THIN PATIENTS</td>
<td>3.20</td>
<td>4.10</td>
<td>.025</td>
<td>[-1.51, -0.28]</td>
</tr>
<tr>
<td>SIDE DOCKING VERSUS PERINEAL DOCKING</td>
<td>2.86</td>
<td>3.94</td>
<td>.016</td>
<td>[-1.68, -0.48]</td>
</tr>
<tr>
<td>RUNNING AN EFFICIENT OR</td>
<td>2.84</td>
<td>3.67</td>
<td>.03</td>
<td>[-1.46, -0.20]</td>
</tr>
<tr>
<td>SUTURING</td>
<td>3.46</td>
<td>4.06</td>
<td>.075</td>
<td>[-1.34, 0.15]</td>
</tr>
<tr>
<td>PELVIC VESSEL SEALING</td>
<td>3.29</td>
<td>3.96</td>
<td>.018</td>
<td>[-1.06, -0.20]</td>
</tr>
<tr>
<td>COMPLEX CASES</td>
<td>2.55</td>
<td>3.35</td>
<td>.025</td>
<td>[-1.36, -0.24]</td>
</tr>
<tr>
<td>4TH ARM UTILIZATION</td>
<td>3.13</td>
<td>4.00</td>
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<tr>
<td>ADVANCED ENERGY USE</td>
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<td>3.95</td>
<td>.01</td>
<td>[-1.10, -0.44]</td>
</tr>
<tr>
<td>PELVIC LYMPH NODE DISSECTION</td>
<td>2.97</td>
<td>3.85</td>
<td>.023</td>
<td>[-1.47, -0.30]</td>
</tr>
<tr>
<td>PARA-AORTIC LYMPH NODE DISSECTION</td>
<td>2.16</td>
<td>3.29</td>
<td>.027</td>
<td>[-1.94, -0.31]</td>
</tr>
<tr>
<td>COMPLICATIONS &amp; MANAGEMENT</td>
<td>2.43</td>
<td>3.48</td>
<td>.004</td>
<td>[-1.34, -0.76]</td>
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<tr>
<td>TROUBLESHOOTING</td>
<td>2.44</td>
<td>3.79</td>
<td>.001</td>
<td>[-1.52, -1.20]</td>
</tr>
</tbody>
</table>

*Confidence level based on 5-point scale

2603 - Poster Session

Gynecology oncology inpatient emergency simulations to improve patient outcomes
C. Lewis, V. Archer, C. Proctor and E. Marko. Inova Fairfax Hospital, Falls Church, VA, USA

Objective: We sought to determine the effectiveness of mock rapid-response simulation scenarios in gynecologic oncology inpatient emergencies to improve team confidence, knowledge, and responsiveness to improve patient outcomes.

Method: A prospective pre- and post-educational study was performed with 3 simulated scenarios of inpatient gynecologic oncologic emergencies: hypotension due to postoperative hemorrhage, pulmonary embolism, and neutropenic sepsis. Participants included multidisciplinary staff working on medical-surgical gynecologic oncology inpatient wards in a large northern Virginia hospital system. A moulaged manikin with high-fidelity vital signs was used for mock rapid-response in situ simulations. Participant data were statistically compared for pre- and post-curriculum differences including knowledge test, confidence survey, and team performance assessments based on validated checklists. Clinical impacts were measured through hospital patient safety data before and after the curriculum was initiated.

Results: Seventeen multidisciplinary participants participated in 4 mock rapid-response events over 3 months. In each scenario, statistically significant improvement was found in knowledge, confidence, and team performance (Table 1). The most significant team improvements were seen with the sepsis scenario. During the study period hospital-wide patient safety data demonstrated a reduction in both intensive care unit (ICU) stays and mortality rates for sepsis. Course evaluations were overwhelmingly positive, and team members thought the mock codes were very valuable.
Conclusion: Simulation is an effective method for preparing multidisciplinary teams to respond to gynecologic oncology inpatient emergencies. This is an ongoing study, and initial results indicate that mock codes may result in earlier recognition and management of inpatient gynecologic oncology emergencies resulting in reduced morbidity and mortality.

Table 1. Data Summary for Gynecologic Inpatient Emergency Simulations

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Pre-Test</th>
<th>Post-Test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension Scenario</td>
<td>45%</td>
<td>92.5%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Participant Knowledge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Confidence</td>
<td>2.05</td>
<td>1.43</td>
<td>0.0005</td>
</tr>
<tr>
<td>Team Performance</td>
<td>72.5%</td>
<td>85.42%</td>
<td>0.0204</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Pre-Test</th>
<th>Post-Test</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Pulmonary Embolus Scenario</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Knowledge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Confidence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Team Performance</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Pre-Test</th>
<th>Post-Test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis Scenario</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Knowledge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Confidence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Team Performance</td>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Impacts</th>
<th>Pre-Curriculum</th>
<th>Post-Curriculum</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU Days for Sepsis</td>
<td>11.88</td>
<td>5.86</td>
<td>0.005</td>
</tr>
<tr>
<td>Sepsis Mortality</td>
<td>17.24%</td>
<td>7.14%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

2604 - Poster Session
A hands-on training course for cervical cancer screening and management of pre-invasive disease in Lesotho, africa
N. Phoolcharoen, E. Baker, M. Lopez, P. Bonongwe, S.G. Parra, J. Carns, K. Cherry, M.F. Munsell, J. Thomas, C. Smith, R. Richards-Kortum, C. Lorenzoni, M.P. Salcedo and K.M. Schmeler. aGynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, bChulalongkorn University, Bangkok, Thailand, cThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, dMalawi college of medicine, Blantyre, Malawi, eRice University, Houston, TX, USA, fMaputo Central Hospital, Maputo, Mozambique

Objective: Southern Africa has the highest age standardized rate of cervical cancer in the world (43.1 per 100,000 women). There is an urgent need to provide quality care for women with cervical precancerous and cancerous lesions in this region. Our objective was to provide introductory training to health care providers from the region to perform screening, diagnosis, and management of cervical dysplasia.

Method: In July 2018, JHPIEGO, MD Anderson, and Rice University held a training course at the African First Ladies 12th Stop Cervical, Breast & Prostate Cancers in Africa Conference in Maseru, Lesotho. The course included lectures and hands-on training using simulation models to improve knowledge and demonstrate skills needed for screening, diagnosis, and management of cervical dysplasia. The training included didactic lectures and hands-on training stations for visual inspection with acetic acid (VIA), HPV testing, cryotherapy, colposcopy, cervical biopsy, and loop electrosurgical excision procedure.
(LEEP). Pre- and post-course knowledge was evaluated, and the data were collected in the Research Data Capture (REDCap) system.

**Results:** There were 92 participants from all 10 districts of Lesotho (nurses, physicians, and other health care professionals) and 10 International Gynecology Cancer Society (IGCS) gynecologic oncology fellows and mentors from 3 African countries. The 10-question knowledge assessment evaluated cervical and breast cancer prevention knowledge. The mean scores, pre 4.35, and post 7.64, demonstrated a 76% improvement. From observations and debriefing, participants and facilitators were satisfied with the course.

**Conclusion:** The technical update with practical demonstration improved basic knowledge on cervical cancer screening and diagnosis. However, long-term partnerships and ongoing learning and mentoring programs are necessary to translate knowledge into practice and sustain health care provider capabilities and skills in low-resource settings.

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**2605 - Poster Session**

**Multiprofessional approach in advanced cervical cancer as a prognostic factor in survival - exenterative surgery and chemotherapy with bevacizumab**

J.S. Silva. State University of Amazon, Manaus, Brazil

**Objective:** We sought to demonstrate the good results in patients with advanced and metastatic colorectal cancer after a good interprofessional relationship and protocol in the ducts to the line of systemic therapy.

**Method:** The purpose of this study was to report all stages of evolution and conduct of the patient with advanced cervical cancer, from diagnosis to total pelvic exenteration and subsequent failure of control in the metastatic phase, and the response to systemic therapy with bevacizumab.

**Results:** A 55-year-old obese patient from the northern region of Brazil, hypertensive and diabetic, diagnosed in 2009 with a finding of CIN III by colpocitological examination, was submitted to conization in the same year, confirming the diagnosis with free margins. In 2012, because of the persistence of a high-grade lesion, the patient underwent an enlarged total hysterectomy associated with bilateral anexectomy, and was confirmed as a scale-cell carcinoma (SCC) with 1-cm diameter and free margins (FIGO stage IB1) but with pelvic lymph node disease without evaluation of the retroperitoneum, followed afterward for external radiotherapy with chemosensitization concomitant with platinum and brachytherapy for treatment consolidation. In 2014, it evolved with acute renal failure due to central recurrence and bilateral parametrial infiltration that was spontaneously resolved after vesico-vaginal fistula and indication of supra-elevating total pelvic exenteration and reconstruction in double-barrelled wet colostomy, evolving without complications to hospital discharge in 7 days. In 2016, it presented a new recurrence located in the vaginal dome, pelvic floor, and mediastinum, identifying systemic dissemination by PET-CT. As a therapeutic approach, it was decided to initiate palliative chemotherapy with bevacizumab, presenting complete response of the metastatic lesions. Patient currently remains asymptomatic and in clinical follow-up, with only nonobstructive bilateral renal lithiasis and no uretero-hydronephrosis. See Figure 1.

**Conclusion:** Although in the advanced stages of cervical cancer there are few treatment options and the prognosis is poor, the literature shows that when bevacizumab is added, there is an increase in clinical benefit of 67% in a population previously treated for persistent and metastatic disease. In addition to clinical stability, imaging tests (PET-CT) for follow-up of the patient showed control of the metastatic activity of the disease after the addition of the chemotherapeutic agent. Patients diagnosed with cervical cancer at an advanced or recurrent stage, regardless of financial resources, present an OS of approximately 12 months, although there was no difference in the impact on quality of life. This report shows the survival and quality of life far superior to the published statistics, since it has already been asymptomatic for 2 years and with no signs of disease.
Objective: Optimal adjuvant treatment of patients with FIGO 2009 stage IB grade 2 or 3 endometrioid endometrial cancer (EEC) is controversial. We sought to assess the outcomes of patients with FIGO 2009 stage IB grade 2 or 3 EEC treated with comprehensive surgical staging (CSS) and vaginal brachytherapy (VBT) as sole adjuvant treatment.

Method: Stage IB grade 2 or 3 EEC patients treated with VBT following CSS at an academic institution from 2005 to 2017 were retrospectively reviewed. Patients who had received pelvic radiotherapy, chemotherapy, or hormonal therapy in combination with VBT were excluded. Pearson χ² test was used to compare patients with grade 2 versus grade 3 with respect to clinicopathological variables. OS and DFS were calculated with the Kaplan-Meier estimator. Multivariable Cox proportional hazards regression was used to analyze factors associated with OS and DFS.

Results: Included were 111 patients with grade 2 (n = 82) or grade 3 (n = 29) EEC. The median age at diagnosis was 67 years (range 30–94 years). Pelvic lymph node (LN) dissection was performed in 98.2% (n = 109; median LNs dissected, 17; 79.3%, n = 88, had ≥10 LNs removed). With a median follow-up of 36 months, the 3-year OS and DFS were 89.6% and 90.1%, respectively. Of 17 total recurrences, three were isolated locoregional failures (1 distal vagina, 1 pelvic sidewall and vaginal...
cuff, and 1 pelvic sidewall), and 14 had a distant component. Median time to recurrence was 25.5 months (range 11–51 months): 94.1% (n = 16) of those with a recurrence had lower uterine segment involvement (LUSI), and 76.5% (n = 13) had invasion of the outer third of the myometrium. LUSI (P = 0.031), tumor size larger than 4 cm (P = 0.024), and fewer than 10 LNs removed (P = 0.031) were significantly associated with reduced DFS on multivariate analysis (MVA). Larger tumor size (P = 0.001) and higher nuclear grade (P = 0.005) were associated with poorer OS on MVA. There were no differences in DFS or OS between grade 2 and grade 3.

**Conclusion:** We found overall excellent outcomes for surgically staged FIGO stage IB grade 2 or grade 3 EEC patients treated with VBT alone. Adjuvant VBT should be considered among the options of treatment for this population, particularly in patients without additional adverse risk factors (i.e., LUSI, tumor size >4 cm) who have ≥10 LNs removed.

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**2607 - Poster Session**

**Early-stage endometrial cancer with lymphovascular space invasion: Chemotherapy improves progression free survival and reduces distant metastases**


**aJohns Hopkins Hospital, Baltimore, MD, USA, bJohns Hopkins School of Medicine, Baltimore, MD, USA, cThe Cleveland Clinic Foundation, Cleveland, OH, USA, dCleveland Clinic, Cleveland, OH, USA, eUniversity of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, fThe University of Oklahoma, Stonewick Cancer Center, Oklahoma City, OK, USA, gUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, hMayo Clinic, Rochester, MN, USA, iUniversity of Virginia Health System, Charlottesville, VA, USA, jDuke University Medical Center, Durham, NC, USA, kDuke University School of Medicine, Durham, NC, USA, lWashington University School of Medicine in St. Louis, St. Louis, MO, USA, mUniversity of Cincinnati Academic Health Center, Cincinnati, OH, USA, nUniversity of Cincinnati, UC Health Medical Arts Building, Cincinnati, OH, USA**

**Objective:** Lymphvascular space invasion (LVI) is a risk factor for lymph node involvement, recurrence, and poor survival in early-stage endometrial cancer. The optimal treatment for patients with LVI is unknown. We aimed to determine the recurrence and survival outcomes of patients with stage I and II endometrial endometrioid carcinoma (EEC) and LVI treated with observation (OBS), radiation alone (RAD), or chemotherapy (CHEMO) with or without RAD after surgery.

**Method:** This is a multiinstitutional, retrospective cohort study of women with FIGO stage IA, IB, or II EEC with LVI who underwent hysterectomy and staging from 2005 to 2015 and received either OBS, RAD (vaginal brachytherapy or whole pelvic), or CHEMO ± RAD after surgery. Data were analyzed using Kaplan-Meier estimates and Cox proportional hazards models.

**Results:** In sum, 478 patients were identified. Median patient age was 64 years, and median follow-up period was 50.3 months. After surgery, 103 (21.5%) patients received CHEMO ± RAD, 232 (48.5%) received RAD, and 143 (30%) had OBS. No differences were noted in patient age, race, BMI, tumor size, and number of lymph nodes among the cohorts. Both CHEMO and RAD had more stage II disease compared to the OBS cohort (P < 0.01), and more grade 3 tumors were present in the CHEMO (43.7%) compared to the RAD (25.4%) or OBS (14.7%) cohorts (P < 0.001). There were 101 recurrences diagnosed with 16.8%, 43.6%, and 39.6% of patients in the CHEMO, RAD, and OBS groups, respectively (P = 0.02). Patterns of recurrence differed by treatment with the lowest rate of distant/multisite recurrence in CHEMO (5.9%) compared to RAD (18.2%) and OBS (22.5%) cohorts (global P = 0.02). Further, PFS (P = 0.02) differed by adjuvant treatment (Figure 1). On multivariate analysis, patients treated with CHEMO had the lowest hazard of progression (HR = 0.19, 95% CI 0.09–0.39), with those receiving RAD also reducing the risk of progression (HR = 0.35, 95% CI 0.21–0.59) compared to OBS (ref).

**Conclusion:** Systemic chemotherapy with or without radiation postoperatively may be associated with improved recurrence and survival outcomes for early-stage EEC with LVI compared to OBS or RAD. Larger, prospective trials are needed to confirm these findings.
Fig. 1. Progression-Free Survival