Abstracts Presented for the 47th Annual Meeting of the Society of Gynecologic Oncology

Opening Scientific Plenary Session I
Saturday, March 19, 2016
Moderators: Sang Ryu, MD, *Korea Cancer Center Hospital, Seoul, South Korea*
Kathleen N. Moore, MD, *The University of Oklahoma, Oklahoma City, OK, USA*

1 - Scientific Plenary
Mutations in homologous recombination genes and response to treatment in GOG 218: An NRG Oncology study
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Objectives: Gynecologic Oncology Group (GOG) 218 was a phase III, randomized trial of advanced primary ovarian, fallopian tube, and peritoneal carcinoma (OC), examining the role of adding bevacizumab to every-21-day carboplatin and paclitaxel. Our objective was to examine whether mutations in homologous recombination (HR) genes affect response to treatment.

Methods: We sequenced germline (from blood) and/or somatic (from neoplastic tissue) DNA from 1,195 women enrolled in GOG 218 using the targeted capture and multiplex sequencing assay BROCA-HR. Defects in HR were defined as damaging germline or somatic mutations in 16 genes predicted to affect HR, including *BRCA1*, *BRCA2*, and others. Proportional hazards models were used to provide estimates of relative hazards for progression-free survival (PFS) and overall survival (OS).

Results: Of 1,195 women with OC, germline or somatic mutations were identified in 148 (12.4%) patients with *BRCA1*, 78 (6.5%) with *BRCA2*, and 81 (6.8%) with other, non-*BRCA* HR genes. Total mutation frequency (all genes) in those with high-grade serous histology was 27.0% (262/971), but this was not significantly higher than the mutation frequency in endometrioid (10/42, 23.8%), clear cell (6/28, 21.4%), or unspecified carcinoma (20/90, 22.2%). Median PFS and OS by group were as follows: *BRCA1*: 15.7 and 55.3 months; *BRCA2*: 21.6 and 75.2 months; non-*BRCA* HR: 16.0 and 56.0 months; and no mutation: 12.6 and 42.1 months. Adjusting for treatment, stage, residual disease, and performance status, hazards for progression and death compared with those without mutations were significantly lower for those with mutations, specifically *BRCA1* mutations (HR 0.80, 95% CI 0.66–0.97, $P = .02$ for PFS; HR 0.74, 95% CI 0.59–0.94, $P = .01$ for OS), *BRCA2* mutations (HR 0.52, 95% CI 0.40–0.67, $P < .0001$ for PFS; HR 0.36, 95% CI 0.25–0.53, $P < .0001$ for OS), and non-*BRCA* HR mutations (HR 0.73, 95% CI 0.57–0.94, $P = .01$ for PFS; HR 0.67, 95% CI 0.49–0.90, $P = .007$ for OS). The analysis of PFS and OS by mutation status and treatment arm is under way.

Conclusions: Women with OC with either germline or somatic mutations affecting HR had significantly longer PFS and OS than those without mutations. Histology was not predictive of mutation status. The effect of mutation status on response by treatment arm will be presented.

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2 - Scientific Plenary
Homologous recombination deficiency score shows superior association with outcome compared with its individual score components in platinum-treated serous ovarian cancer
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Objectives: Response to DNA-damaging agents, such as platinum, is associated with defects in the homologous recombination (HR) pathway. Recently, an HR deficiency (HRD) score has been developed as the sum of 3 independent measures of HRD: loss of heterozygosity (LOH) score, telomeric-allelic imbalance (TAI) score, and large-scale state transitions (LST) score. Previous studies have suggested that the combined HRD score is a more powerful

prognostic marker than any of the individual components. Here, we present the first direct evaluation of the combined score and the individual score components in platinum-treated serous ovarian cancer (SOC).

Methods: An HRD threshold was previously developed in a training cohort of chemotherapy naïve ovarian and breast tumors using a cutoff of 95% sensitivity to detect *BRCA1/2*-deficient tumors. Tumors with a high HRD score (≥42) were defined as HR deficient. A threshold for each HRD component was determined using the same training cohort, with a cutoff of 95% sensitivity (LOH ≥8, TAI ≥10, LST ≥18). Cox proportional hazards models stratified by cohort were applied in a retrospective analysis of 859 samples from 4 independent studies examining the use of platinum agents in SOC. The dichotomized scores (high, low) were tested individually and then compared with the combined HRD score in bivariate models.

Results: The combined HRD score predicted PFS ($P = 2.2 \times 10^{-6}$) and OS ($P = 1.0 \times 10^{-8}$) in the combined platinum-treated cohorts. Although the individual component scores were also associated with progression-free and overall survival, the combined HRD score was more significant. In a bivariate analysis of HRD with each component, none of the individual component scores reached significance for either progression-free or overall survival (Table 1), whereas the HRD score adds significantly to each of the individual scores.

Conclusions: This analysis demonstrates that HRD is a superior predictor of outcome in platinum-treated SOC than any of the individual score components (LOH, TAI, LST).

Table 1
Bivariate analysis of dichotomous scores in model of PFS and OS.

	PFS		OS	
High/Low	**P Value**	**Hazard Ratio**	**P Value**	**Hazard Ratio**
HRD	0.0089	0.72	2.2x10-4	0.60
LOH	0.34	0.89	0.39	0.89
HRD	0.0073	0.68	0.0032	0.62
TAI	0.79	0.96	0.36	0.87
HRD	0.045	0.73	0.0082	0.62
LST	0.36	0.87	0.42	0.88

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3 - Scientific Plenary

Efficacy and safety of trabectedin or dacarbazine for the treatment of patients with uterine leiomyosarcoma after prior chemotherapy: A subgroup analysis of the randomized phase 3 SAR-3007 study

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Objectives: In ET743-SAR-3007, the efficacy of trabectedin in patients with advanced leiomyosarcoma (LMS) or liposarcoma (LPS), after chemotherapy failure, was compared with the active comparator dacarbazine. As reported, trabectedin exhibited improved disease control with median progression-free survival (PFS) of 4.2 months (vs 1.5 months for dacarbazine) (HR 0.55; $P < .0001$), with similar efficacy in both LMS and LPS cohorts. An analysis was conducted to assess the efficacy and safety of trabectedin or dacarbazine in the largest subgroup of the study, the 232 women with uterine LMS, who comprised 40.2% of the study participants.

Methods: In this multicenter phase-3 study, patients were randomized (2:1) to receive trabectedin by 24-hour intravenous infusion (n = 384) or dacarbazine by 1-hour intravenous infusion (n = 193), once every 3 weeks. The primary endpoint was overall survival (OS). Secondary endpoints were PFS, time to progression, objective response rate, duration of response, symptom severity, and safety.

Results: A total of 232 patients with uterine LMS were randomized (trabectedin: 144; dacarbazine: 88) and all were included in this analysis. Baseline disease characteristics were well-balanced between the 2 treatment arms: ECOG performance status 0 (trabectedin: 48% vs dacarbazine: 47%); prior anticancer therapies (surgery [trabectedin: 97%

vs dacarbazine: 97%]); radiation (trabectedin: 49% vs dacarbazine: 36%); and median lines of previous chemotherapy (trabectedin: 3 vs dacarbazine: 3). The median number of study drug treatment cycles received in the trabectedin group was double that of the dacarbazine group (median trabectedin: 4 vs dacarbazine: 2), with greater proportion of patients receiving 6 or more treatment cycles (trabectedin: 39.3% vs dacarbazine: 18.5%). A significant improvement in PFS was observed in the trabectedin group (trabectedin: 4.0 vs dacarbazine: 1.5 months; HR 0.576, 95% CI 0.41–0.81, *P* = .0012). More patients achieved partial response (trabectedin: 15 [11%] vs dacarbazine: 7 [9%]). OS was similar (HR 0.899, 95% CI 0.65–1.24, *P* = .5107), with median OS of 13.4 months (trabectedin) vs 12.9 months (dacarbazine). Most patients in both treatment arms received postprotocol systemic therapies (trabectedin: 76%, dacarbazine: 75%). Toxicities were consistent with the well-characterized profiles of both treatments.

Conclusions: Among patients with uterine LMS, treatment with trabectedin resulted in superior disease control, with significantly longer PFS compared with dacarbazine. The efficacy and toxicity profiles of trabectedin in uterine LMS patients were similar to the profiles of the overall study population.

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4 - Scientific Plenary

Personalized circulating tumor DNA biomarkers dynamically predict treatment response and survival in gynecologic cancers

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Objectives: The measurement of circulating tumor DNA (ctDNA), the so-called "liquid biopsy," represents a powerful emerging technology capable of providing accurate assessment of both tumor behavior and disease burden. We sought to explore the usefulness of ctDNA as both a surveillance and prognostic biomarker in gynecologic cancers and to compare ctDNA efficiency, sensitivity, and lead time against serum CA-125 values and computed tomography (CT) scans.

Methods: Forty-four patients were enrolled for this institutional review board–approved study, including 27 patients with high-grade serous carcinoma (HGSC; ovary, peritoneal, and fallopian tube) and 17 with uterine cancer (UCEC). All UCECs were high-grade with only one exception. Serum and tumor samples were collected at the time of surgery and then throughout the treatment course. Patient/tumor-specific mutations were identified using whole-exome and targeted gene sequencing. ctDNA levels were quantified using droplet digital polymerase chain reaction (PCR) and correlated with clinical disease status, CA-125 levels, CT results, surgical findings, and progression-free (PFS) and overall survival (OS).

Results: Tumor-specific mutations were identified in 36 of 44 patients (28/36 from targeted sequencing, 8/8 by WES). Droplet digital PCR assays meeting QC were generated for 32 patients (19 with HGSC and 13 with UCEC). ctDNA was detected in 93.8% of patients, and sensitivity and specificity were highly correlated with CA-125 and CT scanning, with a number of interesting exceptions. Specifically, in 6 patients with negative CT scans, ctDNA identified the presence of cancer. All were later found to have cancer. On average, ctDNA had a predictive lead time of 7 months (range, 1–11 months) over CT imaging. Most notably, undetectable levels of ctDNA at the completion of primary therapy were associated with markedly improved PFS (*P* = .0048) and OS (*P* = .0194).

Conclusions: Detection of residual disease represents a diagnostic dilemma and potential critical inflection point in precision medicine. We demonstrate for the first time that personalized ctDNA biomarkers in gynecologic cancers can detect the presence of residual tumor earlier than currently used serum and imaging studies and are an independent predictor of survival. Ultimately, these studies open the door for clinical studies to define the usefulness of ctDNA as a surveillance tool in gynecologic cancers.

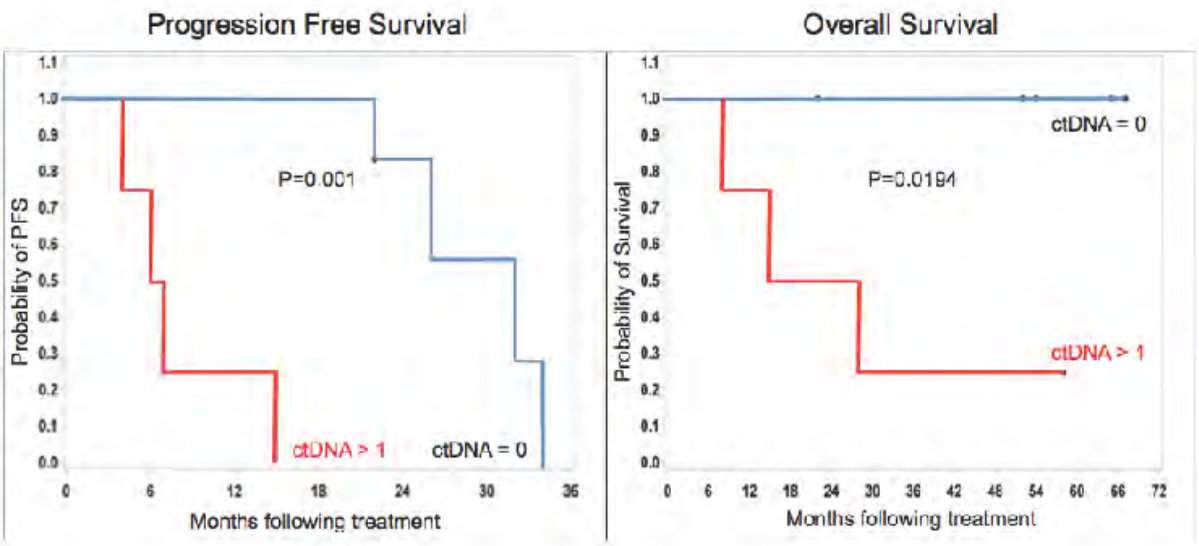

Fig. 1
Progression Free Survival vs. Overall Survival.

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5 - Scientific Plenary
Variations in HPV vaccination rates of adolescent and young adult females by provider specialty
M.B. Wilbur, M. Clarke, B. Chou and D. Phelan-Emrick. *Johns Hopkins Hospital, Baltimore, MD, USA*

Objectives: To quantify human papillomavirus (HPV) vaccine initiation and completion rates for 10- to 26-year-old females in a major metropolitan area and determine the association between HPV vaccination and provider specialty.

Methods: Data from the electronic health records of a large affiliated academic community were collected. All clinic visits for females ages 10 to 26 years between 2006 and 2013 were queried. Data on patient age, race, insurance type, clinic location, and provider were extracted from the electronic health records. The exposure was HPV vaccination and the outcome of interest was the specialty of the listed provider. Logistic regression analysis was used to look at associations of HPV vaccine initiation and completion by provider specialty, controlling for age, race, and insurance type.

Results: A total of 49,709 girls were seen at least once at a clinic site during the study period. Females were excluded from the analysis if they were pregnant or had previously received the vaccine at an outside location, and were not "at risk" for the exposure of interest. This left 47,075 females eligible for HPV vaccine initiation. A total of 11,812 (25.1%) females were vaccinated. Of these, 9,558 (20.1%) received the second shot in the series and 7,059 (15%) completed the 3-shot series. For females initiating the HPV vaccination, the ordering providers varied by specialty. With family practice providers as referents, pediatricians (OR 1.41) and internal medicine/pediatricians (OR 1.51) were more likely to initiate vaccination, whereas obstetrician/gynecologists (OR 0.47) and internal medicine specialists (OR 0.46) were less likely to do so. Similarly, compared with family practitioners, females seen by pediatricians (OR 1.53) and internal medicine/pediatricians (OR 1.09) were more likely to complete the vaccine series than those seen by obstetrician/gynecologists (10.6%, OR 0.67) and internal medicine practitioners (OR 0.66).

Conclusions: The overall HPV vaccine initiation rate of young females seen at this large affiliated multisite academic community was low (25.1%), with only 15% completing the vaccine series overall. Obstetrician/gynecologists and internal medicine providers were less likely to order the HPV vaccine than their pediatrics and family practice colleagues. Studies to determine patient and health care provider–related barriers to HPV vaccine administration are warranted.

Scientific Plenary II: Moving targets; Defining pathways in gynecologic cancers
Saturday, March 19, 2016
Moderators: Tashanna K. N. Myers, MD, *Baystate Medical Center/Tufts University School of Medicine, Springfield, MA, USA*
Ronald D. Alvarez, MD, *University of Alabama at Birmingham, Birmingham, AL, USA*

6 - Scientific Plenary
Limited access safety lead-in of the MEK inhibitor trametinib in combination with GSK2141795, an AKT inhibitor, in patients with recurrent or persistent endometrial cancer: A Gynecologic Oncology Group study
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Objectives: Endometrial cancer has multiple molecular aberrations, especially in the PI3K and RAS pathways. Single-agent activity for agents targeting these pathways has been modest, potentially because of resistance caused by cross-talk. We sought to determine safety and preliminary efficacy of the MEK inhibitor trametinib, combined with the AKT inhibitor GSK2141795, in patients with endometrial cancer.

Methods: Patients with measurable recurrent or persistent endometrial cancer were eligible. One to two prior cytotoxic regimens were allowed, but prior use of a MEK or PI3K pathway inhibitor was prohibited. The initial trial was a *KRAS* mutation–stratified randomized phase 2 design, with a safety lead-in evaluating the combination. For the safety lead-in, the recommended phase 2 dose (trametinib 1.5 mg, GSK2141795 50 mg) was dose level 1 (DL1). Agents were taken orally once daily; one cycle was 28 days.

Results: One of the 26 enrolled patients was ineligible because of pathology. Fourteen patients were treated at DL1 and 12 patients were treated at DL-1. Median age was 62 years (range, 29–80 years) and 54% had 2 prior therapies. Most common cell types were endometrioid (58%) and serous (27%). Four (16%) of 25 patients had *KRAS* mutations. Dose-limiting toxicities (DLTs) were assessed during cycle 1. DL1 had 8 DLTs: hypertension (n = 2), mucositis (n = 2), rash (n = 2), dehydration (n = 1), and acute kidney injury (n = 1). DL1 was deemed nontolerable, so a second dose level was explored (DL-1: trametinib 1.5 mg, GSK2141795 25 mg). No DLTs were seen at DL-1. Sixty-one percent of patients had grade 3 toxicity, including gastrointestinal (n = 8), hypoalbuminemia (n = 4), dehydration (n = 3), fatigue (n = 3), renal (n = 2), anemia (n = 2), anorexia (n = 2), edema (n = 2), infection (n = 2), nausea/vomiting (n = 2), hyperkalemia (n = 1), hypokalemia (n = 1), hyponatremia (n = 1), leukocytosis (n = 1), allergic reaction (n = 1), and vaginal fistula (n = 1). There were no responses in DL1 (0% 1-sided; 90% CI 0–15.2) and 1 response in DL-1 (8.3% 2-sided; 90% CI 0.4–33.9). Progression-free survival at 6 months was 14% for DL1, and has not been reached for DL-1 (Figure 1). No clinical benefit was seen in patients with *KRAS* mutations.

Conclusions: The combination of trametinib and GSK2141795 had high levels of toxicity in endometrial cancer at the original recommended phase 2 dose. A reduced dose was better tolerated, but the preliminary efficacy is inadequate to warrant further study. Analysis is ongoing to identify molecular correlates to clinical benefit.

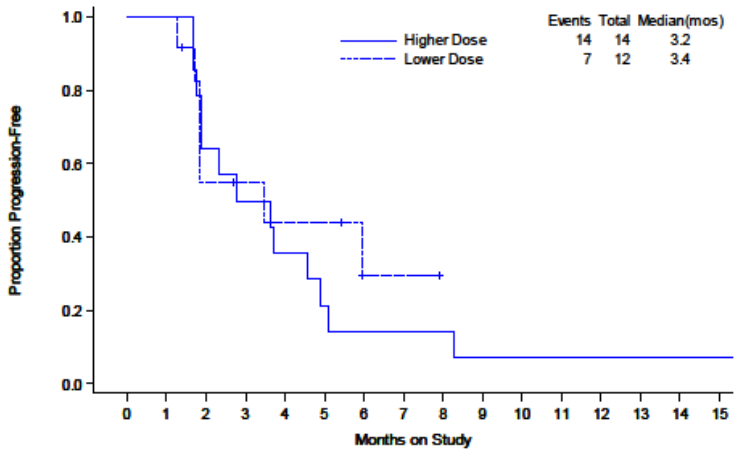

Fig. 1
Progression-Free Survival by Treatment Levels.

7 - Scientific Plenary

Two to tango: Biological activity and companion predictive markers for a novel dual AKT and P70S6K inhibitor in ovarian and uterine malignancies

R.A. Previs, G.N. Armaiz-Pena, C. Ivan, H.J. Dalton, J. Huang, J.M. Hansen, W. Hu, R.L. Coleman and A.K. Sood. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: Compensatory pathways and feedback loops activated by pharmacologic inhibition of AKT or TORC1 alone have tempered the clinical efficacy of these drugs. Here, we examined the biological effects of MSC2363318A, a novel dual inhibitor of AKT(1,3), and P70S6K.

Methods: In vivo (orthotopic murine models of ovarian and uterine cancer) and in vitro (MTT, Western blot analysis, and plasmid transfection) were used to determine the biological and mechanistic effects of MSC2363318A. High-throughput analyses (reverse-phase protein arrays [RPPA]) were carried out to identify underlying mechanisms and biomarkers of response.

Results: Single-agent MSC2363318A significantly decreased tumor growth and metastases in murine orthotopic models of ovarian (SKOV3ip1 and Igrov1) and uterine (Hec1a) cancer. Intrinsically, the agent reduced proliferation (Ki67) and angiogenesis (CD31) indices, and increased cell death (cleaved caspase 3) markers. Clinically relevant survival models were also investigated, and paclitaxel or bevacizumab were combined with MSC2363318A. Significantly prolonged overall survival (OS) was achieved with combination MSC2363318A and paclitaxel in the SKUT2 (endometrioid) uterine cancer mouse model ($P < .001$) (Figure). Regression and stabilization of established tumors in the Ishikawa (endometrioid) model was observed in mice treated with combination MSC2363318A and paclitaxel. Synergy between MSC2363318A and paclitaxel was identified in vitro in protected (IC50 ≥5 μM) cell lines. RPPA identified YAP1 as a candidate biomarker to predict cell lines that were most sensitive to MSC2363318A ($R = 0.675$, $P = .0015$). The effect of MSC2363318A on angiogenesis was further explored in combination experiments with bevacizumab. In an orthotopic ovarian cancer model (HeyA8), we observed robust tumor growth inhibition and less frequent metastasis. Because of the emergence of resistance to antiangiogenic therapy, a previously described novel murine ovarian cancer model of adaptive antiangiogenic resistance (SKOV3ip1-luciferase) was used to demonstrate resensitization to bevacizumab with the addition of MSC2363318A, resulting in improved OS ($P = .01$).

Conclusions: MSC2363318A has therapeutic efficacy in multiple preclinical models of ovarian and uterine cancer. These findings support clinical development of dual AKT/P70S6K inhibition.

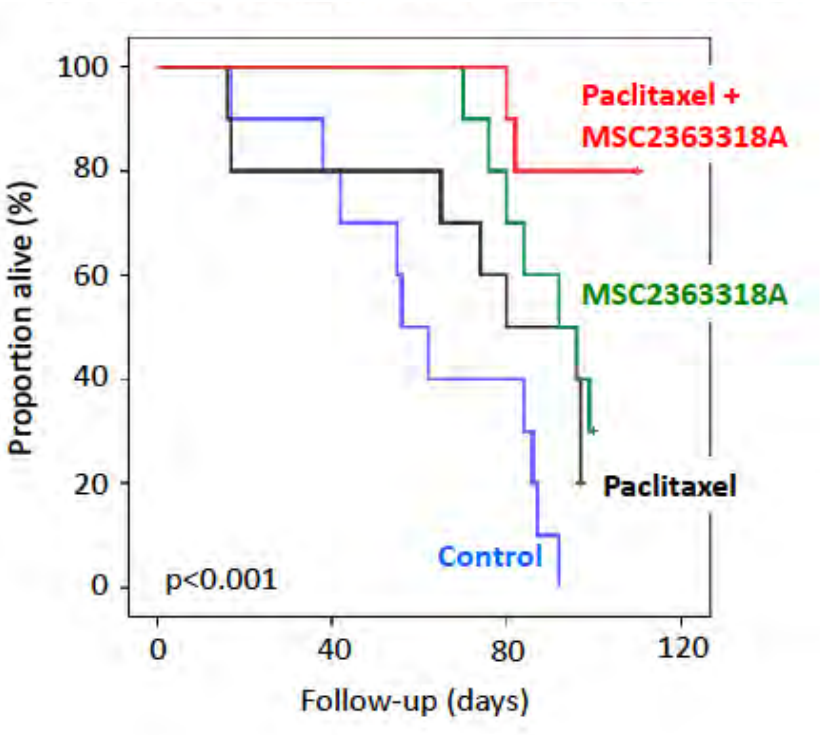

Fig. 1
Overall survival for MSC2363318A ± paclitaxel in a uterine orthotopic model of SKUT2.

8 - Scientific Plenary
PTEN loss predicts response to Notch pathway inhibition in endometrial cancer
J.M. Hansen, R.A. Previs, Y.A. Lyons, Y. Wang, C. Ivan, W. Hu, K.A. Baggerly and A.K. Sood. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: Previous work has shown nonoverlapping expression of the Notch and PI3K/AKT pathways in endometrial cancer. Here, we examined the clinical and biological relevance of Notch2, Notch3, and DLL3 alterations in endometrial cancer. Moreover, we tested the relevance of PTEN as a predictive marker for response to therapies targeting the Notch pathway. We hypothesized that loss of PTEN would lead to resistance to such therapies.

Methods: Clinical, gene expression, copy number, and exome sequencing data for patients with endometrial cancer were obtained from The Cancer Genome Atlas. Overall survival (OS) based on upregulation or amplification of Notch2, Notch3, and/or DLL3 was determined using log-rank tests. In vitro cell viability assays were performed after treating a panel of uterine cell lines with a monoclonal antibody (mAb) to Notch2 and Notch3. Using an in vivo uterine orthotopic PTEN-null model, mice were treated with the mAb to Notch2/3.

Results: Clinical, gene expression, copy number, and sequencing data were analyzed for 221 patients with endometrial cancer. Of these, 39 patients (18%) had upregulation or amplification of Notch2, Notch3, and/or DLL3. These patients had significantly shorter OS than the patients without upregulation or amplification of these genes (P = .003). In vitro, uterine cancer cell lines with PTEN loss (Ishikawa, SPEC-2) had increased cell viability after Notch2/3 inhibition compared with cell lines with intact PTEN expression (Hec1a, KLE). In vivo SPEC-2 (PTEN-mutant) tumor-bearing mice treated with Notch2/3 mAb showed no significant difference in tumor growth compared with controls.

Conclusions: Notch2, Notch3, and/or DLL3 upregulation or amplification in uterine cancer is associated with poorer survival. Consistent with our hypothesis, loss of PTEN function leads to resistance to in vitro and in vivo Notch inhibition and may serve as an important biomarker during further development.

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9 - Scientific Plenary
Endometrial cancer subtypes and immunotherapy: Is the immune microenvironment different in microsatellite instable endometrial cancer?
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Objectives: Tumors with microsatellite instability (MSI), including colorectal and gastric cancers, have shown increased immunogenicity and response to immunotherapy treatments compared with microsatellite-stable (MSS) tumors. The purpose of our study was to evaluate immune gene expression in high MSI (MSI-H) endometrial cancers (EC) compared with MSS ECs using data from The Cancer Genome Atlas (TCGA) and further validate the findings with immunohistochemistry (IHC).

Methods: Uterine TCGA data were used to study MSI-H ECs compared with MSS tumors. Differential gene expression was further investigated using the Ingenuity pathway analysis. Primary endometrioid EC tissues were identified from archived tumor bank specimens. MSI-H ECs (n = 37) were matched to MSS (n = 66) tumors by grade, stage, age, and body mass index (BMI). IHC analysis was conducted on formalin-fixed, paraffin-embedded EC sections using a multiplex staining system with anti-granzyme B antibodies for activated cytotoxic T lymphocytes (CTL) and nuclear staining with DAPI. The percentage of positive intratumoral cells was calculated and compared quantitatively with an automated imaging system. Statistical analysis was performed using STATA software. Nonparametric Mann-Whitney test was used to determine differences in activated CTLs; $P < .05$ signified statistical significance.

Results: Using TCGA data, MSI-H (n = 118) EC showed overall activation of the granzyme B signaling pathway compared with MSS (n = 160) EC (P = .002) along with upregulation of granzyme B in MSI-H tumors. Of the MSI-H cases included for IHC analysis, 32 (86%) showed loss of MLH1 by promoter methylation and 5 (14%) were identified as Lynch syndrome with germline defects in MSH2. There was no significant difference in age, stage, grade, or BMI between the groups. MSI-H tumors demonstrated 1.12% positive intratumoral staining for granzyme B compared with 0.60% in MSS tumors (P = .62).

Conclusions: Uterine TCGA data demonstrated increased expression of granzyme B in MSI-H tumors, suggesting activation of CTLs. Based on our findings, we will initiate a MSI-H–stratified clinical trial of immune checkpoint inhibition. Additional studies are also ongoing using a large panel of immune cell markers to further investigate differences in the immune microenvironment of MSI-H compared with MSS EC.

10 - Scientific Plenary

GOG 186H: A randomized phase II evaluation of weekly paclitaxel versus weekly paclitaxel with oncolytic reovirus (Reolysin) in the treatment of recurrent or persistent ovarian, fallopian tube, or primary peritoneal cancer

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Objectives: To assess whether the addition of oncolytic reovirus (Reolysin) to weekly paclitaxel treatment prolonged progression-free survival (PFS) in women with recurrent or persistent ovarian, tubal, or primary peritoneal cancer.

Methods: This phase IIB trial randomized patients to: (1) paclitaxel 80 mg/m^2 on days 1, 8, and 15, versus (2) paclitaxel plus Reolysin 3×10^{10} $TCID_{50}$ per day intravenously on days 1 to 5, both regimens every 4 weeks. The primary endpoint was PFS. The study was designed to detect a HR of 0.625 with 80% power. The maximum sample size of the study was 110 patients.

Results: The study enrolled 108 patients (54 in each arm), with PFS events seen in 91 patients. In this pretreated population (with >40% of patients having received 2 prior regimens for recurrence), 42% of cases had previously received bevacizumab. Platinum-resistant disease was present in 67% of cases, with 24% having recurrence between 6 and 12 months from prior platinum exposure. There was no significant relationship between treatment-related deaths and treatment group, with a HR of 1.11 (95% CI, 0.78–1.59, *P* = .687 when stratified by measurable disease and platinum-free interval). There was no significant relationship between overall survival and treatment group, with a HR of 0.945 (95% CI, 0.625–1.428, *P* = .823, with no significant change when stratified by measurable disease). The proportion responding on the Reolysin arm was 17%, whereas the proportion responding on the paclitaxel alone arm was 20% (OR 0.84, 90% exact CI 0.30–2.33). In addition, the proportion of patients showing a CA-125 response was just over 30% for each treatment group. The 2 regimens were comparable in severe toxicities, though Reolysin administration appeared to be associated with severe neutropenia (grade ≥4) (12% vs 0%), and severe respiratory adverse events (grade ≥3) (25% vs 2%). No grade 5 deaths were considered treatment related.

Conclusions: Although the addition of Reolysin to weekly paclitaxel in the treatment of women with recurrent or persistent ovarian, tubal, or peritoneal cancer did not significantly change the toxicity profile of paclitaxel alone, it did not sufficiently reduce the hazard of progression or death to warrant further investigation.

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11 - Scientific Plenary

Genetic and therapeutic targeting of the receptor tyrosine kinase discoidin domain receptor 2 inhibits invasion and metastasis in ovarian cancer

L.M. Divine, W.R. Grither, A. Lohrey, E.H. Meller, A.R. Hagemann, P.H. Thaker, M.A. Powell, D.G. Mutch, G.D. Longmore and K.C. Fuh. *Washington University School of Medicine in St. Louis, St. Louis, MO, USA*

Objectives: A collagen-binding receptor tyrosine kinase, discoidin domain receptor 2 (DDR2), has been implicated in the regulation of breast and lung cancer metastasis and DDR2-dasatinib is a subarm in the National Cancer Institute's MATCH trial. Our objective is to evaluate the biological role of DDR2 in metastatic ovarian cancer.

Methods: Tumor specimens from tissue microarrays were evaluated for DDR2 expression with immunohistochemistry. Ovarian cancer cell lines, A2780 and ES2, were used. shRNA was used to genetically inactivate DDR2 (shDDR2) and scrambled control (shControl). Mesothelial clearance assays were performed using primary mesothelial cells and tumor cell spheroids. Matrigel invasion assays were performed. Xenograft models using A2780 shControl and shDDR2 cells were used. Western blot was performed to evaluate DDR2, SRC, E- and N-cadherin, and SNAIL expression. One-way analysis of variance and the Student unpaired *t* test were used to analyze data.

Results: High immunohistochemical expression of DDR2 was found in 28 (74%) of 38 advanced-stage, high-grade tumors, compared with 79 (44%) of 179 early-stage, high-grade tumors *P* < .0001. All metastatic tumor specimens had high DDR2 expression (n = 12). DDR2 was also found to regulate invasion and migration. Matrigel invasion assays showed a decrease in tumor cell invasion in shDDR2 compared with shControl in ES2 and A2780 cells (27 vs 110

cells/high power field [hpf], $P < .001$ and 23 vs 40 cells/hpf, $P = .0027$, respectively). Inhibition with dasatinib showed a significant decrease in invasion of shControl cells similar to shDDR2 ($P = .5925$). DDR2-mediated tumor cell invasion is associated with epithelial mesenchymal transition; DDR2-deficient cells had lower mesenchymal markers and higher epithelial marker (E-cadherin) expression compared with DDR2-expressing cells. In addition, an intraperitoneal A2780 xenograft model (n = 10 per group) showed that DDR2-deficient cells had significantly less tumor burden than DDR2-expressing cells (1.1 vs 2 g, $P = .01$).

Conclusions: DDR2 is highly expressed in advanced-stage ovarian cancer, and plays a significant role in clearance, migration, and invasion. Dasatinib inhibition of DDR2-expressing, SRC-independent tumor cell invasion suggests that DDR2 serves as a potential therapeutic target of dasatinib in ovarian cancer.

Surgical Forum
Saturday, March 19, 2016
Course Directors: Luis Chiva, MD, PhD, *MD Anderson International, Madrid, Spain*
Mario Leitao, MD, *Memorial Sloan Kettering Cancer Center, New York, NY, USA*
Xiaohua Wu, MD, *Fudan University Shanghai Cancer Center, Shanghai, China*

12 – Surgical Forum
The laparoscopic perspective of the Querleu-Morrow classification system of radical hysterectomy
R. Ribeiro[a], W. Kondo[b], J.C. Linhares[a], E. Leblanc[c] and D. Querleu[d]. *[a]Erasto Gaertner Hospital, Curitiba, Brazil, [b]Sugisawa Hospital, Curitiba, Brazil, [c]Centre Oscar Lambret, Lille, France, [d]Institut Bergonié Cancer Center, Bordeaux, France*

13 – Surgical Forum
Nerve-sparing radical hysterectomy: Open and robotic approaches
N. Sakuragi. *Hokkaido University School of Medicine, Sapporo, Japan*

14 – Surgical Forum
Comprehensive therapeutic extraperitoneal aortic lymphadenectomy: Basic technique
K.A. O'Hanlan. *Laparoscopic Institute for Gynecology and Oncology, Portola Valley, CA, USA*

15 – Surgical Forum
Liver mobilisation and vascular isolation, diaphragmatic stripping and resection, periportal lymphadenectomy, liver resection
S. Misirlioglu[a], C. Taskiran[a], A. Alper[a], M. Kerem[b] and M. Arvas[c]. *[a]VKF Koc University School of Medicine/VKF American Hospital, Istanbul, Turkey, [b]Gazi University School of Medicine, Ankara, Turkey, [c]VKF American Hospital, Istanbul, Turkey*

16 – Surgical Forum
Minimally invasive staging for high grade serous ovarian cancer utilizing the newest robotic surgical platform, highlighting para-aortic lymph node dissection
V. Broach and M.M. Leitao. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

17 – Surgical Forum
Robotic radical trachelectomy in an early cervical cancer patient
H.J. Lee, J.Y. Park, S.W. Lee, D.Y. Kim, D.S. Suh, J.H. Kim, Y.M. Kim, Y.T. Kim and J.H. Nam. *University of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea*

18 – Surgical Forum
Laparoscopic bilateral pelvic lymphadenectomy for external iliac and obturator ovarian cancer recurrences extending to the inguinal lymph nodes
R. Ribeiro[a], A.T. Tsunoda[b], W. Kondo[c] and J.A. Guerreiro[a]. *[a]Erasto Gaertner Hospital, Curitiba, Brazil, [b]Barretos Cancer Hospital, Barretos, Brazil, [c]Sugisawa Hospital, Curitiba, Brazil*

Education Forum I: Current (Smoking Hot) Topics in Palliative Care
Saturday, March 19, 2016
Course Directors: Stephanie V. Blank, MD, *New York University School of Medicine, New York, NY, USA*
Kerri S. Bevis, MD, *University of Alabama at Birmingham, Birmingham, AL, USA*
Faculty: Carolyn J. Lefkowits, MD, MPH, *University of Colorado Denver, Aurora, CO, USA*
Christopher V. Lutman, MD, *Miami Valley Hospital South, Dayton, OH, USA*

19 - Education Forum

Room for improvement: An examination of advance care planning documentation among gynecologic oncology patients

A.J. Brown[a], M.J. Shen[b], D. Urbauer[a], J.S. Taylor[a], P. Parker[c], C. Carmack[a], L.S. Prescott[a], C.C.L. Sun[a], L.M. Ramondetta[a]and D.C. Bodurka[a]. *[a]The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [b]Weill Cornell Medical College, New York, NY, USA, [c]Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: To evaluate patients' knowledge regarding advance directives and patient completion rates of advance directives; and to examine the association between death anxiety, disease symptom burden, and patient initiation of advance directives.

Methods: One hundred and ten gynecologic cancer patients were surveyed regarding their knowledge and completion of advance directives. Patients also completed the MD Anderson Symptom Inventory (MDASI) scale and Templer's Death Anxiety Scale (DAS). Descriptive statistics were used to examine characteristics of the sample. The Fisher exact test and 2-sample *t* test were used to examine associations between key variables.

Results: Table 1 lists demographic data. The majority of patients had heard of "do not resuscitate" (DNR; 95%). Only 33% had completed a DNR order. Most had heard about living wills or medical power of attorney documents (75%). Only 49% had completed these documents. Of those receiving treatment, 33% had a DNR and 51% had completed a living will or medical power of attorney. A higher MDASI Interference Score was associated with patients being less likely to have a DNR ($P = .02$) and a living will or medical power of attorney ($P = .003$). A higher DAS score was associated with patients being less likely to have completed a living will or medical power of attorney ($P = .03$).

Conclusions: Most patients were familiar with advance directives, but less than half had created these documents. Among patients currently receiving treatment for a gynecologic cancer, few had an advance directive in place. Disease-related interference with daily activities and a higher level of death anxiety were associated with decreased rates of advance directive completion. These findings indicate that disease-related interference with daily activities and increased death anxiety may be barriers to advance care planning documentation. There is room to improve advance care planning documentation among gynecologic oncology patients. Providers must identify and address barriers to advance care planning documentation to assist patients with achieving their end-of-life care goals. Patients receiving active treatment for their cancer and those with increased disease symptom burden and death anxiety should be targeted for advance care planning discussions, because they may be less likely to engage in advance care planning.

Table 1

Demographic and Clinical Summary.

		N (%)
Age	N	110
	Mean (SD)	58.82 (12.06)
	Median	61
	Min - Max	24 – 82
Race	White	84 (76.36%)
	African American	4 (3.64%)
	Hispanic	18 (16.36%)
	Asian	3 (2.73%)
	Other	1 (0.91%)
Partnered Status	No Partner	37 (33.94%)
	Partner	72 (66.06%)
	Unknown/Missing	1
Associate Degree or Higher	Elementary, HS, GED	31 (28.18%)
	Associate, Undergraduate, Graduate	79 (71.82%)
Identify with a Religion	No	6 (5.45%)
	Yes	104 (94.55%)
Cancer Site	Ovarian	51 (46.36%)
	Uterine	38 (34.55%)
	Cervical	17 (15.45%)
	Vulvar/Vaginal	4 (3.64%)
Stage	Not Staged	12 (11.01%)
	Stage I	31 (28.44%)
	Stage II	9 (8.26%)

	Stage III	43 (39.45%)
	Stage IV	14 (12.84%)
	Unknown/Missing	1
Cancer Management	Surveillance	55 (50.00%)
	Primary/Recurrence	55 (50.00%)
Current Treatment	Current Treatment	55 (50.00%)
	No Treatment or Maintenance	55 (50.00%)
Heard about DNR	No	6 (5.45%)
	Yes	104 (94.55%)
Heard about Advance Directive	No	27 (24.77%)
	Yes	82 (75.23%)
	Unknown/Missing	1
Heard about Hospice	No	0 (0.00%)
	Yes	110 (100.00%)
Have DNR	No	74 (67.27%)
	Yes	36 (32.73%)
Have Advance Directive	No	56 (50.91%)
	Yes	54 (49.09%)
DNR in Medical Record	No	109 (99.09%)
	Yes	1 (0.91%)
Advance Directive in Medical Record	No	90 (81.82%)
	Yes	20 (18.18%)

Education Forum III: How to Define and Deliver Value-based Care in Gynecologic Cancer
Saturday, March 19, 2016
Course Directors: Laura J. Havrilesky, MD, *Duke University Medical Center, Durham, NC, USA*
Larissa Meyer, MD, *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*
Faculty: Jason Wright, MD, *Columbia University College of Physicians and Surgeons, New York, NY, USA*

20 – Education Forum
The ASCO Value Framework highlights relative value of treatment options in ovarian cancer
J.R. Foote, A.A. Secord and L.J. Havrilesky. *Duke University Medical Center, Durham, NC, USA*

Objectives: The American Society of Clinical Oncology (ASCO) Value Framework provides an objective measure that allows physicians and patients to compare the relative value of new treatments based on clinical benefit, toxicity, and costs. Our aim was to assess the value of 3 frontline ovarian cancer therapies using the ASCO Value Framework to determine the net health benefit (NHB) for each approach.

Methods: Using the 2015 ASCO Value Framework for assessment of cancer treatments and phase III randomized controlled clinical trial (RCT) data, the NHB for 3 frontline ovarian cancer treatment options were calculated: concurrent and maintenance bevacizumab, intraperitoneal (IP)/intravenous (IV) chemotherapy, and dose-dense paclitaxel. The ASCO Value Framework calculates the NHB using 4 criteria: clinical benefit based on improvement in overall survival or progression-free survival, toxicity difference, symptom palliation, and treatment-free interval. Clinical benefit calculation uses ASCO-assigned importance weights for OS and PFS. The maximum possible NHB points for each therapy is 130. NHB was presented alongside the drug-acquisition cost (DAC) of each therapy, as per ASCO's intended use of the value framework. We calculated a benefit-cost ratio of NHB points per additional dollars in treatment costs.

Results: The NHB of dose-dense paclitaxel (Japanese Gynecologic Oncology Group [JGOG] 3016) was 68 of 130 possible NHB points, with 9% more severe toxicities, at an additional cost of $355 per cycle for dose-dense therapy. IP cisplatin/IV+IP paclitaxel (Gynecologic Oncology Group [GOG] 172) received 32 NHB points, with 36% more severe toxicities, at an additional cost of $592 per cycle for outpatient IP chemotherapy. Concurrent plus maintenance bevacizumab received 22 NHB points, with 18% more severe toxicities, at an additional cost of $6,678 per cycle (GOG 218) or 11 NHB points/$3,385 per cycle (ICON 7). The ratios of NHB points per dollar cost were: 0.19 for dose-dense paclitaxel (highest value), 0.05 for IP chemotherapy, and 0.003 for bevacizumab (lowest value) (see Figure).

Conclusions: Using the ASCO Value Framework, we have constructed a value snapshot of 3 major frontline therapeutic interventions in ovarian cancer. Dose-dense paclitaxel provided the most value when accounting for NHB and cost. However, further research is needed to include individual patients' preferences and provide personalized value assessments.

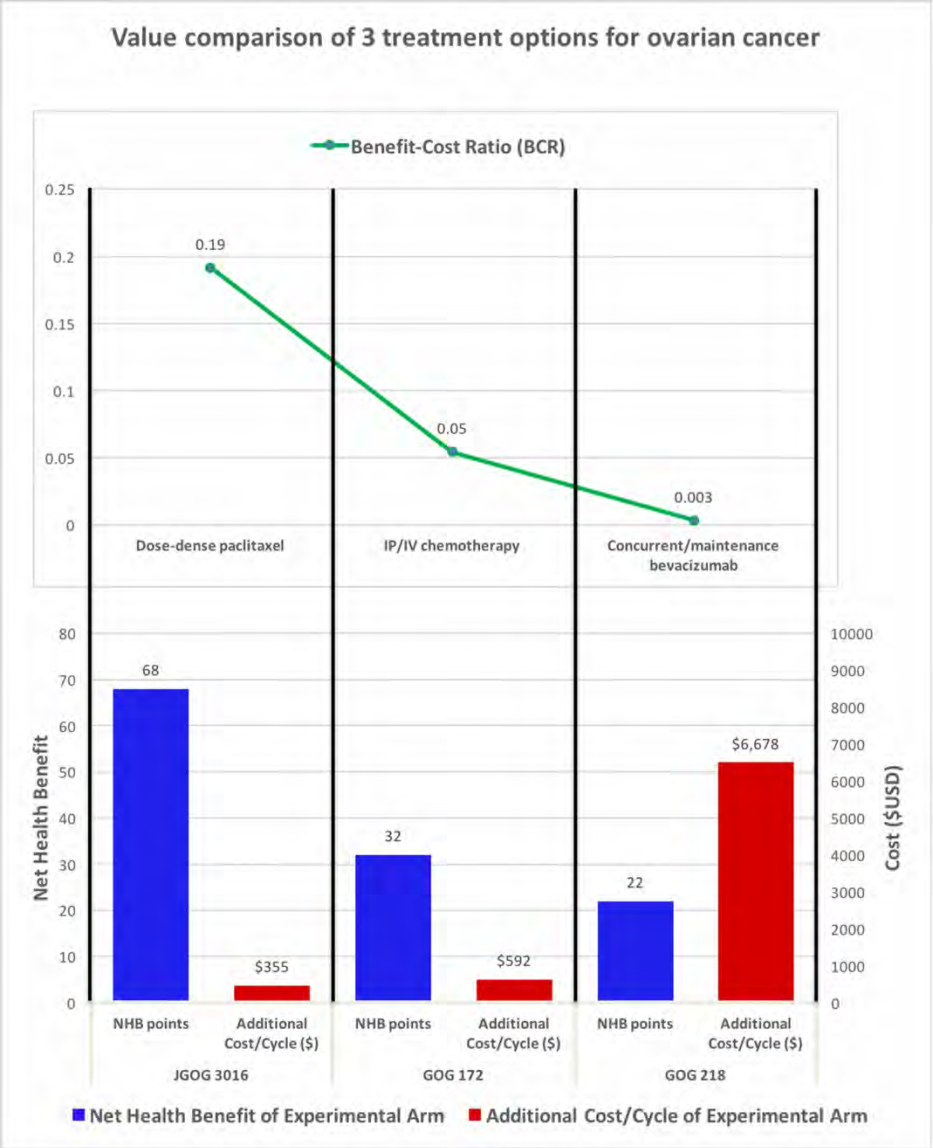

Fig.1
Value Comparison of 3 Treatment Options for Ovarian Cancer.

Scientific Plenary IV: Genetic Risk Assessment
Sunday, March 20, 2016
Moderators: B.J. Rimel, MD, *Cedars-Sinai Medical Center, Los Angeles, CA, USA*
Christian Marth, MD, PhD, *Medical University Innsbruck, Innsbruck, Austria*

21 – Scientific Plenary
The implementation of video-assisted genetic counseling for ovarian, fallopian, and peritoneal cancer patients
C.H. Watson[a], M. Ulm[b], T. Tillmanns[b], M.E. Reed[b], L. Smiley[b] and R. Covington[b]. [a]*University of Tennessee Health Science Center, Memphis, TN, USA,* [b]*University of Tennessee West Clinic, Memphis, TN, USA*

Objectives: To compare the frequency of genetic testing in patients with ovarian, fallopian, or peritoneal cancer after observing a condensed genetic counseling video at their initial visit versus traditional referral for genetic counseling and testing at physician discretion.

Methods: A retrospective chart review was performed of all patients initially seen at the West Cancer Center for evaluation of ovarian, fallopian, or peritoneal cancer from July 2014 to August 2015. Patients seen between July 2014 and December 2014 were offered standard genetic counseling and testing at physician discretion during their initial appointment. Counseling and testing were performed at a separate appointment with a certified genetic counselor. A subsequent group of patients seen from March 2015 to August 2015 were instead shown a condensed, standardized counseling video on an iPad. At the end of the video, patients were given the option of *BRCA* testing alone or with a reflex to a comprehensive 25-gene panel if *BRCA* was negative. We compared the number and frequency of patients who received genetic testing in both groups. SPSS software was used to analyze the data, and χ^2 test was used to compare the discrete variables.

Results: A total of 299 patients received traditional counseling with referral and testing at the physician's discretion between August 2014 and December 2014. Two hundred ninety-five patients viewed the condensed genetic counseling video, with the option to receive testing the same day between March 2015 and August 2015. Ninety-four patients (31%) who received traditional referral ultimately underwent genetic testing. Among patients who viewed the counseling video and were offered testing on the same day as their initial visit, 162 (55%) received testing. The transition from a referral method to the video-counseling method resulted in a significant increase in the percentage of patients tested (31% to 55%; $P < .001$).

Conclusions: Using a condensed genetic counseling video and providing an option for genetic testing during a patient's initial appointment significantly increased the frequency of genetic testing used by patients with ovarian, fallopian, or peritoneal cancer. Current technology can be used to provide immediate and interactive methods of counseling and may dramatically increase the utilization of genetic testing in patients with ovarian, fallopian, or peritoneal cancer.

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22 - Scientific Plenary

Bone density testing underutilized in *BRCA* population following risk-reducing salpingo-oophorectomy

E.N. Prendergast, M. Green, M. Zakhour, J. Lester, A.J. Li, C. Walsh, B.J. Rimel, R.S. Leuchter, B.Y. Karlan and I. Cass.
Cedars-Sinai Medical Center, Los Angeles, CA, USA

Objectives: Characterize bone health surveillance patterns, bone mineral density (BMD) outcomes, and fracture risk after risk-reducing salpingo-oophorectomy (RRSO) in patients with *BRCA*mutations.

Methods: An institutional review board–approved, retrospective review was performe of health surveillance among *BRCA1/2*mutation carriers after RRSO from the years 2000 to 2013. Women with occult carcinoma at RRSO were excluded from analysis. The primary outcome was the number of women who had a dual-energy X-ray absorptiometry (DEXA) scan after RRSO. Secondary outcomes included new diagnoses and time to diagnosis of osteopenia and osteoporosis. Incidence of fracture was also included. Information regarding hormone replacement therapy (HRT) was also recorded. Use of aromatase inhibitors, chemotherapy, and osteoporotic agents was not recorded.

Results: A total of 192 *BRCA* mutation carriers underwent RRSO. Median age at the time of RRSO was 48 years. Approximately, 65% of the cohort was premenopausal at the time of surgery. Median follow-up was 6.5 years from date of surgery. DEXA scanning was performed in 97 (51%) women after RRSO, of which 48 patients had 1 or more test. Age, preoperative menopausal status, use of HRT, and length of follow-up were comparable between *BRCA* mutation carriers who had DEXA surveillance and those who did not. Seventy-six (78%) women had abnormal findings. Fifty-eight (60%) had osteopenia and 19 (20%) had osteoporosis. Median time to abnormal bone density was 24 months (range, 1–151). Fracture was seen in 10 patients (5%). In women younger than 50 years, the frequencies of osteopenia and osteoporosis were 66% and 11% compared with 50% and 31% in postmenopausal women ($P = .08$]. Thirty-five women (46%) who had DEXA surveillance used HRT. Women who used HRT had lower frequencies of osteopenia and osteoporosis than women who did not use HRT, 74% and 0.06% vs 83% and 22%, respectively ($P = .09$; OR 0.26, CI 0.06–1.22).

Conclusions: Significant bone loss is common and develops rapidly in women after RRSO. Women with *BRCA* mutations who undergo RRSO are underscreened for BMD. HRT is associated with a lower risk of significant bone loss osteoporosis. Guidelines for screening in these individuals should be firmly established to reduce osteoporotic-related fracture risk in this population.

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23 - Scientific Plenary
Higher rates of clinically actionable multigene panel results in Ashkenazi Jewish patients
M.K. Frey, G. Sandler, R. Sobolev, S.H. Kim, R. Chambers, R.Y. Bassett, J. Martineau and S.V. Blank. *New York University School of Medicine, New York, NY, USA*

Objectives: Many of the multigene panels used for oncology patients include low- to moderate-risk genes, for which there are no established consensus management guidelines. Because the clinical usefulness of identifying nonactionable mutations is unclear, we sought to determine if there are specific patient populations in which positive findings on multigene panels would be more likely to affect clinical management.

Methods: We reviewed the medical records of all patients who underwent multigene panel testing at a single institution between May 2012 and December 2014.

Results: Four hundred and fifty-four patients underwent multigene panel testing. The median patient age was 54 years (range, 25–91 years) and 435 (96%) were women. One hundred and thirty-three patients (29%) were Ashkenazi Jewish (AJ) and 93 (21%) were not Caucasian. Three hundred and fifty-four patients (78%) had a personal history of cancer. Forty-nine patients had ovarian cancer, 26 endometrial cancer, and 251 breast cancer. We identified 62 pathogenic mutations in 56 patients (12%) and 291 variants of uncertain significance in 196 patients (43%). Overall, 41 pathogenic mutations identified (66%) were actionable. Having a personal or family history of cancer or a specific diagnosis of ovarian, endometrial, or breast cancer did not affect the likelihood of identifying a clinically actionable mutation. Twenty pathogenic mutations were identified in 19 AJ patients, 18 of which were in genes other than *BRCA1/2*. Among those with pathogenic mutations, AJ patients were significantly more likely than non-AJ patients to harbor an actionable mutation (17 [85%] vs 24 [57%], $P = .04$).

Conclusions: With the rapid acceptance of multigene panels, there is a pressing need to understand how this testing will affect patient management. We found that screening and prevention recommendations existed for 66% of the pathogenic mutations identified. In the AJ population, 85% of identified mutations were actionable, only 2 of which were in the *BRCA1/2* genes. Our findings suggest that panel testing may be especially useful in the AJ population.

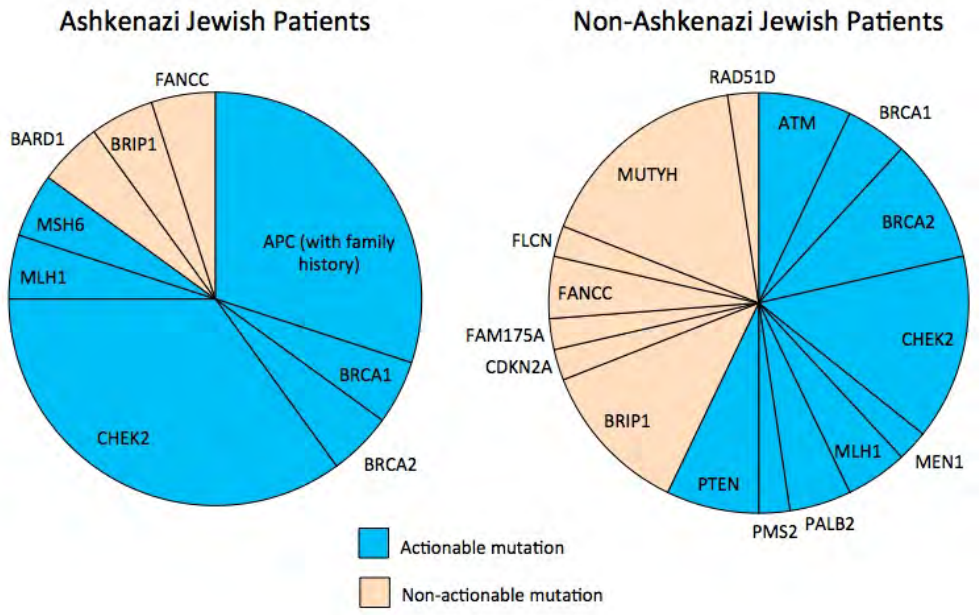

Fig. 1
Mutations in Ashkenazi Jewish and non-Ashkenazi Jewish Patients.

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24 - Scientific Plenary
Hereditary cancer panel testing in an unselected endometrial carcinoma cohort
K.L. Ring[a], A.S. Bruegl[a], B.A. Allen[b], E.P. Elkin[b], N.U. Singh[b], A.R. Hartman[b], M.S. Daniels[a] and R. Broaddus[a]. [a]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA,* [b]*Myriad Genetics, Inc., Salt Lake City, UT, USA*

Objectives: Hereditary endometrial carcinoma (EC) is associated with germline mutations in Lynch syndrome (LS) genes. The role of other cancer predisposition genes in EC is unclear. We aimed to determine the prevalence of cancer predisposition gene mutations in an unselected EC patient cohort.

Methods: Mutations in 25 cancer genes were identified using a next-generation sequencing–based panel applied to 381 unselected EC patients who had previously undergone tumor testing to screen for LS.

Results: Thirty-five patients (9.2%) had a germline deleterious mutation (DM), 22 (5.8%) with DM in LS genes (3 *MLH1*, 5 *MSH*2, 2 *EPCAM-MSH2*, 6 *MSH6*, 6 *PMS2*) and 13 (3.4%) with DM in 10 non-LS genes (4 *CHEK2*, 1 each in *APC*, *ATM*, *BARD1*, *BRCA1*, *BRCA2*, *BRIP1*, *NBN*, *PTEN*, *RAD51C*). Compared with patients with no DM, patients with DM in LS genes were younger at diagnosis (mean 51.7 vs 61.5, $P < .01$), less likely to be overweight (63.6% vs 85.5%, $P = .01$), more likely to have tumor arising in the lower uterine segment (30.0% vs 7.5%, $P < .01$), and more likely to meet 5% to 10% of the Society of Gynecologic Oncology (SGO) criteria for genetic assessment referral (59.1% vs 24.3%, $P = .01$). Three patients (13.6%) with DM in LS genes were diagnosed after age 60 years. Of 20 patients with DM in LS genes and tumor testing, 2 (10%) had tumor testing results suggestive of sporadic cancer but with DM in *MSH2* and *MSH6*. Of 10 patients with DM in *MLH1*, *MSH2*, and *EPCAM-MSH2*, 80.0% were younger than 50 years at diagnosis, 90.0% met SGO criteria, and 90.0% had a family history of LS-associated cancer. Of 12 patients with DM in *MSH6* and *PMS2*, 83.3% were diagnosed after age 50 years, 66.7% did not meet SGO criteria, and 66.7% did not have a family history of LS-associated cancers. Patients with DM in non-LS genes were more likely to have serous tumor histology (23.1% vs 6.4%, $P = .02$) than those with no DM. The 3 patients with non-LS DM and serous histology had mutations in the *BRCA2*, *BRIP1*, and *RAD51C* genes that have been previously linked to hereditary ovarian cancer.

Conclusions: Current genetic testing criteria for endometrial cancer fail to identify a portion of actionable mutations in both LS and other hereditary cancer syndromes. As many as 67% of cases in our study with *MSH6* and *PMS2* mutations were not diagnosed at a young age and did not have a family history of cancer. Universal tumor testing should be used to identify patients who may be missed with clinical criteria. Multigene panel testing demonstrates the ability to identify additional mutations, several of which have been previously linked to hereditary ovarian cancer.

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25 - Scientific Plenary

Common single nucleotide polymorphisms associated with ovarian cancer risk contribute to the racial disparity in incidence

A. Berchuck[a], M. Mullins[b], P.D.P. Pharoah[c], M. Pike[d], J.M. Schildkraut[e] and C.L. Pearce[b]. *[a]Duke University Medical Center, Durham, NC, USA, [b]The University of Michigan Hospitals, Ann Arbor, MI, USA, [c]University of Cambridge, Cambridge, United Kingdom, [d]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [e]University of Virginia, Charlottesville, VA, USA*

Objectives: Data from the US Surveillance, Epidemiology and End Results (SEER) registry has shown that ovarian cancer incidence is 35% lower in blacks than in whites. Differences in oophorectomy rates and epidemiologic risk factors such as parity and oral contraceptive use explain about 30% of this disparity. The Ovarian Cancer Association Consortium (OCAC) has identified 18 genome-wide significant ($P < 5 \times 10^{-8}$) common low-penetrance single nucleotide polymorphisms (SNPs) that increase ovarian cancer risk. We examined whether these risk alleles are more common in whites than blacks to determine whether this contributes to the racial disparity in ovarian cancer incidence.

Methods: Ancestry was defined by SNP genotyping, and the study was restricted to those with more than 90% European ancestry or more than 80% African ancestry. OCAC performed genotyping of 211,155 SNPs using a custom Illumina array. The study included 37,908 Europeans (13,233 cases, 24,675 controls) and 352 Africans (200 controls, 152 cases). The risk SNPs were fit as additive variables to determine the per-allele odds ratios (ORs). A genetic risk score was computed by summing the number of risk alleles for each participant. Using the distribution of this risk score in controls, quintiles were determined to generate ovarian cancer relative risks.

Results: Among the 18 risk SNPs, the increased risk-allele frequencies of 4 did not vary between Europeans and Africans, 3 were higher in Africans, and 11 were higher in Europeans. The risk score was a statistically significant predictor in both groups (Table 1), and strikingly, 27% of European cases fell into the highest genetic risk quartile compared with only 3% of African cases. Using the combined OR for the risk score, the resulting attributable risk of genetic factors was 15.1% in Africans compared with 29.1% in Europeans. After correcting for oophorectomy rates and nongenetic and genetic risk factors, the population-adjusted rates were 5.3 and 5.0 per 100,000 for Europeans and Africans, respectively. This leaves only 3.5% of the difference in incidence rates between Europeans and Africans unaccounted for.

Conclusions: Common genetic variants that confer increased ovarian cancer risk are more frequent in Europeans than Africans. These genetic differences explain almost all of the racial disparity in ovarian cancer incidence that cannot be attributed to differences in oophorectomy rates and epidemiologic risk factors.

Table 1
Relative Risk Associated with Genetic Risk Score Quintile by Genetic Ancestry Group.

		European			African			
Riskscore	**Case**	**Control**	**OR**	**95% CI**	**Case**	**Control**	**OR**	**95% CI**
Quintile 1	2,119	4,867	1.00	1.00 - 1.00	59	105	1.00	1.00 - 1.00
Quintile 2	2,591	4,917	1.23	1.14 - 1.33	48	60	1.34	0.81 - 2.23
Quintile 3	2,928	4,952	1.37	1.27 - 1.48	31	24	1.92	1.02 - 3.63
Quintile 4	3,183	4,967	1.48	1.38 - 1.60	9	8	2.24	0.78 - 6.43
Quintile 5	4,079	4,974	1.93	1.79 - 2.08	5	3	3.52	0.78 - 15.7
P trend			**4.26E-72**				**0.007**	

Scientific Plenary V: Optimizing Surgical Outcomes
Sunday, March 20, 2016
Moderators: David M. Boruta II, MD*, Massachusetts General Hospital/Harvard University, Boston, MA, USA*
Kian Behbakht, MD*, University of Colorado Denver, Aurora, CO, USA*

26 - Scientific Plenary
A multicenter assessment of surgical findings associated with gross residual disease at primary debulking surgery for advanced epithelial ovarian cancer
R.S. Suidan[a,b], P.T. Ramirez[a], O. Zivanovic[b], K.C. Long[b], Q. Zhou[b], M. Pangasa[b], C.F. Levenback[a], G.J. Gardner[b], Y. Sonoda[b] and D.S. Chi[b]. [a]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA,* [b]*Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: To identify surgical findings associated with gross residual disease (RD) at primary debulking surgery (PDS) for advanced epithelial ovarian cancer.

Methods: A multicenter prospective assessment of patients who underwent PDS for stage III–IV ovarian, fallopian tube, and peritoneal cancer previously identified 5 criteria associated with suboptimal (>1 cm residual) cytoreduction. In that study, surgical findings were recorded by a gynecologic oncologist at laparotomy. This was a secondary post hoc analysis looking at the ability to predict any RD. Thirteen surgical criteria were assessed, and a model predictive of RD was developed.

Results: From July 2001 to December 2012, 382 patients met inclusion criteria. Of those, 134 (35%) had complete gross resection with no RD. On multivariate analysis, 5 criteria were found to be associated with RD: widespread small bowel serosal involvement (OR 11.2, 95% CI 10.4–12.1); presacral extraperitoneal disease (OR 4.2, 95% CI 1.2–14); lesions in the gallbladder fossa/liver intersegmental fissure (OR 2.2, 95% CI 2–2.3); disease in the small bowel mesentery, around its root, or the root of the superior mesenteric artery (OR 2, 95% CI 1.3–3); and parenchymal splenic/perisplenic tumor (OR 1.3, 95% CI 1.3–1.3). Because of the high association between widespread small bowel involvement and RD (OR 11.2), a 2-step predictive model was developed. In the first step, the cohort was assessed for the presence of widespread small bowel involvement; among the 102 patients with that finding, the rate of having any RD was 96%. In the second step, among the remaining 280 patients, a 'predictive score' was assigned to each of the 4 other criteria, which was based on their multivariate OR. A total predictive score was then calculated for each patient using their individual findings, and the rate of having any RD for patients who had a total score of 0–1, 2–3, 4–5, and 6 or more was 42%, 63%, 75%, and 89%, respectively (Table 1). A receiver operating characteristic curve generated for the model showed an AUC of 0.77.

Conclusions: In 2 high-volume ovarian cancer centers, we identified 5 surgical criteria associated with RD at PDS. We developed a multivariate model in which the rate of having any RD was directly proportional to a predictive score. With further confirmation, this model could form the basis of a laparoscopic assessment to help determine resectability and triaging to laparotomy and attempted PDS versus neoadjuvant chemotherapy.

Table 1
Total Predictive Score and Gross Residual Disease.

Total Predictive Score	Total Patients * n (%)	No residual disease (n)	Gross residual disease (n)	Rate of having gross residual disease
0 - 1	151/382 (40%)	88	63	42%
2 - 3	92/382 (24%)	34	58	63%
4 - 5	28/382 (7%)	7	21	75%
≥ 6	9/382 (2%)	1	8	89%

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27 - Scientific Plenary
The optimal primary management of bulky stage IIIC ovarian, fallopian tube, and peritoneal carcinoma: Are the only options complete gross resection at primary debulking surgery or neoadjuvant chemotherapy?
V. Sioulas, M.B. Schiavone, O. Zivanovic, K. Long Roche, R. O'Cearbhaill, N.R. Abu-Rustum, D.A. Levine, Y. Sonoda, G.J. Gardner and D.S. Chi. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: To explore the effect of primary cytoreduction on minimal but gross residual disease (RD) in women with bulky stage IIIC ovarian/fallopian tube/primary peritoneal cancer.

Methods: We identified all patients with bulky stage IIIC ovarian/tubal/peritoneal cancer who underwent primary debulking surgery (PDS) at our institution between 2001 and 2010. Patients with nonepithelial histologies, borderline tumors, and nodal metastasis as their only criteria for stage IIIC disease were excluded. Clinicopathologic data were abstracted. Appropriate statistical tests were used.

Results: We identified 496 patients with a median age of 62 years (range, 23–96 years). Serous histology was noted in 451 (91%) of 496 patients. Median operative time was 265 minutes (range, 34–893 minutes). At least 1 cycle of primary or consolidation intraperitoneal (IP) chemotherapy was given to 228 (46%) of 496 patients. We assigned patients to 4 groups based on reported RD: 184 (37%) had no gross RD (group 1); 127 (26%) had 1- to 5-mm RD (group 2); 54 (11%) had 6- to 10-mm RD (group 3); and 131 (26%) had more than 10-mm RD. With a median follow-up of 53 months (range, 0.3–171 months) for the entire cohort, median progression-free survival (PFS) was 18.6 months (95% CI 16.7–20.4). Median PFS was 26.7 months for group 1, 20.7 months for group 2, 16.2 months for group 3, and 13.6 months for group 4 ($P \leq .001$). Overall survival (OS) for the entire cohort was 54.7 months (95% CI 50.8–58.7 months). Median OS was 83.4 months for group 1, 54.5 months for group 2, 43.8 months for group 3, and 38.9 months for group 4 ($P \leq .001$). Median OS for the patients who received at least 1 cycle of primary or consolidation IP chemotherapy was 70 months compared with 41 months for those who did not receive any cycle of it ($P \leq .001$). For the subset of patients who received primary IP or consolidation chemotherapy, median OS was 79 months for group 1, 67 months for group 2, and 57 months for group 3.

Conclusions: Although PDS to no gross RD was associated with the longest PFS and OS, cytoreduction to 1- to 5-mm and 6- to 10-mm RD was also associated with significantly prolonged PFS and OS compared with more than 10-mm RD. Given that the PFS and OS rates for patients with more than 10-mm RD was very similar to those reported in the literature for patients treated with neoadjuvant chemotherapy, the administration of neoadjuvant chemotherapy should not automatically be the option chosen for patients who cannot undergo primary cytoreduction to no gross RD, especially if IP chemotherapy can be given after the PDS.

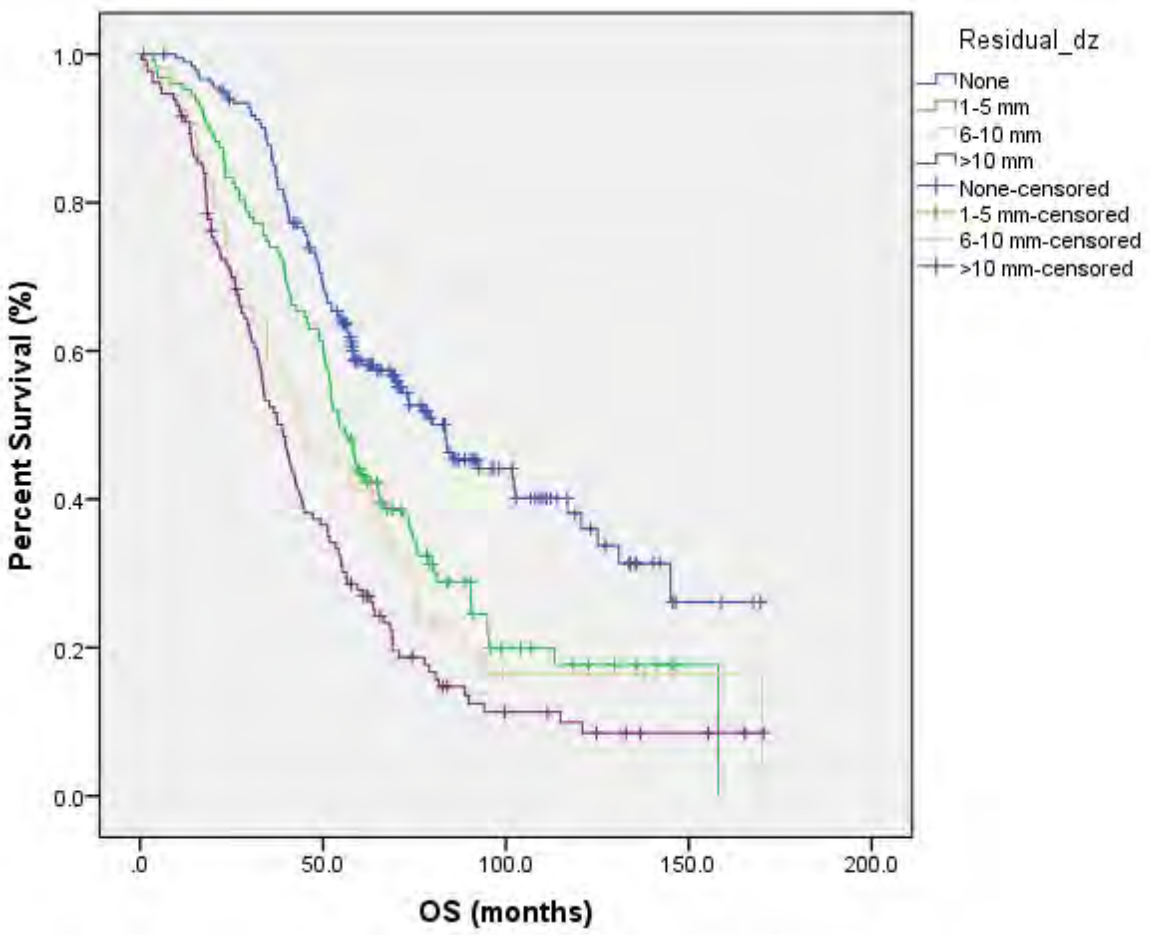

Fig. 1
Overall Survival by Residual Disease Volume.

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28 - Scientific Plenary
Clipping during distal external iliac lymphadenectomy increases lower leg lymphedema in patients with carcinoma of the cervix
S.J. Lee and J.H. Yoon. *St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, South Korea*

Objectives: The distal external iliac lymph nodes were reported to be closely related with lower leg lymphedema (LEL). We hypothesized that complete obstruction of lymphatic channel induced from clipping during distal external iliac lymph node dissection could affect lymphedema after radical hysterectomy performed for cervical cancer.

Methods: A retrospective review of 553 patients with carcinoma of the cervix who underwent radical hysterectomy with pelvic lymphadenectomy from January 1993 to December 2012 was performed. The authors included patients with FIGO stage I to stage IIA2 cervical cancer and excluded cases with a history of radiation therapy for cervical cancer to evaluate the pure effect of surgery alone. Lymphadenectomy for distal external iliac lymph nodes was defined as dissection of lymph nodes located on the psoas muscle within 3 cm from the inguinal canal. We evaluated the existence and number of clips in the area of the distal external iliac lymph nodes using magnetic resonance imaging and computed tomography.

Results: Of a total of 553 cervical cancer patients, clipping on distal external iliac lymph nodes was performed in 283 patients and nonclipping in 270 patients. The patient's age, body mass index, and the number of removed lymph nodes were not different between the 2 groups. Interestingly, LEL occurred in 15.2% (43 of 283 cases) of the patients who underwent clipping on distal external iliac lymph nodes compared with 5.2% (14 out of 270 cases) of the nonclipping cases ($P < .01$, OR 3.28, 95% CI 1.75–6.14). The total duration of LEL was significantly longer in the clipping group compared with the nonclipping group ($P < .05$). Lymphocyst formation was less frequently noted in the clipping group (3.2%, 9 out of 283 cases) compared with the nonclipping group (7.7%, 21 of 270 cases) ($P < .05$, OR 0.39, 95% CI 0.18–0.87).

Conclusions: We found that clipping on distal external iliac lymph nodes during lymphadenectomy in cervical cancer patients was significantly associated with LEL as a postoperative complication. Therefore, for the prevention of LEL, nonclipping on distal external iliac lymph nodes can be suggested as a routine method for pelvic lymphadenectomy in cervical cancer patients.

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29 - Scientific Plenary
Liposomal bupivacaine reduces total opioid requirements, rescue IV opioids, and PCA use after laparotomy for gynecologic malignancies
E. Kalogera, J.N. Bakkum-Gamez, A.L. Weaver, J.P. Moriarty, B.J. Borah, C.L. Langstraat, C.J. Jankowski, J.K. Lovely, B.A. Cliby and S.C. Dowdy. *Mayo Clinic, Rochester, MN, USA*

Objectives: To examine the efficacy of liposomal bupivacaine (LB) via surgical site infiltration compared with bupivacaine HCL (BH) within an established enhanced recovery pathway (ERP).

Methods: A modified ERP replacing local BH infiltration with LB was adopted division-wide. Patients undergoing staging laparotomy (hysterectomy, lymphadenectomy and omentectomy; n = 72) or complex cytoreductive surgery (staging laparotomy with extensive cytoreduction; n = 121) under the modified ERP were compared with historical controls treated under the original ERP (n = 84 and n = 81, respectively). Cumulative pain scores (CPS) were assessed by measuring the area under the curve of pain intensity through 48 hours. Cumulative opioids were measured in oral morphine equivalents (OME). Standardized direct medical costs were compared between groups.

Results: In the complex cytoreductive cohort, CPS was no different between groups at 24 hours ($P = .48$) or 48 hours ($P = .97$). Median OMEs were significantly lower in the LB group through 24 hours (30 vs 54 mg, $P = .002$), 48 hours (38 vs 83 mg, $P = .005$), and remaining length of stay (LOS) (62 vs 101 mg, $P = .006$). The proportion of opioid- and tramadol-free patients was significantly higher in the LB group at 24 hours (19 vs 12%, $P = .01$), 48 hours (40 vs 28%, $P = .04$), and remaining of LOS (39 vs 26%, $P < .001$). Use of LB injection reduced the need for intravenous (IV) rescue opioids (29 vs 56%, $P < .001$) and patient-controlled analgesia (PCA) (4 vs 33%, $P < .001$). Postoperative nausea was less frequent in LB patients at 24 hours (25 vs 61%, $P < .001$) and 48 hours (30 vs 56%, $P < .001$), and the ileus rate was lower (12 vs 22%, $P = .04$). There was no difference between groups in the rate or severity of 30-day complications or LOS (median, 5 days). Median 30-day adjusted total costs (LB vs BH $31,562 vs $33,498, $P = .97$) and pharmacy costs ($2,575 vs $3,007, $P = .45$) did not differ significantly. Similar reductions in OME requirements, nausea, and the need for patient-controlled analgesia (PCA) and IV rescue opioids were observed in the staging laparotomy cohort.

Conclusions: LB injection reduced ileus, nausea, need for PCA, and rescue IV opioids after cytoreductive surgery for gynecologic malignancies, with similar pain relief and costs compared with BH. Only 4% of patients required a PCA and 40% required no opioids at 48 hours after surgery.

Education Forum IV: How to Incorporate Quality Measures into Your Practice
Sunday, March 20, 2016
Course Directors: Matthew A. Powell, MD, *Washington University School of Medicine in St. Louis, St. Louis, MO, USA*
Summer B. Dewdney, MD, *Rush University Medical Center, Chicago, IL, USA*

30 - Education Forum
Poor nationwide utilization of minimally invasive surgery in early-stage uterine cancer: An HCUP-National Inpatient Sample database study
D.B. Mannschreck[a], R. Matsuno[b], S.C. Dowdy[c], A.K. Sinno[d], E.J. Tanner III[d], R.L. Stone[d], K. Levinson[d] and A. Nickles Fader[d]. [a]*Johns Hopkins School of Medicine, Baltimore, MD, USA,* [b]*University of California San Diego Medical Group, La Jolla, CA, USA,* [c]*Mayo Clinic, Rochester, MN, USA,* [d]*Johns Hopkins Hospital, Baltimore, MD, USA*

Objectives: Minimally invasive surgery (MIS) is a Society of Gynecologic Oncology and American College of Surgeons Commission on Cancer quality measure for early-stage endometrial cancer (EC). Our objective was to perform a contemporary analysis of the nationwide uptake of MIS for EC and associated inpatient complications and costs.

Methods: The National Inpatient Sample Database was used to analyze patients with nonmetastatic endometrial adenocarcinoma who received a hysterectomy in 2012. Vaginal, laparoscopic, and robot-assisted hysterectomies were considered MIS. Open surgery was defined as subtotal or total abdominal hysterectomy. Hierarchical multiple logistic regression was used to compare complications among patients treated with open surgery versus MIS and to

identify patient and hospital factors associated with choice of surgical approach. Costs of care were compared between open surgery and MIS using linear regression.

Results: In sum, 5,239 patients were identified; 51.3% underwent open surgery and 48.7% had MIS. Open surgery was more likely to be performed in rural hospitals (OR 8.64), in the Midwest and South (OR 1.24 and 1.40, respectively), and in government hospitals (OR 1.70). Patients were significantly less likely to receive open surgery in high- and medium EC-volume hospitals (OR 0.31 and 0.29, respectively). Patient factors associated with open surgery include black race (OR 1.34) and self-pay status (OR 1.66). In addition, open surgery was associated with increased overall complications (OR 3.47), surgical complications (OR 2.83), major blood loss (OR 4.20), and hospital stay more than 2 days (OR 66.70). Other factors associated with complications included household income and payer status. Overall costs were similar between MIS and open surgery ($14,153 and $14,047, respectively). Surgical complications resulted in a median increase in cost of $3,067 per surgery.

Conclusions: Despite level I data supporting the use of MIS hysterectomy for the treatment of early-stage EC, in 2012, the rate of open abdominal hysterectomy in the United States remains alarmingly high. These data indicate identical costs of care for MIS and open surgery, but a 3.5 times greater risk of complications with open surgery. We anticipate that the rate of MIS and corresponding quality of care will improve with the adoption of the recent Commission on Cancer measures.

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31 - Education Forum

Unplanned 30-day readmission rates as a quality measure: Risk factors and costs of readmission to a gynecologic oncology service

M.B. Wilbur[a], D.B. Mannschreck[b], E.J. Tanner III[a], B. Stone[c], K. Levinson[a], S.M. Temkin[a], F. Grumbine[d], P. Pronovost[b] and A.N. Fader[b]. *[a]Johns Hopkins Hospital, Baltimore, MD, USA, [b]Johns Hopkins School of Medicine, Baltimore, MD, USA, [c]Johns Hopkins University, Baltimore, MD, USA, [d]Johns Hopkins Medical Institutions, Baltimore, MD, USA*

Objectives: The rate of unplanned 30-day hospital readmission after discharge is considered a quality measure across US hospitals, and affects Medicare-based reimbursements for inpatient care. Our study objectives were to calculate the 30-day readmission rate to our gynecologic oncology (GON) service, to identify risk factors for readmission, and to determine related costs.

Methods: All admissions to a high-volume, academic GON surgical service during a 2-year study period (2013–2014) were queried. Minor surgical procedures were excluded. Patients requiring hospital readmission within 30 days of discharge were identified. Index admissions were compared for patients with and without readmission. Risk factors and costs of readmission were identified. Gatrointestinal (GI) disturbance was defined as high ostomy output, small bowel obstruction, or ileus. Infection was defined as surgical site infection, including fever and/or leukocytosis. Data were collected on a diverse array of patients, with various demographic and clinical factors, psychosocial factors, and an institutional discharge screen survey findings (Table 1). Multiple logistic regression was used to identify factors associated with 30-day readmission.

Results: A total of 1,606 women underwent surgical admission to the GON service. A total of 178 readmissions (11.1%) were observed. The average readmission interval was 11.82 days and average length of stay was 5.16 days. The most common reasons for readmission were GI disturbance (43%) and surgical site infection (30%). Factors correlated with readmission included ovarian cancer cyotreductive surgery (OR 2.33, 95% CI 1.23–4.35), creation of an ostomy (OR 7.67, 95% CI 2.99–19.69), and positive discharge screen (OR 3.1, 95% CI 1.48–6.5). The mean cost of each readmission was $25,415; the costs associated with readmission for a GI disturbance were the highest, at $32,432. The total inpatient cost related to readmission was $4,523,959.

Conclusions: Readmission to a high-volume GON service was most associated with cytoreductive surgery for ovarian cancer, ostomy-related complications, and postdischarge complex patient care needs, as identified by institutional discharge screening surveys. The costs of readmission represent a substantial financial burden for hospitals. These data may inform intervention studies to improve the quality of cancer care and reduce health care costs.

Table 1
Institutional Discharge Screening Survey.

1. No discharge needs identified
2. Anticipated complex needs
3. Anticipated disposition other than home self-care
4. Anticipated need from home care infusion
5. Anticipated need for durable medical equipment

6. Unplanned hospitalization/Emergency Department visit >1 in past 6 months
7. Difficulty filling prescriptions in the past 12 months

Legend: A "positive discharge screen" was a defined as "yes" to any of the questions 2-7. This survey tool was utilized in all patients admitted to the gynecologic oncology service to identify complex care needs or poor social support after discharge.

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32 - Education Forum
Readmission after ovarian cancer surgery: Are we measuring surgical quality?
E.L. Barber, K.M. Doll and P.A. Gehrig. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: Readmission after surgery is a quality metric hypothesized to reflect the quality of care and complications in the index hospitalization. Benchmark procedure-specific readmission rates are being set by CMS with financial penalties for underperformance. Recently reported national hysterectomy readmission rates are low (4%). We examined the link between readmissions and surgical quality in ovarian cancer patients.

Methods: Patients who underwent surgery for ovarian cancer from 2012 to 2013 were identified from the National Surgical Quality Improvement Project (NSQIP). Patients were selected using CPT and ICD-9 codes. Major complications were defined as grade 3 or higher complications on the validated Claviden-Dindo scale and included both NSQIP and non–NSQIP-recorded complications based on readmission ICD-9 code. Readmissions and complications within 30 days of surgery were recorded. Descriptive statistics and rate ratios were used for analysis.

Results: We identified 2,806 ovarian cancer patients, of whom 9.2% (n = 259) experienced an unplanned readmission. Overall major complication rate was 11.1% (n = 312): 54.8% in the index hospitalization and 45.2% after discharge. Major complications in the index hospitalization were not associated with subsequent readmission (RR 1.2, 95% CI 0.7–1.9). Overall, 41.4% of readmissions were not attributable to any major postoperative complication. Of the unplanned readmissions, 55.2% (n = 143) never experienced a NSQIP-recorded major complication. Of these 143 patients, the reason for readmission was known for 107 patients and were as follows: non–NSQIP-recorded major complications (i.e., ileus, obstruction, 28.0%); cancer or medical factors (i.e., pleural effusion, neutropenia, 16.8%); minor complications that do not generally require readmission (i.e., urinary tract infection or superficial wound infection, 22.4%); and symptoms (i.e., pain, vomiting) without a diagnosis of complication (32.7%).

Conclusions: Forty percent of unplanned readmissions after ovarian cancer surgery are not due to a major postoperative complication. Ovarian cancer patients may have more medical or cancer-driven readmissions than other postoperative patients. Quality metric benchmarks for readmission and financial penalties should account for this high percentage of non–complication-associated readmissions.

Education Forum VI: Overcoming Barriers to Clinical Research
Sunday, March 20, 2016
Course Directors: Brian M. Slomovitz, MD, *University of Miami Miller School of Medicine, Miami, FL, USA*
Mark Shahin, MD, *Hanjani Institute for Gynecologic Oncology, Abington Memorial Hospital, Abington, PA, USA*

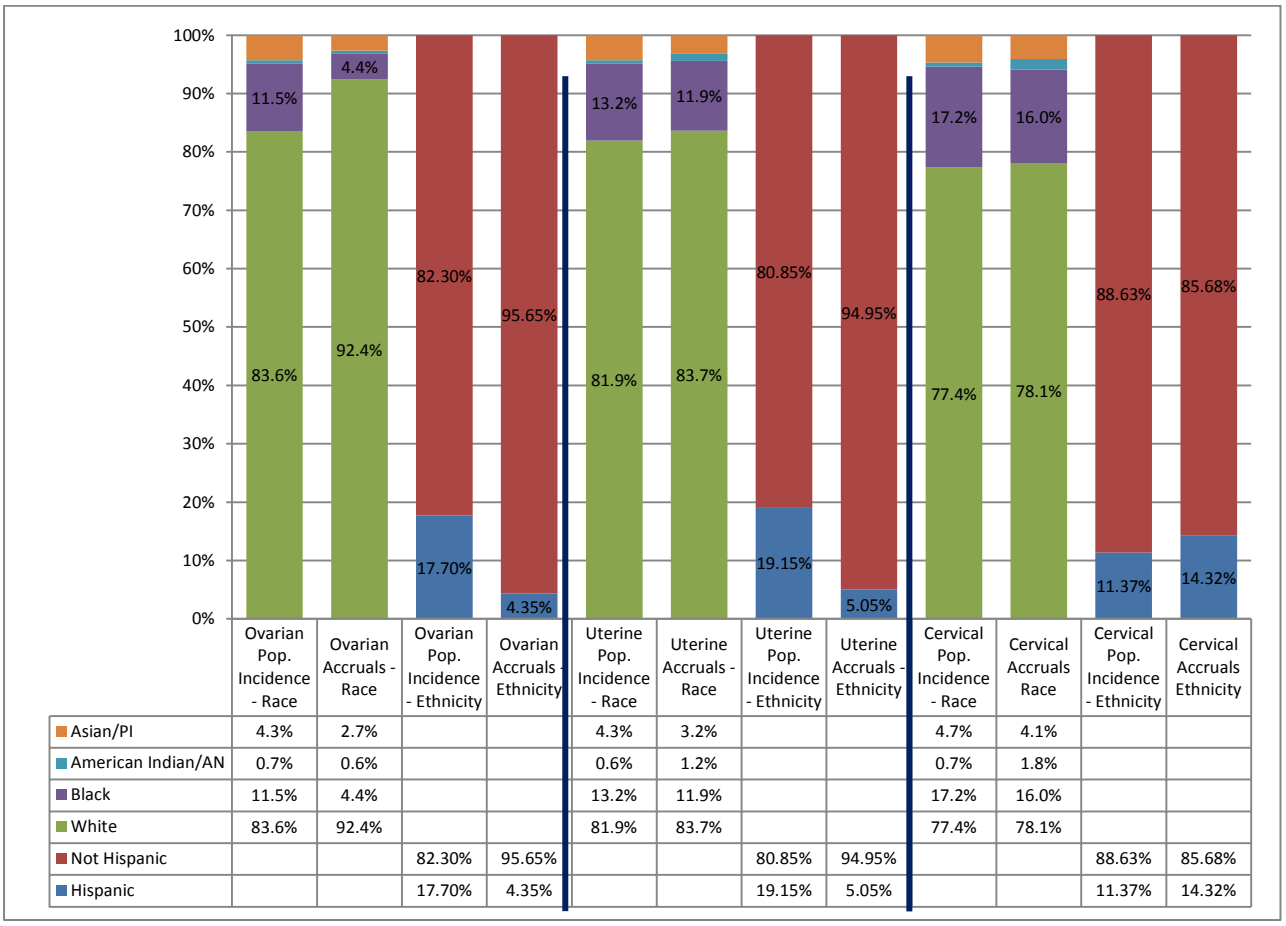
33 - Education Forum
The generalizability of NCI-sponsored clinical trials accrual amongst women with gynecologic malignancies
G. Mishkin, L. Minasian, E.C. Kohn and S.M. Temkin. *National Cancer Institute, Bethesda, MD, USA*

Objectives: Enrollment of a representative population to cancer clinical trials is essential to ensure the scientific validity and generalizability of results. This study evaluated the representativeness of patients enrolled in gynecologic cancer trials.

Methods: Accruals to National Cancer Institute (NCI)–sponsored ovarian, uterine, and cervical cancer treatment trials between 2003 and 2012 were examined. Patient demographics (race, ethnicity, age, and insurance status) were compared with the analogous US patient population estimated using Surveillance, Epidemiology and End Results (SEER) incidence rates and census data. Demographic differences between the proportion of trial participants and incident cancer patients were measured.

Results: There were 19,422 accruals to 165 NCI-sponsored cooperative group gynecologic cancer treatment trials. Accruals were to ovarian (54%), uterine (31%), and cervical (12%) cancer trials. Ovarian cancer trials included relatively less racial, ethnic, and age diversity. Black patients were underrepresented in trials of all disease sites, most notably ovarian cancer (4% vs 11% of the population for black patients, 17% vs 39% for >70-year-old patients). Hispanic patients were very underrepresented in ovarian and uterine cancer trials (4% and 5% vs 18% and 19% of the population, respectively) but not in cervical cancer trials (14 vs 11%). Elderly patients (age >70 years) represented only 17% of the total clinical trial accruals compared with 31% of the gynecologic cancer population. Ovarian cancer patients with private insurance were overrepresented among accrued patients, but the uninsured were overrepresented among women with uterine or cervical cancers enrolled in trials. These patterns were similar in the years 2008 to 2012 compared with the period 2003 to 2007.

Conclusions: Several notable differences were observed between the patients accrued to NCI-funded trials and the incident population. Improving representation of racial and ethnic minorities and elderly patients in cancer clinical trials continues to be a challenge and priority.



	Ovarian Pop. Incidence - Race	Ovarian Accruals - Race	Ovarian Pop. Incidence - Ethnicity	Ovarian Accruals - Ethnicity	Uterine Pop. Incidence - Race	Uterine Accruals - Race	Uterine Pop. Incidence - Ethnicity	Uterine Accruals - Ethnicity	Cervical Pop. Incidence - Race	Cervical Accruals Race	Cervical Pop. Incidence - Ethnicity	Cervical Accruals Ethnicity
Asian/PI	4.3%	2.7%			4.3%	3.2%			4.7%	4.1%		
American Indian/AN	0.7%	0.6%			0.6%	1.2%			0.7%	1.8%		
Black	11.5%	4.4%			13.2%	11.9%			17.2%	16.0%		
White	83.6%	92.4%			81.9%	83.7%			77.4%	78.1%		
Not Hispanic			82.30%	95.65%			80.85%	94.95%			88.63%	85.68%
Hispanic			17.70%	4.35%			19.15%	5.05%			11.37%	14.32%

Fig. 1
Relative Population Incidence and Clinical Trial Participation by Race and Ethnicity.

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34 - Education Forum
Factors that influence gynecologic cancer patient participation in clinical trials
S. Hammer, M.E. McDonald, T. Ginader, S. Stockman, D.P. Bender, J.G. Bosquet, J.M. Stephan and M.J. Goodheart.
University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Objectives: Fewer than 5% of cancer patients enroll in clinical trials and this is especially true for those with gynecologic cancer. Our study aimed to determine what motivates gynecologic cancer patients to participate in clinical trials, and what barriers or misconceptions remain. We hypothesize that there are demographic and clinical differences between patients who participate in clinical trials and those who do not.

Methods: A prospective questionnaire-based study was administered to gynecologic cancer patients seen in our division. The questionnaire obtained demographic information, past experience, understanding about, willingness to participate in and receive information on clinical trials, and the reasons the patient would or would not be willing to participate if offered a clinical trial. Additional clinical and demographic information was obtained from the medical record. Statistical analysis included the Student's *t* test and Cox multivariate analysis.

Results: Of the 115 respondents, 90% had heard the term "clinical trial," mostly from different media outlets (36%) or the medical community (50%), and 95 (82.6%) would participate or consider participating in a clinical trial if offered. Only 44% knew that it compared different treatments and only 45% knew that they were often randomized. More than half (54%) felt they would directly benefit from participating in a clinical trial, and 61.7% felt "society in general" would benefit. When asked if they would participate in a clinical trial, only 35 (30%) responded "yes." Those who were treated 1 or more years ago were more likely to say yes than those treated less than 1 year ago (85% vs 14%; *P* = .01), whereas those who live 60 miles or more from the medical center were more likely to say "no" (70% vs 30%; *P* = .05). When asked if they would like additional information, patients diagnosed with cervical and uterine cancer were inclined to respond "no" compared with patients with ovarian and vulvar cancer (*P* = .05). Only 16 patients (14%) participated in a clinical trial.

Conclusions: Most patients have heard about clinical trials, but few participate. Different media outlets and the medical community should continue to educate patients about clinical trials. There still remains confusion about clinical trials, but most feel they are beneficial personally and/or to society. Distance traveled to the hospital and time since last treatment are factors that influence trial enrollment. Continued education regarding clinical trials will hopefully increase enrollment.

Scientific Plenary VI: Farr Nezhat Surgical Innovation Session
Monday, March 21, 2016
Moderators: Pedro T. Ramirez, MD*, The University of Texas MD Anderson Cancer Center, Houston, TX, USA*
Sean C. Dowdy, MD*, Mayo Clinic, Rochester, MN, USA*

35 - Scientific Plenary
Is recovery really 'enhanced' through enhanced recovery programs? An analysis of patient-reported perioperative symptom burden before and after implementation of an enhanced recovery pathway for gynecologic surgery
L.A. Meyer, A.M. Nick, M.D. Iniesta, K.E. Cain, T.W. Earles, J.D. Lasala, Q. Shi, X.S. Wang, K.H. Lu and P.T. Ramirez. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: With the growing focus on patient-centered care, patient-reported outcomes are increasingly important in comparative effectiveness research. Our objective was to compare patient-reported symptom burden and functional recovery in women undergoing surgery before and after implementation of an enhanced recovery pathway (ERP).

Methods: Perioperative patient-reported symptom burden was measured in women undergoing laparotomy on the gynecologic oncology service of a tertiary cancer center before and after implementation of an ERP. Symptoms were assessed using the MD Anderson Symptom Inventory–Ovarian Cancer module (MDASI-OC), a 27-item validated tool. The MDASI-OC was administered as a preoperative baseline, daily while hospitalized, and at least weekly for 8 weeks postoperatively. Fisher exact test and mixed-effect modeling were performed.

Results: A total of 167 patients (74 pre-ERP, 93 post-ERP) completed the MDASI-OC longitudinally. Even though there was a 77% reduction in opioid intake (median morphine equivalents) during the first 3 days after surgery in the ERP group, there was no significant difference in mean pain scores between the pre- and post-ERP cohorts. Compared with traditional perioperative care, patients in the ERP reported significantly lower severity of a composite score of the most highly rated symptoms (fatigue, dry mouth, drowsiness, pain, and abdominal pain) during their hospitalization (*P* = .002). In addition, the ERP cohort had significantly lower composite scores in physical interference (walking, work, activity; *P* = .008), and lower affective interference scores (mood, relations with other people, enjoyment of life; *P* < .0001. During the 8 weeks after discharge, women in the ERP continued to report significantly less fatigue (*P* =.009), drowsiness (*P* < .0009), and pain (*P* = .02). Although no significant differences were noted in physical interference scores in the 8 weeks after discharge, improvements in affective interference continued (*P* =.0009). Memory and ability to concentrate were significantly better in the ERP group both during hospitalization and after discharge.

Conclusions: Adoption of an ERP can significantly reduce opioid consumption without worsening patients' subjective feeling of pain and may improve functional recovery in the immediate and extended postoperative setting.

36 - Scientific Plenary

Accelerating gastrointestinal recovery in women undergoing ovarian cancer debulking: A randomized, double-blind, placebo-controlled trial

J.N. Bakkum-Gamez, C.L. Langstraat, M.A. Lemens, A.L. Weaver, M. McGree, A. Mariani, B.S. Gostout, T.O. Wilson, B.A. Cliby and S.C. Dowdy. *Mayo Clinic, Rochester, MN, USA*

Objectives: To determine the efficacy of alvimopan, a peripherally acting μ-opioid antagonist, on ileus and postoperative outcomes in women undergoing laparotomy for ovarian cancer (OC).

Methods: Women with clinically apparent OC undergoing primary, interval, or secondary debulking via laparotomy were randomized 1:1 to receive alvimopan 12 mg orally twice a day, starting with 1 dose preoperatively versus placebo at the same dosing interval. Study drug was continued for the duration of hospital stay, but did not exceed 7 days. All patients were on a standardized enhanced recovery protocol. Preoperative and intraoperative variables, postoperative complications, analgesic doses, pain scores, nausea, ileus, time to upper and lower gastrointestinal (GI) tract function return, and length of stay (LOS) were recorded. Ileus was defined as surgeon diagnosis, return to nothing-by-mouth (NPO) status, or postoperative placement of nasogastric tube (NGT). Upper GI function return was time to 600-mL oral intake, and lower GI function was time to first bowel movement.

Results: A total of 134 women were randomized to receive either alvimopan (n = 66) or placebo (n = 68) between January 2013 and June 2015. Mean age was 62.1 years; 73 (54.5%) had stage III/IV disease. Of these, 67.9% underwent primary, 14.9% interval, and 17.2% secondary debulking. Twenty-two patients (16.4%) underwent rectosigmoid resection. There were no differences in patient, tumor, or surgical characteristics between the study arms. Patients in the alvimopan arm had return of lower GI function 1 day earlier than those who received placebo (3.0 vs 3.9 days; $P = .014$), were less likely to return to NPO status (4.5% vs 13.2%; $P = .08$), and a lower likelihood of needing a NGT postoperatively (4.5% vs 11.8%; $P = .13$). The rate of ileus was 10.6% in the alvimopan arm compared with 19.1% in the placebo arm ($P = .17$). Consistent with a shorter time to return of lower GI function, there was a higher rate of nausea on postoperative day 2 (66.2% vs 48.4%; $P = .04$) in the alvimopan arm. There was no difference in pain scores, postoperative complications, or readmission rate (Table 1). The overall enteric leak rate was 0.7% (n = 1, placebo arm). There was no difference in LOS; however, mean LOS was only 4.3 (standard deviation, 2.8) days for the entire study cohort.

Conclusions: Alvimopan decreases the time to return of lower GI function among women undergoing laparotomy for OC debulking without increasing complications. The rate of ileus is reduced by nearly half when alvimopan is used in these highly complex surgical cases.

Table 1
30-day Postoperative Complications.

Complications within 30 postop days	Total (N=134) N (%)	Alvimopan (N=66) N (%)	Placebo (N=68) N (%)	P*
Ileus	20 (14.9%)	7 (10.6%)	13 (19.1%)	0.17
Bowel obstruction	2 (1.5%)	0 (0.0%)	2 (2.9%)	0.50
Enteric leak	1 (0.7%)	0 (0.0%)	1 (1.5%)	0.99
Dehydration	3 (2.2%)	3 (4.5%)	0 (0.0%)	0.12
Surgical site infection	5 (3.7%)	3 (4.5%)	2 (2.9%)	0.68
Urinary tract infection	3 (2.2%)	1 (1.5%)	2 (2.9%)	0.99
Venous thromboembolism	5 (3.7%)	2 (3.0%)	3 (4.4%)	0.99
Cardiac event	4 (3.0%)	2 (3.0%)	2 (2.9%)	0.99
Central nervous system event	1 (0.7%)	1 (1.5%)	0 (0.0%)	0.50
Return to operating room	6 (4.5%)	3 (4.5%)	3 (4.4%)	0.99

*Chi-square or Fisher's exact

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37 - Scientific Plenary

Implementation of an enhanced-recovery-after-surgery protocol in gynecologic surgery: Impact on patient satisfaction with pain control and surgical outcomes

S.C. Modesitt[a], B.M. Sarosiek[b], E.R. Trowbridge[b], D.L. Redick[b], R.L. Thiele[b], M. Tiouririne[b] and T. Hedrick[b]. [a]*University of Virginia Health System, Charlottesville, VA, USA,* [b]*University of Virginia, Charlottesville, VA, USA*

Objectives: To standardize and improve perioperative care, we implemented an enhanced-recovery-after-surgery (ERAS) protocol for all patients undergoing major gynecologic surgery at an academic institution.

Methods: A multidisciplinary team implemented 2 ERAS protocols, a full version using regional anesthesia for open procedures and a light version without regional anesthesia for vaginal/minimally invasive procedures. ERAS pathways were predicated on the following: extensive preoperative counseling, carbohydrate loading/oral fluids until 2 hours before surgery, multimodal analgesia with avoidance of intravenous opioids, intraoperative goal-directed fluid resuscitation and immediate postoperative feeding/ambulation. A before- and after-study design was used to measure outcomes after implementation. Complications and expected length of stay (LOS) were drawn from American College of Surgeons National Surgical Quality Improvement Program (NSQIP) data.

Results: A total of 104 consecutive patients underwent surgery within the ERAS full protocol compared with 282 consecutive historical controls (conventional). The LOS was virtually identical (2.8 days) and consistent with the NSQIP-predicted LOS. Substantial and statistically significant reductions in the ERAS full group were seen in morphine equivalents ($P < .0001$), intraoperative and total intravenous fluid administration ($P < .0001$ for both), and immediate postoperative pain scores ($P < .001$). Subset analysis of gynecologic oncology patients (31 ERAS full and 97 conventional) who underwent additional staging/surgical procedures was similar except for an additional trend towards improved LOS (2.97 vs 3.54; $P = .08$). Two hundred twenty-five consecutive patients underwent surgery within the ERAS light protocol, compared with 299 consecutive historical controls; the only significant differences were intraoperative morphine equivalents ($P < .001$) and intraoperative and overall intravenous fluids ($P < .0001$ for each). Press Ganey scores for patient satisfaction showed a marked improvement on the focus question "how well was pain controlled" and increased from the 14th to 96th percentile after ERAS implementation.

Conclusions: Implementation of an ERAS protocol in gynecologic surgery led to substantial reduction in intraoperative fluids and morphine use, with significant improvement in patient satisfaction with pain control.

Focused Plenary I: Endometrial Cancer
Monday, March 21, 2016
Moderators: Erin A. Bishop, MD, *The University of Oklahoma, Oklahoma City, OK, USA*
David Scott Miller, MD, FACOG, *University of Texas Southwestern Medical Center, Dallas, TX, USA*

38 - Focused Plenary
National trends in management of stage IIIC1 and IIIC2 uterine cancer: Chemotherapy and radiotherapy in isolation and sequence
J. Chino[a], J.R. Foote[a], G. Broadwater[a], A.A. Secord[a], M.B. Jones[b], L.J. Havrilesky[a] and S. Gaillard[c]. [a]*Duke University Medical Center, Durham, NC, USA,* [b]*Duke Cancer Center Macon Pond, Raleigh, NC, USA,* [c]*Duke Cancer Institute, Durham, NC, USA*

Objectives: To determine trends in national patterns of care for advanced-stage uterine cancer, with attention to combinations of chemotherapy (CT) and radiation therapy (RT), and correlating with survival outcomes.

Methods: The National Cancer Data Base (NCDB) was queried for women with surgical stage IIIC1 and IIIC2 uterine cancer diagnosed between 1998 and 2012. Treatment modality was categorized as RT alone, CT alone, RT then CT, CT then RT (including "sandwich" regimens), or concurrent CT-RT. Covariates were captured including facility type, disease stage (IIIC1 or IIIC2), race, age, insurance, income, education, histology, and era of treatment (1998–2006 and 2007–2012, corresponding to the publication of Gynecologic Oncology Group [GOG] 122 results), and tested for differences in treatment modality via the X^2 test. Survival was compared among treatment modalities using Cox proportional-hazards regression while adjusting for covariates.

Results: A total of 4,137 women met the inclusion criteria: 3,103 had complete data for inclusion into multivariate survival models. Of these, 1,865 received RT alone, 820 CT alone, 409 RT then CT, 886 CT then RT, and 157 concurrent CT-RT. The use of RT alone declined dramatically after 2006 (62.6% before, 12% after, $P < .001$), with the most common modalities after 2006 being CT then RT (43.9%) and CT alone (33.0%). Academic programs and comprehensive community programs were less likely to use RT alone (43.5% and 44.9%) than community programs (56.9%), and more likely to use CT alone (22.0% academic programs, 18.9% comprehensive community programs, 12.4% community programs) ($P < .001$). Stage IIIC2 disease was more likely than stage IIIC1 to be treated with CT alone (38%) or CT then RT (42%); stage IIIC1 was most frequently treated with RT alone (50.1%), ($P < .001$). In multivariate survival modeling, both CT alone and RT alone were associated with worse survival than any combination therapy (HR 0.87, $P = .036$). In patients treated after 2007, CT then RT was superior to CT alone (HR 2.3, 95% CI 1.5–3.5), however other pairwise treatment comparisons were not significant (Figure 1).

Conclusions: National patterns of care for node-positive uterine cancer are variable, and changed after the publication of GOG 122 in 2006. After correcting for confounding factors, multimodality treatment appears superior to monotherapies, with CT then RT being the most common means of integrating therapy.

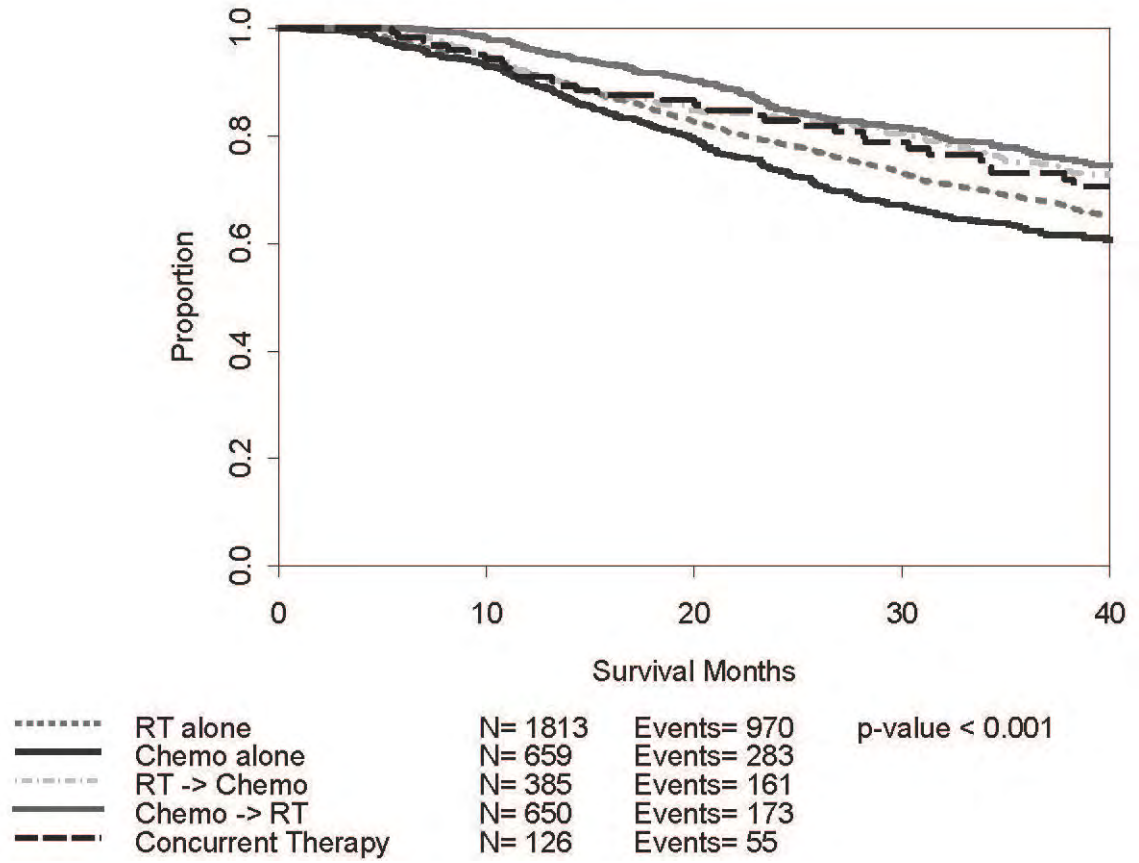

Fig. 1
Overall Survival by Treatment Approach in Stage IIIC1 and IIIC2 Uterine Cancer.

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39 - Focused Plenary
CTNNB1 (beta-catenin) mutation in grade 1-2 endometrioid endometrial cancer identifies a high-risk subgroup
K.C. Kurnit, B. Fellman, D. Urbauer, G.B. Mills and R. Broaddus. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: *CTNNB1* (encodes β-catenin) mutation is 1 of the more common mutations in endometrial cancer (EC). The purpose of this study was to determine pathologic and demographic characteristics of *CTNNB1* mutant ECs with an emphasis on survival outcomes.

Methods: We performed a retrospective chart review of all patients with histologically confirmed EC who sought care at University of Texas MD Anderson Cancer Center and underwent either clinical (46/50 gene panel) or research-based (200 gene panel) next-generation sequencing of their tumors since 2000. Clinical information, including demographic information, pathology information, and clinical outcomes, was extracted using a chart review. Statistical analyses included the Fisher exact, X^2, and Kruskal-Wallis tests, and the Kaplan-Meier product-limit estimator was then used to calculate recurrence-free survival (RFS).

Results: A total of 343 patients were included in this analysis, of whom 17% had tumors with an exon 3 *CTNNB1* mutation. Patients with tumors that had *CTNNB1* mutations were younger and had a higher body mass index. *CTNNB1* tumors more frequently had an endometrioid (EEC) histology, more often grade 1, and less often had lymphovascular space invasion (Table 1). FIGO stage was not significantly different between the 2 *CTNNB1* groups. Among low-grade (grade 1 or 2) EEC, *CTNNB1* mutants had higher rates of recurrence (44% vs 25%, $P = .017$). Within this same low-grade EEC group, *CTNNB1* mutants had worse RFS than *CTNNB1* wild-type tumors (median 6.1 vs 11.3 years, $P =$

.039). There were no differences in rates of adjuvant therapy, advanced stage, or *TP53* mutations between the *CTNNB1* groups within the low-grade EEC group, though *KRAS* mutations were more common among *CTNNB1* wild-type tumors.

Conclusions: EC with *CTNNB1* mutations represent a distinct subset of low-grade EEC with more aggressive clinical characteristics. Assessment of these mutations may be useful in the upfront identification of women with low-grade EC for risk of recurrence.

Table 1
Patient and tumor characteristics stratified by *CTNNB1* mutation status.

	***CTNNB1* wild type (N = 283)**	***CTNNB1* mutant (N = 60)**	***p*-value**
Age (mean), in years	62.3	52.8	< 0.001
BMI (mean), in kg/m²[1]	33.3	35.9	0.037
Race			0.361
White	204 (72.1)	42 (70.0)	
Black	26 (9.2)	2 (3.3)	
Hispanic	42 (14.8)	12 (20.0)	
Asian	10 (3.5)	4 (6.7)	
Other	1 (0.4)	0 (0)	
Tumor size (mean), in mm[2,3]	4.9	4.4	0.189
Histology, N (%)			0.001
Endometrioid	193 (68.2)	53 (88.3)	
Mixed	44 (15.5)	6 (10.0)	
Non-endometrioid	46 (16.3)	1 (1.7)	
Grade, N (%)[2]			< 0.001
1	15 (5.6)	16 (27.1)	
2	146 (54.3)	35 (59.3)	
3	108 (40.1)	8 (13.6)	
Grade, endometrioid histology only, N (%)[2]			0.007
1 or 2	145 (75.5)	49 (92.5)	
3	47 (24.5)	4 (7.5)	
Lymphovascular space invasion, N (%)[2,4]			0.003
Absent	106 (41.2)	33 (63.5)	
Present	151 (58.8)	19 (36.5)	
Myometrial invasion, N (%)[2,5]			0.073
< 50%	146 (55.3)	37 (68.5)	
≥ 50%	118 (44.7)	17 (31.5)	
FIGO Stage, N (%)[6]			0.210
I or II	169 (60.8)	41 (69.5)	
III or IV	109 (39.2)	18 (30.5)	

[1]Infomation regarding BMI was not available for 2 patients.
[2]15 patients received neoadjuvant treatment, thereby making tumor size, histologic grade, myometrial invasion, and lymphovascular space invasion difficult to determine at the time of hysterectomy.
[3]Infomation regarding tumor size was not available for 42 patients.
[4]Infomation regarding lymphovascular space invasion was not available for 19 patients.
[5]Information regarding myometrial invasion was not available for 10 patients.
[6]Information regarding FIGO stage either by surgical staging, biopsy, or definitive imaging was not available for 6 patients.

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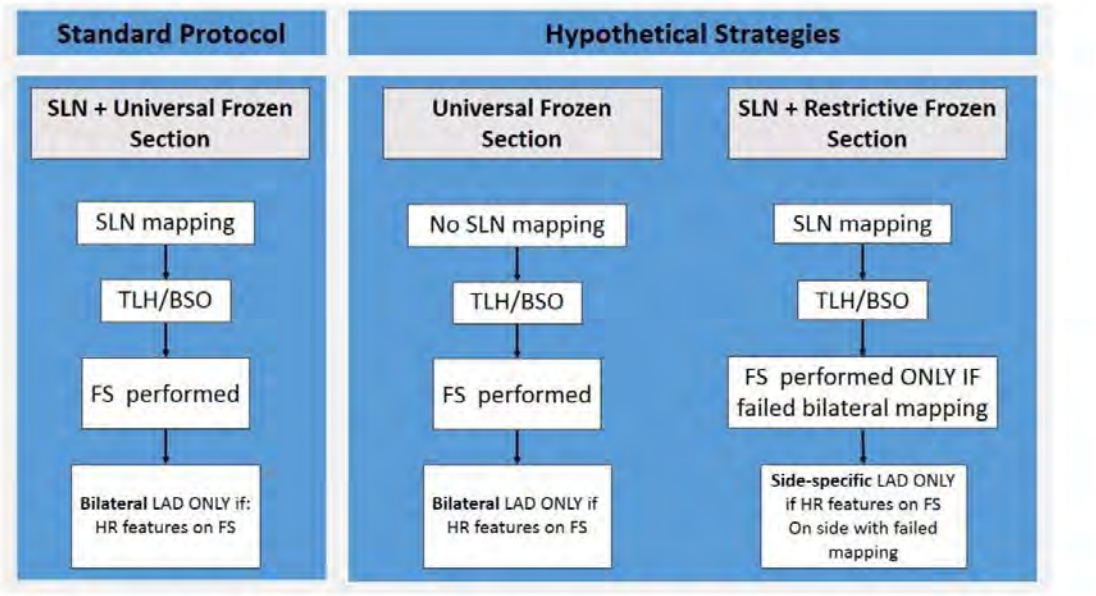
40 - Focused Plenary
Reducing overtreatment: A comparison of 3 lymph node assessment strategies for endometrial cancer using sentinel lymph node mapping and intraoperative frozen section
A.K. Sinno[a], E. Peijnenburg[b], A. Nickles Fader[a], A.M. Angarita[c], A.L. Beavis[a], R.L. Stone[a], S.M. Temkin[a], K. Levinson[a] and E.J. Tanner III[a]. *[a]Johns Hopkins Hospital, Baltimore, MD, USA, [b]Johns Hopkins School of Medicine, Baltimore, MD, USA, [c]Johns Hopkins Medical Institutions, Baltimore, MD, USA*

Objectives: To compare the ability of 3 lymph node (LN) assessment strategies to accurately identify lymphatic metastases while reducing the overall rate of completion lymphadenectomy (LAD) in patients with low-grade endometrial cancer (EC).

Methods: This was a single institution study performed at a high-volume academic center**.** Within our standard protocol (SP), all patients with congenital adrenal hyperplasia (CAH) or early-stage, grade 1/2 EC undergo sentinel lymph node (SLN) mapping, laparoscopic hysterectomy, and intraoperative uterine frozen section (FS). LAD is performed if high-risk uterine features are identified on FS. Using SP data from patients treated from 2012 to 2015, 2 hypothetical strategies were applied retrospectively to assess the impact of alternative FS and SLN utilization on the LAD rate and detection of LN metastases: (1) a universal FS strategy, in which SLN mapping is omitted and FS is performed on all patients to determine the need for LAD, and (2) an SLN-restrictive FS strategy (SLN-RFS), in which FS and subsequent side-specific LAD are only performed when bilateral SLN mapping fails.

Results: Of 114 patients who received the SP, SLNs were identified in 74% of hemipelvises. FS was performed in 105 patients (92.1%) and LAD in 42 patients (36.8%). LN metastases were identified in 8 patients using the SP (7%): 3 by means of SLN and 5 with LAD ± SLN. When applying the hypothetical strategies to this patient cohort, using the universal FS strategy results in a poorer detection of LN metastases compared with the SP or the RFS-SLN (5/8, 8/8, and 8/8 patients, respectively). Alternatively, the SLN-RFS strategy leads to an LAD rate significantly lower than the SP and universal FS strategies (9.2%, 36.8%, and 36.8%, respectively; $P = .004$), without a reduction in detection of LN metastases compared with the SP (8/8 for both). With 9 months median follow-up, 6 patients had recurrences; most (83%) developed in patients who had a negative LAD (n = 4; mean LNs, 18) or no LAD indication (stage IA, grade 1; n = 1). Of the 8 patients in whom lymphatic metastasis were identified, only 1 recurrence was noted after 23.8 months' median follow-up.

Conclusions: An operative strategy that omits universal FS and restricts its use to cases with failed SLN mapping is associated with a decrease in LAD rates, without compromising the detection of LN metastases in patients with low-grade EC. This strategy should be further explored to determine if it safely reduces overtreatment in this cohort.



SLN: Sentinel lymph node mapping. TLH/BSO: Total laparoscopic hysterectomy, bilateral salpingo-oophorectomy. FS: Frozen section of the uterus. LAD: lymphadenectomy. HR: High risk.

Fig. 1
A Comparision of Three Lymph Node Assessment Strategies for Endometrial Cancer Using Sentinel Lymph Node Mapping and Intraoperative Frozen Section.

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41 - Focused Plenary
Challenging the paradigm of progesterone-only therapy for early endometrial cancer: Results of a prospective trial of the levonorgestrel intrauterine system
S.N. Westin, C.C.L. Sun, R. Broaddus, N. Pal, M. Woodall, D. Urbauer, L.M. Ramondetta, K.H. Lu, R.L. Coleman and D.C. Bodurka. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To prospectively evaluate efficacy of the levonorgestrel intrauterine system (LIUS) to treat complex atypical hyperplasia (CAH) and grade 1 endometrioid endometrial carcinoma (EEC).

Methods: A single-institution, single-arm, phase II study of the LIUS was conducted in patients with CAH or EEC with 1 of the following: (1) medical comorbidities precluding surgery, (2) morbid obesity, or (3) desire to retain fertility. After confirmation of no extrauterine disease, dilation and curettage was performed and LIUS placed. Endometrial biopsies were performed every 3 months. The primary endpoint was pathological response rate at 12 months, defined as complete response (CR, no abnormality or hyperplasia without atypia in CAH or EEC patients) and partial response (PR, CAH in EEC patients).

Expression of estrogen-induced genes was assessed in pre- and post-treatment tissue to predict response at 3 months. Clinical and molecular characteristics were compared between responders and nonresponders, defined as stable and progressive disease.

Results: To date, 69 patients have been enrolled; 57 received the LIUS. Of these, 37 had CAH (65%) and 20 had EEC (35%). Median age was 48.2 years (range, 19–85 years) and median body mass index (BMI) was 46.8 kg/m^2 (range, 21-79 kg/m^2). Adverse events were mild, primarily irregular bleeding and cramping.

Of the 41 patients evaluable at 12 months, the overall response rate was 78%: 90% for CAH and 50% for EEC. At 12 months, there were 32 responders (31 CR, 1 PR) and 9 nonresponders (4 with stable and 5 with progressive disease). Seven patients are on trial but have not reached 12 months.

There were no differences in responders versus nonresponders in median age (47.2 vs 55.9 years, $P = .20$) or BMI (45.3 vs 54.5 kg/m^2, $P = .16$). However, 91% (29/32) of responders had pathologic evidence of exogenous progesterone effect at 3 months compared with only 33% (3/9) of nonresponders (P = .001). Among patients with evaluable molecular data, responders had significantly higher baseline expression of SFRP1, SFRP4, IGF1, and RALDH2. At 3 months, responders showed significantly decreased expression of SFRP1 and increased expression of RALDH compared with the nonresponders.

Conclusions: The LIUS demonstrates differential activity in CAH and EEC. Further, a combination of clinical and molecular factors is associated with response to therapy. These findings are being validated in a randomized discontinuation trial of the LIUS ± everolimus.

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42 - Focused Plenary

Improving hormonal therapy in uterine cancer: Efficacy of onapristone (phosphor-PR) and trametinib

Y. Huang, W. Hu, J. Huang, S. Pradeep, H.J. Dalton, R.A. Previs, J.M. Hansen, A.M. Nick, R.L. Coleman and A.K. Sood. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: Although progesterone receptor (PR)–targeted therapies are modestly active in patients with uterine cancer, their underlying molecular mechanisms are not well understood. We examined the biological effects and related mechanisms of onapristone, a novel progesterone receptor antagonist, in uterine cancer.

Methods: We evaluated the antitumor activity of onapristone alone and in combination with rationally selected drugs (trametinib) in orthotopic mouse models of uterine cancer and examined their underlying mechanisms.

Results: Onapristone significantly increased apoptosis by 14% over controls in PR-high-expressing cells (ISHIKAWA), but not in PR-weak-expressing cells (SKUT2). The expression of phospho-PR (S294, S345) and a PR target gene (p21) was significantly modulated by onapristone in ISHIKAWA cells. Surprisingly, onapristone induced p-p44/42 MAPK signaling in ISHIKAWA cells, which prompted us to consider that MEK inhibition might enhance the efficacy of onapristone in uterine cancer. MTT and isobologram analyses showed a synergistic effect of onapristone and trametinib in ISHIKAWA cells. The combination therapy significantly inhibited cell proliferation by 12% over controls, increased apoptosis by 13.2%, and increased G1/S arrest. Nuclear translocation of PR has been reported to be ligand-dependent or -independent; notably, we identified that EGF-induced nuclear translocation of phospho-PR(S294) in ISHIKAWA cells. Trametinib and onapristone inhibited nuclear translocation of EGF-induced phospho-PR (S294). Further in vivo studies showed that the combination of onapristone and trametinib significantly inhibited tumor growth compared with controls (96.5% reduction, $P < .01$), onapristone alone (65.5%; $P < .05$), and trametinib alone (86.2%; $P < .05$).

Conclusions: Targeting PR pathways with onapristone in combination with trametinib significantly inhibited tumor growth in preclinical uterine cancer models and is worthy of further clinical investigation.

Focused Plenary II: Old Drugs, New Tricks: Modifying Cancer Risk
Monday, March 21, 2016
Moderators: Amanda S. Bruegl, MD, *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*
Jayanthi S. Lea, MD, *University of Texas Southwestern Medical Center, Dallas, TX, USA*

43 - Focused Plenary
Effect of low-dose aspirin on survival outcome of endometrial cancer
K. Matsuo[a,b], S.S. Cahoon[b], M. Kakuda[c], S. Adachi[d], A. Moeini[b], H. Machida[b], J. Garcia[a], Y. Ueda[c], L.D. Roman[a,b] and A.K. Sood[e]. [a]*LAC+USC Medical Center, Los Angeles, CA, USA,* [b]*University of Southern California, Los Angeles, CA, USA,* [c]*Osaka University Graduate School of Medicine, Osaka, Japan,* [d]*Niigata University Graduate School of Medicine, Niigata, Japan,* [e]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: Although aspirin may reduce the risk of endometrial cancer occurrence, prognostic effects of aspirin on endometrial cancer are not well known. The aim of this study was to examine survival outcomes of endometrial cancer patients taking low-dose aspirin (81–100 mg/day).

Methods: A multicenter retrospective study was conducted examining surgically staged endometrial cancer patients (n = 1,294). Demographics, comorbidities, medication type, tumor characteristics, and treatment patterns were correlated with survival outcome (disease-free [DFS] and disease-specific overall [OS] survival).

Results: The study population included 141 (10.9%) patients taking aspirin. Aspirin use was associated with obesity, hypertension, diabetes mellitus, and hypercholesterolemia (all, $P < .001$). Aspirin users were less likely to receive postoperative radiation and chemotherapy (both, $P < .001$). Aspirin users were more likely to take other antihypertensive, antiglycemic, and anticholesterol agents (all, $P < .05$). Aspirin use was not associated with histology, grade, and stage (all, $P > .05$). After controlling for age, ethnicity, body habitus, histology, grade, stage, medication type, and postoperative adjuvant therapy, aspirin use remained an independent prognostic factor associated with improved 5-year DFS (90.2% vs 79.0%, adjusted HR 0.51, 95% CI 0.26–0.98, $P = .042$) and OS rates (96.7% vs 87.0%, adjusted HR 0.31, 95% CI 0.11–0.85, $P = .023$). Aspirin use in patients who received postoperative whole pelvic radiotherapy was associated with improved 5-year DFS rate (88.2% vs 61.5%, adjusted-HR 0.19, 95% CI 0.06–0.62, $P = .006$) but not associated in patients who received postoperative chemotherapy (68.8% vs 60.2%, $P = .67$).

Conclusions: Our results suggested that aspirin use may have a protective effect on survival outcome in endometrial cancer especially in those receving radiotherapy.

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44 - Focused Plenary
Weight change pattern and survival outcome of women with endometrial cancer
A. Moeini[a], S.S. Cahoon[a], H. Machida[a], M.A. Ciccone[b], B.H. Grubbs[a], L.I. Muderspach[a] and K. Matsuo[a]. [a]*University of Southern California, Los Angeles, CA, USA,* [b]*LAC+USC Medical Center, Los Angeles, CA, USA*

Objectives: To determine the association between weight change patterns and survival outcomes of women with endometrial cancer.

Methods: This retrospective study examined surgically staged endometrial cancer cases with available weight information between 1999 and 2013 (n = 665). Proportional body mass index (δ-BMI) change at 6 months, 1 year, and 2 years after hysterectomy was compared with baseline BMI and correlated with patient demographics, tumor characteristics, treatment type, and disease-free (DFS) and disease-specific overall (OS) survival.

Results: Mean BMI was 35.6, and 69% of cases were obese. At 6 months, 1 year, and 2 years after surgery, 39.1%, 51.6%, and 57.0%, respectively, of the study population gained weight compared with pretreatment baseline. In univariate analysis, 6-month δ-BMI change was significantly associated with DFS and OS (both, $P < .001$): 5-year rates, ≥15% δ-BMI loss (33.5% and 59.1%), 7.5% to 14.9% loss (67.3% and 70.0%), <7.5% loss (87.8% and 95.7%), <7.5% gain (87.2% and 90.3%), 7.5% to 14.9% gain (64.6% and 67.6%), and ≥15% gain (32.5% and 66.7%). In multivariable analysis controlling for age, ethnicity, baseline BMI, histology, grade, stage, chemotherapy, and radiotherapy, 6-month δ-BMI change remained an independent prognostic factor for DFS and OS (all, $P < .05$): adjusted-HRs, ≥15% δ-BMI loss (3.35 and 5.39), 7.5% to 14.9% loss (2.35 and 4.19), 7.5% to 14.9% gain 2.58 and 3.33), and ≥15% gain (2.50 and 3.45) compared with <7.5% loss. Similar findings were observed at the 1-year time point ($P < .05$). Baseline BMI was not associated with survival outcome ($P > .05$).

Conclusions: Our results demonstrated that endometrial cancer patients continued to gain weight after hysterectomy and post-treatment weight change had a bidirectional effect on survival outcome.

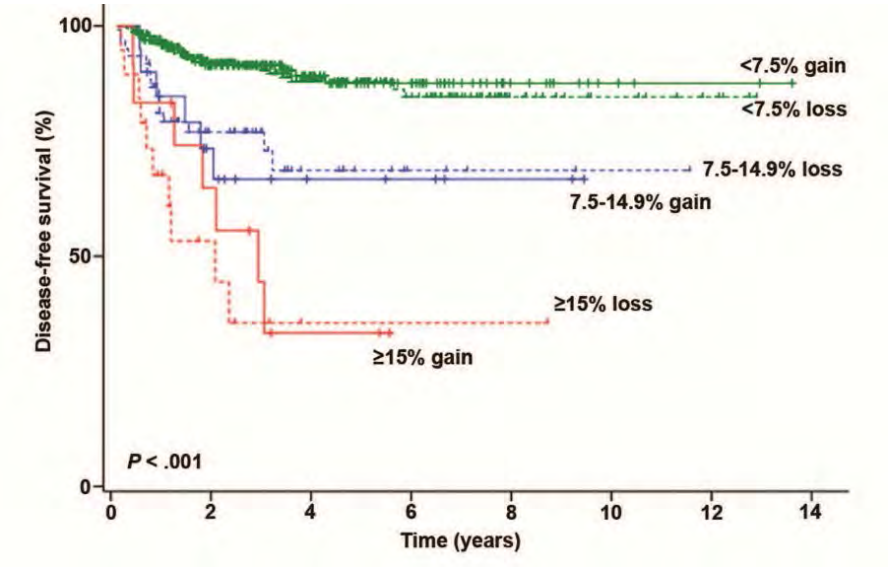

Fig. 1
6-month BMI Change (%).

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45 - Focused Plenary
Statin therapy improves ovarian cancer survival: A SEER-Medicare databasinse analysis
T.J. Vogel[a], C.Y. Jeon[b] and A.J. Li[b]. [a]*Women's Cancer Program/Cedars-Sinai Medical Center, Los Angeles, CA, USA,* [b]*Cedars-Sinai Medical Center, Los Angeles, CA, USA*

Objectives: Observational studies suggest that statin therapy for hyperlipidemia correlates with improved clinical cancer outcome. In vitro studies in gynecologic cancers demonstrate increased cell death with the use of lipophilic statins. We hypothesize that statin therapy influences survival in women with epithelial ovarian cancers.

Methods: We used the linked Surveillance, Epidemiology and End Results (SEER) registries and Medicare claims data (2007–2009) on patients with epithelial ovarian cancer to capture statin administration information during primary treatment for epithelial ovarian cancer. Patients were considered statin users if a prescription was filled after surgical resection. Cox proportional hazards regression models were used to determine the impact of statin use on overall survival.

Results: We identified 1,510 ovarian cancer patients who underwent primary surgical resection. Seven hundred and forty (49.0%) and 373 (24.7%) were stages III and IV, respectively. Six hundred and thirty-six patients (42.1%) filled prescriptions for statin therapy. Most statin users (89%) were prescribed a lipophilic formulation. Mean overall survival in statin users versus nonusers was 32.2 months versus 28.7 months ($P < .0001$). Mean survival for statin users versus nonusers in the stage III cohort was 31.7 months versus 25.9 months ($P < .0001$). After adjusting for age, race, stage, platinum therapy, Charlson score, and heart disease before diagnosis, we observed a 34% reduction in death independently associated with statin therapy (HR 0.66, 95% CI 0.55–0.80). Improved overall survival with statin use was observed for both serous (HR 0.69, 95% CI 0.55–0.87) and nonserous (HR 0.52, 95% CI 0.33–0.82) histologies. When statin treatment was categorized by statin type, lipophilicity, and intensity, an overall survival benefit was only observed in lipophilic statins of moderate to high intensity.

Conclusions: This SEER-Medicare database analysis confirms a statistical improvement in overall survival with lipophilic statin use after surgery in patients with epithelial ovarian cancer. These data support the further study of repositioning statin use as a therapy in women with this disease.

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46 - Focused Plenary

Molecular and metabolic differences of treatment responders versus nonresponders in a phase 0 clinical trial of metformin in endometrial cancer

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Objectives: In a phase 0 clinical trial of metformin in endometrial cancer (EC) patients, we previously reported that metformin decreased proliferation in the tumors of the majority of patients enrolled. We aimed to determine molecular and metabolic differences between responders and nonresponders to metformin treatment.

Methods: Obese women with endometrioid EC were enrolled. Patients took metformin (850 mg QD) for 1 to 4 weeks before surgical staging. Tissue microarrays (triplicate cores) were constructed from formalin-fixed, paraffin-embedded endometrial biopsy and hysterectomy specimens before and after metformin treatment. Expression of the metformin transporters (OCT1, OCT3, PMAT, MATE1, MATE2), phosphorylated (p)-insulinlike growth factor 1 receptor (IGF1R), p-insulin receptor substrate-1 (IRS1), LKB1, and PTEN were evaluated using immunohistochemistry. Global, untargeted metabolomics was performed on serum samples of EC patients before metformin treatment, using combined GC-MS and LC-MS/MS techniques.

Results: Of 20 patients enrolled, 13 (65%) responded to metformin as defined by a significant decrease in Ki-67 staining. In responders, metformin decreased the expression of OCT1 (46%, $P = .003$), OCT3 (40%, $P = .036$), PMAT (66%, $P = .0019$), MATE2 (26%, $P = .0017$), p-IGF1R (24%, $P = .035$), LKB1 (36%, $P = 0.0015$), and PTEN (80%, $P = .033$) but was not associated with changes in MATE1 or p-IRS1. In nonresponders, metformin treatment was not associated with any changes in these molecular targets. Pretreatment MATE2 expression approached significance in predicting response to metformin ($P = .0625$). Metabolomic profiling revealed that responders had higher premetformin treatment levels of amino acids, dipeptides, glycolytic intermediates, arachidonic acid, monohydroxy fatty acids and lysolipids compared with nonresponders ($P < .05$).

Conclusions: Treatment response to metformin was associated with decreased expression of OCT1, OCT3, PMAT, and MATE2 transporters as well as metabolically relevant proteins associated with obesity and EC. Baseline metabolic differences were found between responders and nonresponders to metformin that may serve as biomarkers for ongoing clinical trials of metformin in this obesity-driven disease.

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47 - Focused Plenary

A stratified randomized double-blind phase II trial of celecoxib in the treatment of patients with cervical intraepithelial neoplasia: A Gynecologic Oncology Group (GOG 0207) study with translational biomarkers and drug level monitoring

J.S. Rader[a], M. Sill[b], F. Garcia[c], J.H. Beumer[d], D.M. Benbrook[e], R. Zuna[f], N.M. Spirtos[g], C.A. Hamilton[h], S.B. Lele[i], J. Byron[j], D.S. Alberts[c] and C. Trimble[k]. *[a]Medical College of Wisconsin, Milwaukee, WI, USA, [b]Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, [c]The University of Arizona Cancer Center, Tucson, AZ, USA, [d]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA, [e]The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, [f]The University of Oklahoma, Norman, OK, USA, [g]Women's Cancer Center, Las Vegas, NV, USA, [h]Murtha Cancer Center, Walter Reed National Military Medical Center, Bethesda, MD, USA, [i]Roswell Park Cancer Institute, Buffalo, NY, USA, [j]Southern Pines, Pinehurst, NC, USA, [k]Johns Hopkins Medical Institutions, Baltimore, MD, USA*

Objectives: To examine the effect of celecoxib on cervical intraepithelial neoplasia (CIN) type 3 based on whether or not the patient had regression of disease.

Methods: Patients with CIN 3 and persistent visible lesions were randomized to either celecoxib 400 mg once daily or placebo for 14 to 18 weeks. The primary measure of a successful outcome was histologic regression, defined as complete remission (or partial regression to CIN 1) as evaluated with the post-treatment excisional biopsy and toxicity. A test of equal probabilities of successes between the 2 therapies was conducted after all patients enrolled, using the Fisher exact test at $\alpha = 10\%$ and 90% power when the treatment arm boosted the probability of success by 30%. Translational analysis included cervical tissue human papillomavirus genotyping, COX-2 expression in biopsy specimens, and serum celecoxib and vascular endothelial growth factor (VEGF) levels.

Results: One hundred and thirty patients were randomized (67 to celecoxib; 63 to placebo): 121 patients were evaluable for toxicity, and 91 patients were eligible and evaluable for efficacy (50 to celecoxib; 41 to placebo). There was no statistically significant increase in histologic regression in those treated with celecoxib (40%) versus placebo (34.2%). Using the 8-week time point and presence or absence of celecoxib, the response rate was 46% when

celecoxib was present and 33% when celecoxib was not present (Fisher exact test 2-sided $P = .36$; 1-sided $P = .18$). There was a significant decline in COX-2 expression from pretreatment to end of treatment for the celecoxib group (95% CI on change in mean HSCORE −40.3 ± 33.68 = −74.0 ~ −6.7; $P = .02$). The level did not change in the placebo group. A total of 80 patients had serum samples available for VEGF levels before treatment. Patients with high VEGF levels exhibited a greater response of 47.4% in the celecoxib arm compared with 13.6% response in the placebo group ($P < .05$). However, there was no difference in proportion responding between the treatment and placebo groups for patients with low VEGF levels.

Conclusions: Celecoxib at 400 mg once daily for 14 to 18 weeks did not show a significant decrease in the severity of CIN 3 compared with placebo. However, the translational endpoints suggested several measures that can be explored to personalize future chemoprevention trial design for CIN 3.

Focused Plenary III: Cervix
Monday, March 21, 2016
Moderators: Bradley J. Monk, MD, *University of Arizona Cancer Center, Phoenix, AZ, USA*
Marilyn Huang, MD, *Magee-Womens Hospital of UPMC, Pittsburgh, PA, USA*

48 - Focused Plenary
Bilateral SLN mapping for cervical cancer with ICG and robotic fluorescence imaging is associated with greater accuracy in detecting metastatic disease
A.M. Tran[a], W. Yang[b], J.F. Boggess[a], L.D. Kowalski[c], J.M. Scalici[d], L.A. Cantrell[e], K.M. Schuler[f], A. Ivanova[a], R.K. Hanna[g] and E.C. Rossi[a]. [a]*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA,* [b]*University of North Carolina Gillings School of Public Health, Chapel Hill, NC, USA,* [c]*Nevada Surgery and Cancer Care, Las Vegas, NV, USA,* [d]*Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA,* [e]*University of Virginia School of Medicine, Charlottesville, VA, USA,* [f]*Good Samaritan Hospital, Cincinnati, OH, USA,* [g]*Henry Ford Health System, Detroit, MI, USA*

Objectives: Sentinel lymph node (SLN) mapping with indocyanine green (ICG) and near-infrared fluorescence imaging (NIRFI) has been described for cervical cancers. However, only small published series have evaluated the accuracy of this technique in this disease. The FIRES trial is a multicenter prospective cohort study including women undergoing hysterectomy and lymphadenectomy for endometrial and cervical cancer. Our objective was to evaluate the accuracy of this SLN mapping technique in detecting occult metastatic disease in cervical cancer among patients undergoing a standardized technique by surgeons at multiple centers.

Methods: Patients with stage IA2 to 1B1 cervical cancer (all histologies) were enrolled in the study between February 2012 and July 2015. Patients received 1 mg of ICG intracervical injection and underwent SLN mapping using robotic NIRFI as well as completion pelvic lymphadenectomies. Negative SLN specimens underwent ultrastaging with immunohistochemistry to cytokeratin. Detection rate, sensitivity, and false-negative predictive value were calculated. Fisher exact test was used to compare dichotomous variables between node-positive and -negative groups. The study is registered with clinicaltrials.gov.

Results: A total of 67 patients were enrolled at 10 centers by 17 surgeons. Of these, 14 patients (21%) had pelvic nodal metastases. In 60 patients, at least 1 SLN was detected (90%). The rate of bilateral mapping was 61%. Of the 11 patients with metastases who underwent mapping, 7 had positive SLNs (sensitivity 64%), with 4 patients having a false-negative SLN (7.5%), and a negative predictive value (NPV) of 92.5%. Of the 4 patients with false-negative SLNs, 3 mapped unilaterally with the positive non-SLN found on the unmapped side. One patient had an empty unilateral SLN specimen on final pathology (false-positive mapping). Patients who had failed bilateral mapping were significantly more likely to have positive lymph nodes ($P = .01$). Patients with true bilateral mapping had 100% sensitivity and NPV for detecting metastatic disease.

Conclusions: Bilateral SLN mapping achieved with ICG and robotic NIRFI is associated with high accuracy in detecting metastatic cervical cancer. In the case of unilateral mapping or failed mapping, a side-specific complete lymphadenectomy should be performed.

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49 - Focused Plenary
Can sentinel lymph node biopsy replace pelvic lymphadenectomy for early cervical cancer?
G.K. Lennox[a] and A.L. Covens[b]. [a]*University of Toronto, Toronto, ON, Canada,* [b]*Toronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada*

Objectives: To evaluate recurrence-free survival and morbidity in patients with early cervical cancer who undergo bilateral pelvic lymphadenectomy (BPLND) versus those who undergo bilateral sentinel lymph node biopsy (BSLNB) only at primary surgery.

Methods: Patient data were entered prospectively in an ongoing cervical cancer database. Patients with stage IA/IB cervical cancer were included who had bilateral negative lymph nodes on pathology after primary surgery with either BPLND or BSLNB. Nonparametric (Wilcoxon rank test), X^2, and Mantel-Haenszel tests were used to compare groups. Cox regression analysis was performed to determine the variables predictive of recurrence-free survival. Statistical significance was defined as $P < .05$.

Results: A total of 1,193 patients met the inclusion criteria: 1,103 with negative BPLND and 90 negative BSLNB. There was no difference between the BPLND and BSLNB groups in recurrence-free survival (2-year: 95% and 97%, and 5-year: 92% and 93%, respectively), tumor size, histology, depth of invasion, positive margins, lymphovascular space invasion, or intraoperative complications. BPLND compared with BSLNB was associated with increased surgical time (2.75 vs 2.00 hours, $P < .001$), median blood loss (500 mL vs 100 mL, $P < .001$), blood transfusion (17.3% vs 0.0%, $P < .001$), and postoperative infection (10.4% vs 0.0%, $P = .0014$). However, there were significant differences in the temporal date of surgery, the proportion of stage IA versus IB, and the radicality of surgery between the 2 groups. On univariate analysis, clinical stage, depth of invasion, lymphovascular space invasion, and tumor size were prognostic factors for recurrence-free survival. On multivariate analysis, only tumor size was prognostic for recurrence-free survival. Type of lymph node assessment (BPLND or BSLNB) was not prognostic.

Conclusions: A negative BSLNB is not associated with a difference in recurrence-free survival compared with a negative BPLND. Indices of morbidity may also be reduced; however, changes in demographics and surgery over time may also be the cause.

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50 - Focused Plenary

Association between timing of cervical excisional procedure to minimally invasive hysterectomy and surgical complications

S.A. Sullivan, A. Staley, A. Winn, L.H. Clark and K.H. Kim. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: We sought to determine if interval between cervical excisional procedure and definitive surgery affects postoperative complications in minimally invasive surgery (MIS) for cervical cancer.

Methods: A retrospective cohort study was conducted of all cervical cancer patients diagnosed from January 1, 2000, to July 1, 2015. Patients who had a cervical excisional procedure (either loop electrosurgical excisional procedure or cold knife conization) followed by definitive MIS within 90 days were included. Types of definitive surgery included radical or simple hysterectomy (RH or SH), radical or simple trachelectomy (RT or ST), and vaginal hysterectomy. Early definitive surgery was defined as less than 42 days (6 weeks) after excisional procedure and delayed was 43 to 90 days (6 weeks to 3 months). The primary outcome was operative complications defined as intraoperative gastrointestinal (GI)/genitourinary (GU) injury, postoperative cuff dehiscence, abscess, readmission, fistula, or delayed GI/GU injury up to 30 days. Descriptive statistics and modified Poission regression were used for analysis. Operative complications were chosen from published complications for hysterectomy after excisional procedure.

Results: One hundred and forty patients met the inclusion criteria. Of these, 48 (34.3%) had early definitive surgery and 92 (65.7%) delayed. Median age was 42 years (range, 23–72 years), median body mass index (BMI) was 28 kg/m^2 (range, 16–50 kg/m^2). The early surgery cohort had a median time to surgery of 35 days (range, 2–42 days); the delayed cohort had a median of 56 days (range, 43–90 days). There was no difference in age, BMI, insurance status, stage of disease, histology, or medical comorbidities. There was no difference in complication rate between early and delayed excisional procedures (21% vs 15%, $P = .38$). When adjusting for medical comorbidities, age, race, BMI, modality, stage of disease, and histology, there was an increased complication risk in the early surgery group (relative risk [RR] 2.0, 95% CI 1.1–3.6, $P = .03$). A sensitivity analysis was performed among women who had a radical procedure (RH or RT) and the adjusted results remained consistent (RR 2.0, 95% CI 1.1–3.8, $P = .03$).

Conclusions: Performing definitive surgery for cervical cancer within 6 weeks after cervical excision procedure is associated with a higher risk for 30-day complications even when MIS is used.

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51 - Focused Plenary

Significance of risk-weighted surgical-pathological factors on survival of stage IB cervical cancer: An ancillary analysis of Gynecologic Oncology Group study

K. Matsuo[a], J. Java[b], L.I. Muderspach[c], L.D. Roman[d] and J.D. Wright[e]. *[a]Keck School of Medicine of USC, Los Angeles, CA, USA, [b]Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, [c]University of Southern California, Los Angeles, CA, USA, [d]LAC+USC Medical Center, Los Angeles, CA, USA, [e]Columbia University College of Physicians and Surgeons, New York, NY, USA*

Objectives: Although surgical-pathological factors are useful to identify patients with decreased survival in early-stage cervical cancer, the significance of risk factor weighted by the number and its magnitude has not been well studied. The aim of this study was to evaluate survival outcome of surgically -treated stage IB cervical cancer patients examined by risk-weighted surgical-pathological factors.

Methods: This is a Gynecologic Oncology Group (GOG) ancillary data analysis examining 1,538 stage IB cervical cancer patients who underwent primary radical hysterectomy and pelvic lymphadenectomy (GOG-49, 92, and 141). The hazard ratios (HR) associated with disease-free survival (DFS) for 7 surgical-pathological risk factors (nodal metastasis, parametrial involvement, surgical margin, lymphovascular space invasion [LVSI], deep stromal invasion, large tumor, and histology) were examined on multivariate model. A risk-weighted surgical-pathological score (sum of HR score) for DFS was determined and compared to the one of traditional risk factor model.

Results: Risk-weighted HRs for DFS included deep stromal invasion 1.85, large tumor 1.81, parametrial involvement 1.73, LVSI 1.37, histology 1.30, and nodal metastasis 1.29 (all, $P < .05$). Five-year DFS rates based on risk-weighted scores were 85.6% for score 0, 89.1% for 1st quartile, 79.6% for 2nd quartile, 69.3% for 3rd quartile, and 50.2% for 4th quartile ($P < .001$; Panel A). Compared with the traditional risk factor model (5-year DFS rates for low-, intermediate-, and high-risk groups: 87.3%, 68.5%, and 60.9%, respectively; Panel B), a 4th quartile score in the risk-weighted model had a significantly lower 5-year DFS rate compared with the traditional high-risk group (50.2% vs 60.9%, $P < .001$).

Conclusions: A risk-weighted surgical-pathological model was more predictive of a worse DFS than the traditional risk model in women with stage IB cervical cancer.

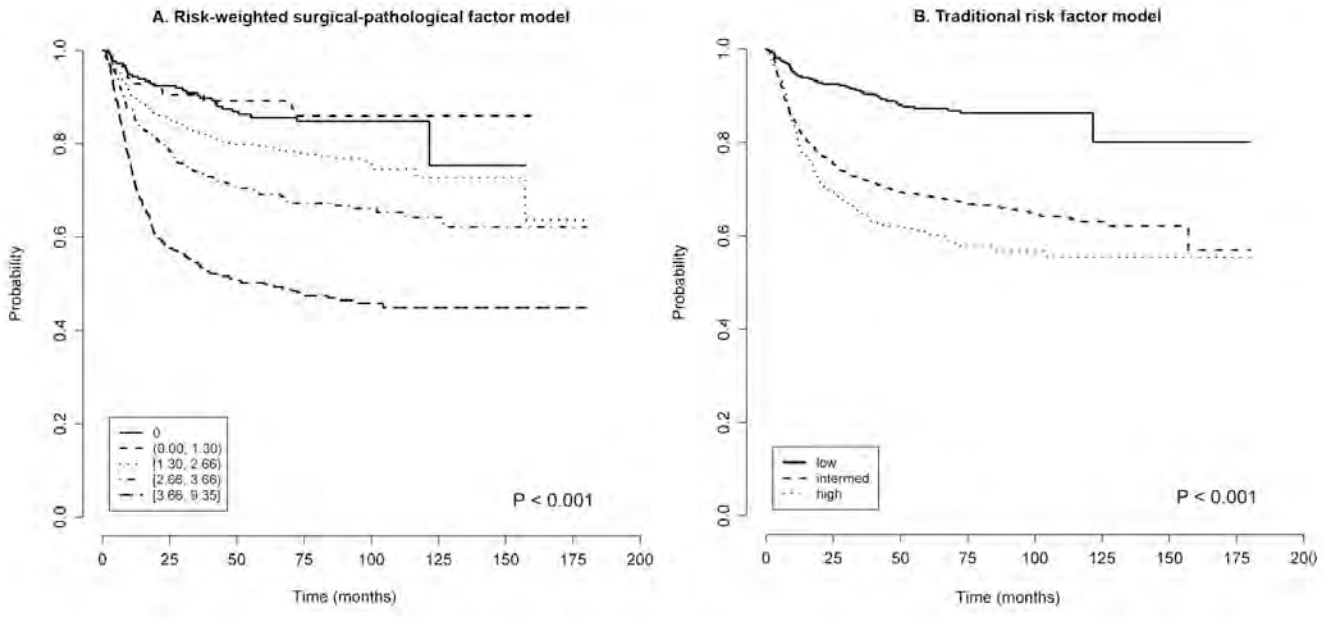

Fig. 1
(A.) Risk-weighted Surgical-pathological Factor Model. (B.) Traditional Risk Factor Model.

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52 - Focused Plenary

Comparison of the prognostic value of F-18 PET metabolic parameters of primary tumors and regional lymph nodes in patients with locally advanced cervical cancer who are treated with concurrent chemoradiotherapy

G.O. Chong, Y.H. Lee, D.G. Hong, Y.S. Lee and Y.L. Cho. *Kyungpook National University Medical Center, Daegu, South Korea*

Objectives: This study investigated the metabolic parameters of primary tumors and regional lymph nodes, as measured by pretreatment F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) to compare the prognostic value for the prediction of tumor recurrence. This study also identified the most powerful parameter in patients with locally advanced cervical cancer treated with concurrent chemoradiotherapy.

Methods: Fifty-six patients who were diagnosed with cervical cancer with pelvic and/or para-aortic lymph node metastasis were enrolled in this study. Metabolic parameters including the maximum standardized uptake value (SUVmax), the metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the primary tumors and lymph nodes were measured with pretreatment F-18 FDG PET/CT. Univariate and multivariate analyses for disease-free survival (DFS) were performed using the clinical and metabolic parameters.

Results: The metabolic parameters of the primary tumors were not associated with DFS. However, DFS was significantly longer in patients with low values of nodal metabolic parameters than in those with high values of nodal metabolic parameters. A univariate analysis revealed that nodal metabolic parameters (SUVmax, MTV, and TLG), para-aortic lymph node metastasis, and post-treatment response correlated significantly with DFS. Among these parameters, nodal SUVmax (HR 4.15, 95% CI 1.1–22, P = .041) and post-treatment response (HR 7.16, 95% CI 1.5–11.3, P = .007) were found to be determinants of DFS according to a multivariate analysis. Only nodal SUVmax was an independent pretreatment prognostic factor for DFS, and the optimal cutoff for nodal SUVmax to predict progression was 4.7.

Conclusions: Nodal SUVmax according to pretreatment F-18 FDG PET/CT may be a prognostic biomarker for the prediction of disease recurrence in patients with locally advanced cervical cancer.

Focused Plenary IV: Living Longer: Living Better?
Monday, March 21, 2016
Moderators: Linda Duska, MD, *University of Virginia, Charlottesville, VA, USA*
Siobhan M. Kehoe, MD, *University of Texas Southwestern Medical Center, Dallas, TX, USA*

53 - Focused Plenary
Survivors' acceptance of treatment side effects evolves as goals of care change over the cancer continuum
A. Ellis[a,b], M.K. Frey[c], L.M. Koontz[b], S. Shyne[a], J.Y. Chern[c], J. Lee[c] and S.V. Blank[c]. *[a]SHARE, New York, NY, USA, [b]Ovarian Cancer National Alliance, Washington, DC, USA, [c]New York University School of Medicine, New York, NY, USA*

Objectives: Women with ovarian cancer can have long overall survival and the goals of treatment change over time from cure to remission to stable disease. Because treatment side effects can compromise quality of life, we sought to determine whether survivors' acceptance of treatment side effects also changes over the disease continuum.

Methods: Women with ovarian cancer completed an online survey focusing on survivors' goals and priorities. The survey was distributed through survivor networks (OCNA Inspire community, SHARE) and social media (Facebook "Sisterhood of Ovarian Cancer Survivors" and a closed Yahoo community group). All participants provided consent.

Results: Four hundred and thirty-four women visited the survey website and 328 (76%) completed the survey. Among participants, 284 (87%) identified themselves as having ever been in remission, 141 (43%) had recurrences, 119 (36%) were undergoing treatment at the time of survey completion, and 86 (26%) had received 4 or more chemotherapy regimens. Respondents' goals of care were cure for 115 women (35%), remission for 157 (48%), and stable disease for 56 (17%). When asked what was most meaningful, quantity or quality of time, 128 women (39%) reported amount of time/lifespan and 192 (58%) reported quality of life. Overall more than 50% of survivors were willing to tolerate the following symptoms for the goal of cure: fatigue n = 283, 86%), alopecia (n = 281, 86%), diarrhea (n = 232, 71%), constipation n = 227, 69%), acne (n = 224, 67%), neuropathy (n = 218, 67%), arthralgia (n = 210, 64%), flulike symptoms (n = 208, 63%), sexual side effects (n = 201, 61%), headache (n = 190, 58%), memory loss (n = 180, 55%), nausea/vomiting (n = 180, 55%), and pain (n = 169, 52%). The rates of tolerance for most symptoms decreased significantly as the goal of treatment changed from cure to remission to stable disease.

Conclusions: Women with ovarian cancer would willingly accept many treatment side effects when the goal of treatment is cure, but they become less accepting when the goal is remission, and even less so when the goal is stable disease. Physicians and patients must carefully consider treatment toxicities and quality-of-life measures when selecting drugs for patients with incurable disease. These findings are being used to create a decision tool for survivors selecting treatment therapies for recurrent disease.

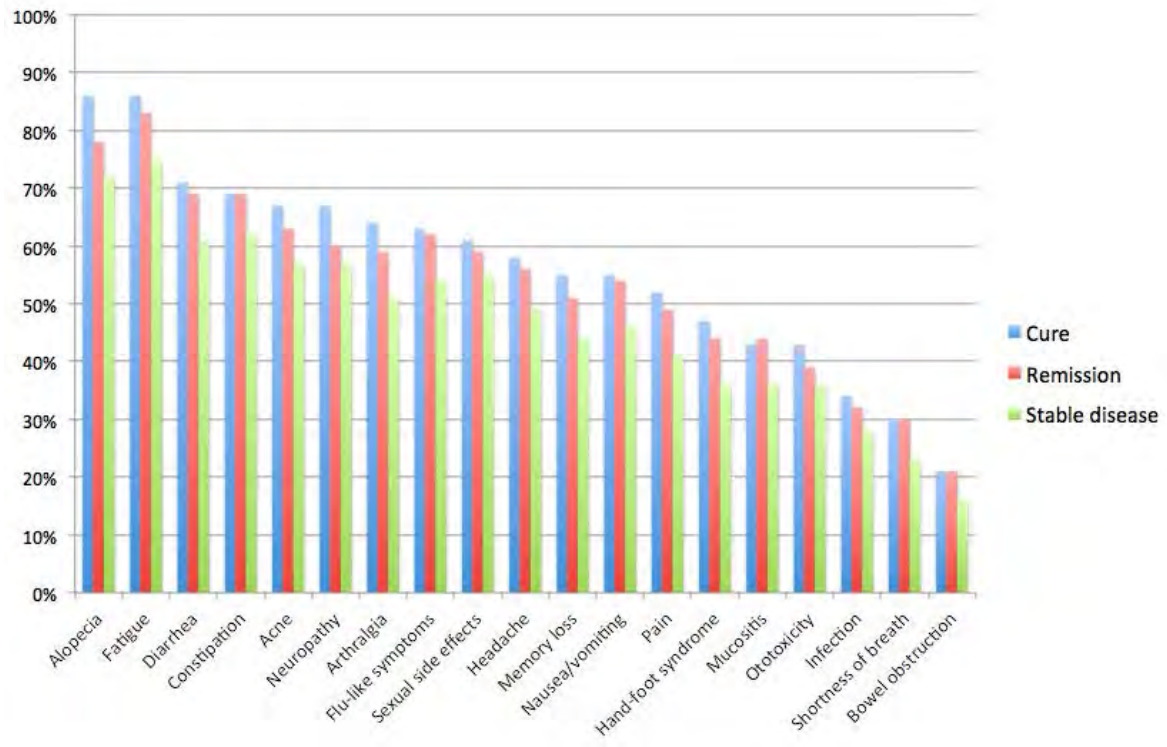

Fig. 1
Percentage of Ovarian Cancer Survivors who Would Accept Treatment Side Effects based on the Goal of Treatment (cure vs. remission vs. disease).

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54 - Focused Plenary
Identifying risk factors for CT-based diagnosed postlymphadenectomy lower-extremity lymphedema in patients with gynecologic cancers
M. Kim[a], J.Y. Choi[a], M.C. Lim[b], D.H. Suh[a], K. Kim[a], J.H. No[a] and Y.B. Kim[a]. [a]*Seoul National University Bundang Hospital, Seongnam, South Korea,* [b]*National Cancer Center, Goyang, South Korea*

Objectives: Most retrospective studies evaluating risk factors for lower extremity lymphedema (LEL) used ambiguous diagnosis of LEL by gynecologic oncologists. We conducted this study to evaluate the feasibility of computed tomography (CT) for objectively diagnosing LEL and risk factors for LEL using CT-based diagnosis.

Methods: We retrospectively reviewed 475 consecutive gynecologic cancer patients (194 cervical, 138 uterine corpus, 140 ovarian, 1 vulvar, and 2 other cancers) undergoing lymphadenectomy between 2009 and 2014. Mean thickness difference (2.3 ± 2.7 mm) of anterior thigh subcutaneous layer on CTs between prelymphadenectomy and LEL diagnosis in 111 (23.4%) who had a definite LEL diagnosis by a specialist was used for the diagnosis in the whole study population. Postlymphadenectomy 1-year CT-based LEL and its association with various clinical characteristics were investigated.

Results: A total of 168 (35.4%) had a postlymphadenectomy 1-year CT-based diagnosis of LEL in the thigh. The LEL group had more open surgery (vs laparoscopic surgery, $P = .001$) and more postoperative adjuvant radiotherapy ($P = .007$) than the non-LEL group. The number of total retrieved pelvic lymph nodes was more in the LEL group than the non-LEL group (24.0 vs 19.9, $P < .001$). However, early ambulation before 24 hours ($P = .013$) and antiembolic stocking application ($P = .016$) were associated with no LEL. Multivariate analysis showed that open surgery (odds ratio [OR] 1.88, 95% CI 1.24–2.88, $P = .003$), more retrieved pelvic lymph nodes (OR 1.02, 95% CI 1.01–1.04, $P = .009$), and no antiembolic stocking application (OR 1.55, 95% CI 1.04–2.30, $P = .030$) were independent risk factors for LEL. The total number of retrieved pelvic lymph nodes was more in open surgery than in pelviscopic surgery (23.2 vs 18.3, $P = .001$).

Conclusions: This study suggests that postlymphadenectomy 1-year CT might provide a reliable objective criterion for LEL diagnosis in gynecologic cancer patients. Patient with open surgery, more retrieved pelvic lymph nodes, and no antiembolic stocking application should be recommended for prophylactic antilymphedema management.

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55 - Focused Plenary
Sexual function and sexual interest in endometrial cancer survivors: Does a physical activity intervention help?
S. Armbruster, J. Song, K.H. Lu and K.M. Basen-Engquist. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To analyze baseline and postintervention sexual dysfunction in endometrial cancer survivors after a 6-month physical activity intervention.

Methods: A total of 63 post-treatment stage I-IIIa sedentary endometrial cancer survivors participated in a single-arm, home-based, physical activity intervention. This structured intervention encouraged gradual attainment of 30 min/day of moderate exercise on most days of the week through telephone counseling, printed material, and pedometers. Quality of life (QOL) measured with the Quality of Life in Adult Cancer Survivors questionnaire (QLACS) and Short Form-36 Health Survey (SF-36), and physical activity, obtained through the CHAMPS questionnaire and by self-report, were collected at baseline and 6 months. Sexual problem (SP) scores, including sexual function (SF) and interest (SI), were extracted from the QLACS. Baseline variables and their relationship to SP were determined using a nonparametric bootstrap procedure. Baseline correlation between SF/SI and QOL components were determined with the Spearman correlation. A logistic regression model was used to assess change in physical activity and SF/SI.

Results: Baseline SPs were significantly higher in women with less than a 4-year college degree compared with those with a higher degree (95% CI –5.95 to –1.38). No significant differences were observed in SP based on obesity status, marital status, treatment type, or race. At baseline, both SF and SI were correlated with the mental component score of QOL (SF -36) (r = –0.25, P < .05; r = –0.29, P = .02), respectively and negative feelings (QLACS) (r = 0.27, P = .03; r = 0.46, P < .001), respectively. Mean postintervention SF significantly improved (95% CI –1.46 to –.025) and 51% of participants experienced an increase in sexual interest. Controlling for age and time since diagnosis, an hour per week increase in physical activity was associated with 6.7% higher odds of experiencing an increase in SI (P = .04).

Conclusions: The positive effect of a physical activity intervention on SF and SI in endometrial cancer survivors is a novel finding. We plan to include SF as an outcome in a larger prospective study on endometrial cancer survivors. Patients should be counseled that increasing physical activity may result in an increase in SF and SI.

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56 - Focused Plenary
Prospective evaluation of quality of life and sexual functioning after radical trachelectomy for early-stage cervical cancer
N.D. Fleming, P.T. Ramirez, P.T. Soliman, K.M. Schmeler, S.N. Westin, A.M. Nick and M. Frumovitz. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To longitudinally assess quality of life (QOL), sexual functioning, and satisfaction with healthcare decisions in women who have undergone radical trachelectomy for early-stage cervical cancer.

Methods: After institutional review board approval, we prospectively enrolled patients with stage IA1-IB1 cervical cancer before undergoing radical trachelectomy to complete validated instruments to assess QOL. These instruments included the General Health-Related QOL (SF-12), the Functional Assessment of Cancer Therapy-Cervix (FACT-Cx), the MD Anderson Symptom Inventory (MDASI), Female Sexual Functioning Index (FSFI), and Satisfaction with Decision (SWD) scale. Instruments were filled out preoperatively (baseline), 4 to 6 weeks postoperatively, at 6 months, at 1 year, and annually thereafter for 4 years. Mixed modeling was used to test for changes from baseline for the survey instruments. A subanalysis was performed comparing QOL scores based on surgical approach.

Results: Thirty-nine patients enrolled in the study, and 35 patients were evaluable. Four patients were excluded because of conversion to radical hysterectomy or limited study participation time. Median age was 30.8 years (range, 21.4–38.7). Median body mass index was 25 kg/m^2 (range, 16.1–44.4). Most patients had stage IB1 disease (51%) and underwent robotic radical trachelectomy (69%). The FSFI-arousal (P = .0001), FSFI-lubrication (P < .0001), FSFI-orgasm (P = .0012), FSFI-satisfaction (P = .02), and FSFI-total (P = .002) showed a significant decline at the 4- to 6-week postoperative visit then returned to baseline levels by 6 months. Similarly, the FACT-Cx physical well-being (P < .0001), FACT-Cx social well-being (P < .0001), SF-12 bodily pain (P < .0001), SF-12 physical functioning (P < .0001), SF-12 physical role (P < 0.0001), and SF-12 social functioning (P = .0002) showed a significant decline at the 4- to 6-week postoperative visit then returned to baseline by 6 months. There were no differences in the MDASI or SWD over the follow-up period. There were no differences in QOL scores based on an open versus minimally invasive surgical approach.

Conclusions: Several QOL, sexual, and functional assessments decline immediately postoperatively after radical trachelectomy. However, they return to baseline measures by 6 months postoperatively, affording these patients long-term satisfaction with their procedural outcomes regardless of surgical approach.

Scientific Plenary VIII: Preventing Cancer: Impact of Screening and Prevention
Tuesday, March 22, 2016
Moderators: Joan L. Walker, MD*, The University of Oklahoma, Oklahoma City, OK, USA*
Audrey T. Tsunoda, MD*, Hospital Erasto Gaertner, Curitiba, Brazil*

57 - Scientific Plenary
Population impact of HPV vaccination in the United States
C.M. Tarney, M. Pagan, J. Klaric, T. Beltran and J.J. Han. *Womack Army Medical Center, Fort Bragg, NC, USA*

Objectives: To determine if the human papillomavirus (HPV) vaccination offers cross-protection against nonvaccine HPV types and whether introduction of the vaccination has offered herd immunity to unvaccinated women.

Methods: We collected and analyzed HPV prevalence data for women aged 18 to 29 years from the prevaccine era (2007–2008) to the postvaccine era (2009–2012) using the National Health and Nutrition Examination Surveys (NHANES); 1,628 female respondents aged 18 to 29 years, representing 21,135,134 women in the US noninstitutionalized civilian population, provided vaginal swabs across 3 consecutive NHANES survey cycles.

Results: Among women aged 18 to 29 years, the prevalence of high-risk HPV among women who received at least 1 dose of the HPV vaccine decreased from 67% in 2007–2008 (95% CI 50.7–81.4) to 41.5% in 2011-2012 (95% CI 30.5–53.1); among women vaccinated for HPV in the postvaccine era, the prevalence of HPV-16 and -18 was 6.4% versus 93.6% for all other high-risk HPV types. There was no difference in high-risk HPV prevalence among women who did not receive the vaccine: 49.5% (95% CI 42.5–56.6) in 2007–2008 versus 50.8% (95% CI 43.0–58.7) in 2011–2012.

Conclusions: The prevalence of high-risk HPV significantly decreased among women aged 18 to 29 years who received the HPV vaccine, but there appeared to be no cross-protection against nonvaccine HPV types. These findings may offer support for use of the investigational 9-valent HPV vaccine. There also was no evidence to suggest protection against HPV infection for unvaccinated women.

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58 - Scientific Plenary
Impact of a multifaceted program targeting key transitions in care on cervical cancer screening within a high-volume safety net health system
M.L. Anderson[a], Y. Cui[a], M. Daheri[b], C.L. Bailey-Delesbore[a], A.N. Ogunwale[a], H. Sangi-Haghpeykar[a], J.R. Montealegre[a], J.M.M. Bump[a], M.Y. Williams-Brown[a], L.M. Ramondetta[c], L. Hanser[b] and M.L. Jibaja-Weiss[a]. *[a]Baylor College of Medicine, Houston, TX, USA, [b]Harris Health System, Houston, TX, USA, [c]The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To assess the impact of a multifaceted program targeting the continuum of cervical cancer screening and prevention for medically underserved women enrolled in Harris Health, the nation's third largest safety net health system.

Methods: Educational videos were developed in English, Spanish, and Vietnamese and used to promote screening at routine points of contact at all 16 Harris Health community health centers (CHCs). Medical homes for screening were implemented at 3 CHCs with poor uptake of the Pap test. Three multilingual navigators and a nurse coordinator were used to educate patients, resolve psychosocial barriers, facilitate scheduling, address financial eligibility, and prompt patient notification and referral. Diagnostic resolution and outcomes were tracked for all patients with abnormal cervical cytology.

Results: Between fiscal years 2010 (baseline) and 2014, the proportion of Harris Health patients who were noncompliant with cervical screening decreased from 17% to 11% ($P < .001$), despite an increase in the total number of age-eligible female enrollees from 108,232 to 156,939. During this interval, the number of Harris Health enrollees diagnosed with abnormal cervical cytology increased from 2,903 to 3,436. After full programmatic implementation, diagnostic resolution for suspicious test results decreased from 9.1 ± 23.5 days to 7 ± 7 days for carcinoma, from 57.2 ± 68.9 days to 44.3 ± 46.2 days for high-grade dysplasia, and from 83.5 ± 94.4 days to 57.6 ± 59.3 days for low-grade

results ($P < .0001$). Only wait time for colposcopy after high-grade Pap test results remained outside its recommended NCSP benchmark. Over the same duration, time from abnormal Pap test to loop electrosurgical excision procedure decreased from 115.2 ± 95.4 days to 77.2 ± 13 days ($P < .001$). Notably, the number of cervical cancer precursors (AIS/CIS) diagnosed and treated at Harris Health facilities nearly doubled (from 113 to 216). Moreover, the number of early-stage (≤IB1) carcinomas increased from 20 (52.6%) to 26 (55.3%), whereas stage IV cancers decreased from 5 (14%) to 4 (8%) ($P < .01$).

Conclusions: System-wide targeting and tracking of key care transitions improves the prevalence and timeliness of screening and shifts cervical cancer burden in a high-volume safety net health system to earlier stage disease. Consideration should be given at a national level to creating regional programs to comprehensively address the multiple psychosocial, educational, and other barriers to cervical cancer screening among medically underserved women.

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59 - Scientific Plenary

Introducing careHPV into a public sector screening program in El Salvador

M. Cremer[a], M. Maza[b], K. Alfaro[b], J.C. Felix[c], J. Gage[d], P.E. Castle[e] and J. Kim[f]. *[a]Cleveland Clinic, Cleveland, OH, USA, [b]Basic Health International, San Salvador, El Salvador, [c]Keck School of Medicine of USC, Los Angeles, CA, USA, [d]National Cancer Institute, Bethesda, MD, USA, [e]Albert Einstein College of Medicine, New York, NY, USA, [f]Harvard University, Boston, MA, USA*

Objectives: The Cervical Cancer Prevention in El Salvador (CAPE) program introduces a low-cost human papillomavirus (HPV) DNA test into a public sector program. El Salvador has one of the lowest screening rates in Latin America (19%). Coverage rates are poor and follow-up for abnormal cytology is inadequate. Started in October 2012, CAPE consists of 3 phases. The aim is to implement a phased program that will ultimately screen 30,000 women. The true impact of this program lies in its final phase wherein the program is handed over to the government of El Salvador, and the Ministry of Health makes it the national screening program. Results of phase 2 of the program (n = 8,050) are presented.

Methods: A total of 8,050 women aged 30 to 49 years were screened in phase 2. Of these, 6,737 had both self- and provider-collected careHPV samples and 1,298 had only provider-testing. The agreement between both forms of sampling was 83.6%, with a k of 0.71. Women with provider-collected HPV-positive results were referred to treatment using the strategy followed by their community. Cohort A was referred to colposcopy, and cohort B had immediate visual triage and was treated with cryotherapy.

Results: Overall, 489 (12.3%) of 3,963 women in cohort A and 465 (11.4%) of 4.087 women in cohort B tested HPV positive. All cohort A patients were referred for colposcopy—387 (79.1%) had colposcopy in less than 6 months, and 203 (41.5%) of 489 were eventually treated (Figure 1). In cohort B, 397 (85%) of 465 received immediate treatment, and 56 (12%) were referred to colposcopy; of these 465 women, 408 (87.0%) were eventually treated (Figure 2).

Conclusions: A pilot program introducing HPV testing was successfully implemented in a low-resource setting. Requiring women to return for a colposcopy made them less likely to complete treatment. Outreach to women who had not been screened recently helped find women at higher risk for HPV.

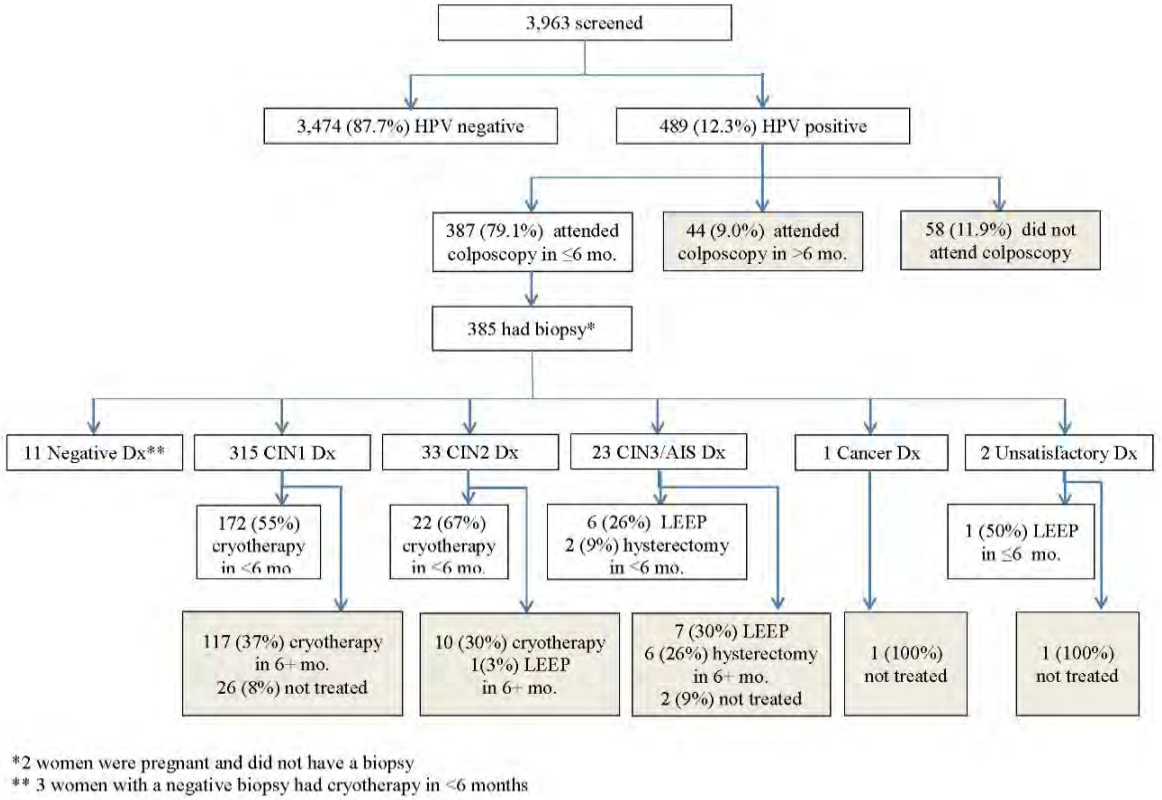

Fig. 1
Colposcopy Management Cohort.

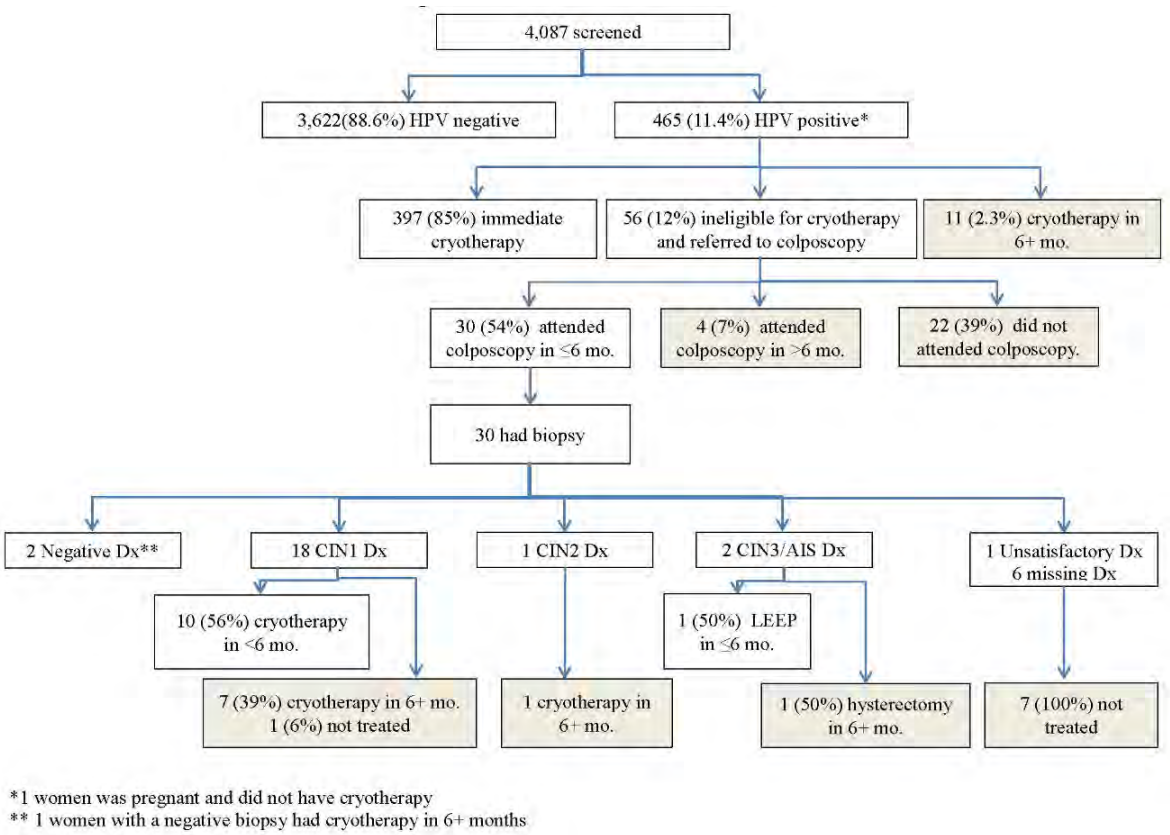

Fig. 2
Screen and Treatment Cohort.

Table 1
Compliance by management cohort.

	Colposcopy Management Cohort		Screen and Treat Cohort		*P*-value
	#	%	#	%	
Totals					
Total scheduled	XXXX		XXXX		
Total screened among scheduled	3,963	XX.X	4,087	XX.X	X.XX
Total HPV positive among screened*	489	12.3	465	11.4	0.18
Completed screening program (i.e. HPV-negative or HPV-positive with follow-up)					
Completed among scheduled	3,690	xx.x	4,033	xx.x	<.001
Completed among screened	3,690	93.1	4,033	98.7	<.001
Completed among HPV positives (completion with follow-up)	2 1 6	44.2	411	88.4	<.001
Screened HPV positive but failed to complete follow-up					
Did not attend colposcopy within 6 months	102	20.9			
Did not receive treatment within 6 months	171	35.0			
Did not get cryotherapy**			11	2.7	
Did not get colposcopy/treatment **			43	76.8	

60 - Scientific Plenary

Fully sialylated alpha-chain of complement 4–binding protein: Diagnostic utility for ovarian clear cell carcinoma

M. Mikami[a], K. Tanabe[b], K. Matsuo[c], M. Miyazawa[a], M. Hayashi[a], S. Asai[a], M. Ikeda[a], M. Shida[a], T. Hirasawa[a] and R. Sho[d].
[a]Tokai University School of Medicine, Isehara, Japan, [b]LSI Medience Corporation, Tokyo, Japan, [c]University of Southern California, Los Angeles, CA, USA, [d]Sho Hospital, Tokyo, Japan

Objectives: Although a certain fraction of endometriomas can develop de novo epithelial ovarian cancer (EOC) such as ovarian clear cell carcinoma (OCCC), currently no useful biomarker exists for early distinction of OCCC from endometriomas. The aim of this study was to describe the diagnostic utility of a novel biomarker for EOC, especially to distinguish OCCC from endometrioma.

Methods: More than 100,000 glycan structures of serum glycoproteins obtained from 134 pretreatment all-stage EOC patients (including 45 OCCCs) and 159 noncancer control women (including 36 endometriomas) were explored for a mass spectrum approach. Diagnostic accuracy of the identified biomarker was compared with that of CA-125 by comparing area under the curve (AUC) and positive and negative predictive values (PPV and NPV).

Results: A2160, a fully-sialylated alpha-chain of complement 4–binding protein, was identified as the candidate target marker. A2160 was significantly elevated in OCCCs at all stages with endometrioma. Diagnostic accuracy of A2160 (cutoff 1.6 U/mL) to distinguish early-stage OCCC from endometrioma is significantly higher than that of CA-125 (cutoff 35 IU/L); for A2160 versus CA-125, AUC: 0.92 versus 0.67; PPV: 95% versus 64%; and NPV: 85% versus 58%. In addition, fully sialylated glycans had a larger accuracy for diagnosing EOC compared with partially sialylated glycans of alpha-chain of complement 4–binding protein.

Conclusions: Our study suggested that A2160 may be a useful biomarker to distinguish early-stage OCCC from endometrioma. This new biomarker can be potentially applied for monitoring endometrioma patients, which could make the early diagnosis of OCCC possible.

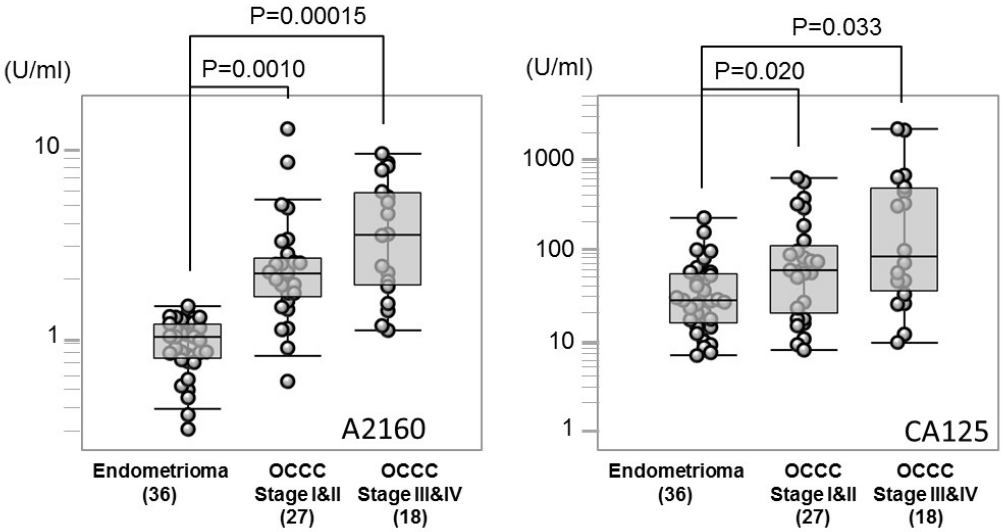

Fig. 1
A2160 and CA-125 levels in endometrioma, stage I-II OCCC, and stage III-IV OCCC.

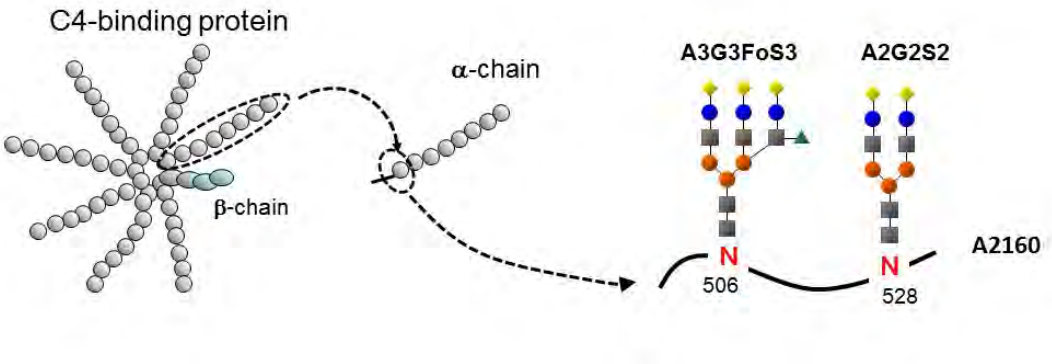

Fig. 2
A2160 glycopeptide and its proposed structure.

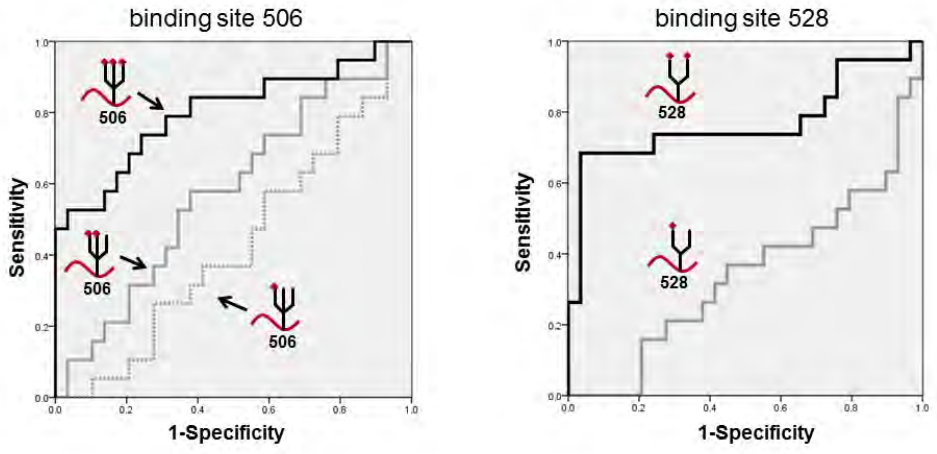

Fig. 3
Comparison of fully vs. partially sialylated alpha-chains of C4BP.

61 - Scientific Plenary

Are U.S. physicians performing salpingectomy? Experience with incorporation of opportunistic salpingectomy in a large community-based health system

C. Garcia[a], M. Martin[b], L. Lyon[c], M.A. Armstrong[c], S. McBride-Allen[c], T.R. Raine-Bennett[c], R.D. Littell[b] and B. Powell[b].
[a]University of Virginia, Charlottesville, VA, USA, [b]Kaiser Permanente San Francisco Medical Center, San Francisco, CA, USA, [c]Kaiser Permanente Northern California Division of Research, Oakland, CA, USA

Objectives: To evaluate the trend in uptake of salpingectomy at the time of hysterectomy and assess physician attitudes toward the practice.

Methods: Retrospective chart review using electronic medical records identified women older than 20 years undergoing hysterectomy from June 2011 to June 2014 in a large community-based US health system. Women undergoing bilateral oophorectomy, with a diagnosis of cancer or a *BRCA1* or *BRCA2* mutation were excluded. The rates of salpingectomy were then calculated per year and compared using a X^2 test. All obstetrics/gynecology physicians were sent an electronic survey assessing attitudes toward opportunistic salpingectomy.

Results: Of the 11,694 hysterectomies performed over the 3-year study period, 4,525 were performed without oophorectomy and were eligible for inclusion. Most were performed without salpingectomy (87%), though there was a statistically significant rise in the rate of salpingectomy from 4.5% during June 2011 to May 2012, to 14.1% during June 2012 to May 2013, and to 32.1% during June 2013 to May 2014 ($P < .001$). There was a significantly shorter median operating room time (187 vs 207 minutes, $P < .001$) and length of stay (22.8 vs 25.2 hours, $P < .001$) for hysterectomy alone compared with bilateral salpingectomy. The difference in estimated blood loss between hysterectomy alone versus salpingectomy was not clinically significant (median 150 mL [75,250] vs 150 mL [100,300], $P < .001$). The survey was completed by 46% (249/543) of physicians: 89% were generalist obstetrician/gynecologists, 77% were women, and 66% reported performing salpingectomy. There were no demographic differences between physicians who reported performing salpingectomy and those who did not (Table 1). Although most physicians felt there were no barriers to performing salpingectomy (54%), the 3 most common barriers identified were difficulty accessing the tube (36%), increased complications (3%), and forgetting to address it with patients (2%).

Conclusions: Most physicians report performing salpingectomy with no identifiable barriers; however, this procedure was only performed in conjunction with hysterectomy 32% of the time in 2013–2014, highlighting an opportunity for further education of physicians in the United States. There was a 2.4-hour increase in median length of stay and a 20-minute increase in median operating room time for salpingectomies.

Table 1
Characteristics of survey respondents by whether they perform salpingectomy.

	Perform Salpingectomy	Do not perform Salpingectomy	P-value
Gender	--	--	P = .171
Female	142 (74.3)	26 (86.7)	--
Male	49 (25.7)	4 (13.3)	--
Type of Practice	--	--	P = .131
Generalist	171 (88.6)	27 (90.0)	--
Oncology	9 (4.7)	0 (0)	--
Perinatology	4 (2.1)	2 (6.7)	--
Reproductive endocrinology and infertility	1 (0.52)	1 (3.3)	--
Urogynecology	8 (4.2)	0 (0)	--
Years in Practice	--	--	P = .745
<5 years	36 (18.7)	5 (16.7)	--
5-10 years	38 (19.7)	4 (13.3)	--
10-20 years	70 (36.3)	11 (36.7)	--
>20 years	49 (25.4)	10 (33.3)	--

62 - Scientific Plenary
Impact of gynecologic screening in Lynch syndrome
C. Cornou, A.S. Bats, G. Vannieuwenhuyse, P. Capmas, C. Bensaid, C. Ngô, C. Nos and F. Lecuru. *Hôpital Européen Georges-Pompidou, Paris, France*

Objectives: Lifetime risk of developing endometrial cancer in Lynch syndrome is higher than in the general population. Gynecologic screening appears interesting, but it is unproven until now. The aim of our study was to determine the value of gynecologic screening for the diagnosis of endometrial complex/atypical hyperplasia and cancer in patients with Lynch syndrome.

Methods: We conducted a prospective study of patients with Lynch syndrome with identified mutations from 1998 to 2015 at the European Georges-Pompidou Hospital in Paris. All patients underwent annual screening, including clinical examination, pelvic ultrasound, endometrial biopsy, and hysteroscopy. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each test and of the global screening strategy were described, as well as endometrial complex/atypical hyperplasia and cancer.

Results: One hundred and seventy-seven patients, with 539 surveillance visits, were included in the study. The median age of patients was 51 years. Mutations identified were MLH1 (38.5%), MSH2 (39.3%), MSH6 (17.9%), and PMS2 (3.4%). Sensitivity, specificity, PPV, and NPV of pelvic ultrasound were 75%, 93.4%, 9.3%, and 99.8%, respectively. For endometrial biopsy, they were 80%, 99.7%, 80%, and 99. 7%, respectively, and for hysteroscopy, they were 100% in all cases. Sensitivity of the global screening strategy was 100%. Five cases of endometrial cancers were diagnosed through the screening. One endometrial cancer case was associated with ovarian cancer (endometrioid carcinoma) that was detected with pelvic ultrasound.

Conclusions: A screening strategy including pelvic ultrasound, endometrial biopsy, and hysteroscopy appears efficient for the diagnosis of gynecologic cancers in Lynch syndrome.

Scientific Plenary IX: Ovary
Tuesday, March 22, 2016
Moderators: Leslie M. Randall, MD*, University of California at Irvine Medical Center, Orange, CA, USA*
Debra L. Richardson, MD*, University of Texas Southwestern Medical Center, Dallas, TX, USA*

63 - Scientific Plenary
Ostomy formation without protective benefit is increased among ovarian cancer patients undergoing cytoreductive surgery with a general surgeon
N. Desravines, E.L. Barber and J.F. Boggess. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: Ostomy formation is rarely necessary during cytoreductive surgery for ovarian cancer and can decrease patient quality of life when compared with primary anastomosis. In contrast, protective ostomies are often used in general surgery. We examined if there was a difference in ostomy creation in patients undergoing primary cytoreductive surgery with a general surgeon or a gynecologic surgeon.

Methods: We used the National Surgical Quality Improvement Program database to identify women who underwent primary cytoreductive surgery for ovarian cancer between 2008 and 2012. We dichotomized patients by the surgical specialty of the primary surgeon and queried the database for concurrent ostomy creation. Demographic variables, surgery characteristics, and patient comorbidities were used as covariants. The externally validated Charlson comorbidity index was used to measure comorbidity. Descriptive statistics and binary logistic regression were used for analysis.

Results: We identified 2,093 patients who underwent primary cytoreductive surgery for ovarian cancer. Gynecologic surgeons performed 88.6% and general surgeons performed 11.4%. Ostomies were created in 6.5% and 23.1%, respectively ($P < .001$). Age and obesity were not associated with ostomy formation; however, lower albumin ($P < .001$), preoperative sepsis ($P < .001$), higher Charlson score ($P = .001$), and emergency surgery ($P < .001$) were associated with ostomy formation. In a logistic regression model controlling for these variables, surgery with a general surgeon was associated with an increased risk of ostomy formation (OR 3.33, 95% CI 2.13–5.14). The decreased rate of ostomy formation by gynecologic surgeons was not associated with increased deep organ space infection (4.6% general, 2.3% gynecologic, $P = .058$) or postoperative sepsis (8.0% general v 2.7% gynecologic, $P < .001$).

Conclusions: Patients undergoing primary cytoreductive surgery for the treatment of ovarian cancer with a general surgeon compared with a gynecologic oncologist had a 3-fold increase in ostomy formation. Increased ostomy formation was not associated with protective effects against surrogate markers for postoperative bowel leak. Further research is needed to elucidate this difference in practice patterns.

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64 - Scientific Plenary

A prospective algorithm to decrease anastomotic leak after rectosigmoid resection during debulking surgery for gynecologic malignancies

E. Kalogera, C.C. Nitschmann, S.C. Dowdy, J.N. Bakkum-Gamez, B.S. Gostout, A. Mariani, B.A. Cliby and C.L. Langstraat.
Mayo Clinic, Rochester, MN, USA

Objectives: To determine whether implementation of a standardized protocol for temporary bowel diversion after rectosigmoid resection (RSR) reduces the rate of anastomotic leak (AL), a catastrophic complication in patients undergoing surgery for gynecologic cancer.

Methods: This was a prospective quality improvement project in patients undergoing RSR during debulking surgery between July 2013 and July 2015. Patients with any of the following underwent temporary diversion: (1) preoperative albumin 3.0 g/dL or less, (2) prior pelvic radiation, (3) more than 1 large bowel resection (LBR), (4) anastomosis (AS) of 6 cm or less from the anal verge, (5) concerns regarding integrity of AS (i.e., leak during proctoscopy without revision of AS) or gross contamination of the pelvis with stool. The AL rate was calculated and compared with the AL rate from a historic cohort (January 1994–June 2011) using the Fisher exact test.

Results: Sixty-four patients underwent RSR during the study period. Twenty-five patients (39.1%) received diverting stomas versus 35 (5.7%) of 609 in the historic cohort. An additional 7 patients met the criteria, but did not have a diversion. The most common indications for diversion were RSR with additional LBR (9/20), AS at 6 cm or less from anal verge (5/20), and leak during proctoscopy (5/20). After implementation of the standardized protocol, the AL rate was 3.1% (2/64), 50% lower than the historic AL rate of 6.2% (38/609; $P = .42$). There were no AL cases among patients who had a diversion. Of note, 1 AL met the criteria for diversion per protocol, but did not have a diversion (theoretical AL rate 1/64, 1.6% vs 6.2%, $P = .16$). Among 38 AL cases in the historic cohort, 90-day mortality was 18.4%; 64% of AL cases would have met criteria for diversion and were thus potentially preventable. Short-term outcomes were not different between patients without an AL who did and did not have a diversion.

Conclusions: Criteria-based temporary bowel diversion for patients undergoing RSR for gynecologic cancer appears to reduce AL. Diversion was not associated with increased short-term morbidity. Long-term outcomes and costs of diversion and re-establishing continuity are currently being evaluated.

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65 - Scientific Plenary

Trends in the use of neoadjuvant chemotherapy for advanced-stage ovarian cancer: A National Cancer Data Base study

E.M. Hinchcliff[a], A. Melamed[b], J.T. Clemmer[b], J.O. Schorge[b], A. Goodman[c], D.M. Boruta II[c], M. del Carmen[c] and J.A. Rauh-Hain[b]. [a]*Harvard Medical School, Boston, MA, USA,* [b]*Massachusetts General Hospital, Boston, MA, USA,* [c]*Massachusetts General Hospital/Harvard University, Boston, MA, USA*

Objectives: To examine the use of neoadjuvant chemotherapy (NACT) for advanced-stage ovarian cancer over time.

Methods: The National Cancer Data Base (NCDB) was used to identify women with advanced-stage (stage III/IV) ovarian cancer who received chemotherapy and debulking surgery from 2003 to 2012, and the annual proportion of women who received NACT was calculated. Join point regression was used to assess trends in annual frequency. Overall differences over the study period were compared between the first and last year using the χ^2 test.

Results: The study sample included 37,448 women, with 27,387 at stage III (73.9%) and 9,680 at stage IV (26.1%). Between 2003 and 2012, the frequency of NACT increased from 7.2% to 20.3% and from 17.3% to 39.0% among women with stage III and stage IV disease, respectively. Frequency of NACT among women with stage III cancer remained constant from 2003 to 2008 ($P = .06$ for trend), and increased annually by 17.0% (95% CI 9.2–25.3, $P = .002$) between 2008 and 2012 ($P = .03$ for change of trend). Among women with stage IV cancer, the frequency of NACT increased steadily throughout the study period (annual percentage change, 8.9%, 95% CI 7.4–10.4, $P < .001$). In addition, the frequency of NACT use increased among all age groups during the study period, but the rise in frequency

varied by age group. The risk difference for patients younger than 50 years was 11.1 (CI 7.6–14.6); between 50 and 59 years, 12.4 (CI 9.3–15.5); between 60 and 69 years, 16.5 (CI 13.2–19.7); and age 70 or older, 19.3 (CI 15.8–22.8).

Conclusions: The use of NACT has increased for advanced-stage ovarian cancer from 2003 to 2012. This rise in frequency was more pronounced with increasing age. NACT use increased steadily for stage IV disease, whereas for stage III disease, an inflection point was seen in 2008 when the rate of increase of NACT use increased significantly.

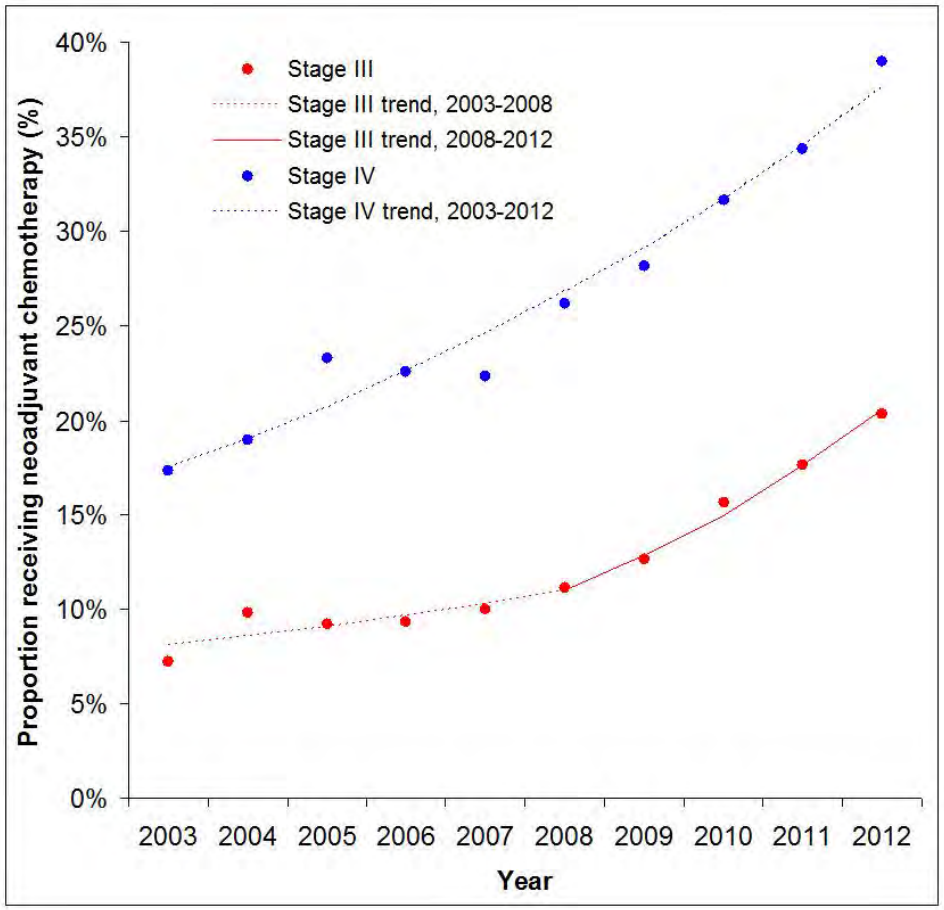

Fig. 1
Trends in the use of neoadjuvant chemotherapy for Stage III/IV ovarian cancer.

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66 - Scientific Plenary
Intraperitoneal chemotherapy outcomes following interval cytoreductive surgery for advanced-stage ovarian cancer at a comprehensive cancer center
J.J. Mueller, A. Kelly, Q. Zhou, A. Iasonos, K. Long Roche, Y. Sonoda, R. O'Cearbhaill, O. Zivanovic, D.S. Chi and G.J. Gardner. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: Multiple trials support the administration of intraperitoneal chemotherapy (IP) after primary debulking surgery (PDS), although it has substantial toxicity. We sought to determine feasibility and outcome of IP delivery after interval debulking surgery (IDS) among patients deemed ineligible for PDS.

Methods: We identified all stage III/IV ovarian cancer patients treated at our institution with neoadjuvant chemotherapy (NACT) from January 2008 to May 2013. Clinicopathologic data were abstracted from medical records. PDS cases, grade 1–2 histology, and nonplatinum/taxane regimens after IDS were excluded. IP was defined as 1 or more cycles of an intravenous (IV)/IP platinum regimen, dose dense treatment (DD) as no IP, and 1 or more cycles of a platinum/weekly paclitaxel regimen, and standard chemotherapy (SC) as an every-3-week PLT-based treatment with no IP or DD. Appropriate statistical tests were performed.

Results: Of 154 cases selected for NACT, 5 (3%) did not undergo IDS because of disease progression. Twenty-one cases (14%) had a post-IDS regimen that did not meet inclusion criteria. Of the remaining 128 cases, 118 (92%) had less than 1 cm residual disease at IDS, and 74 (58%) achieved complete gross resection; rates were similar across groups. An IP port was placed in 57 (45%) of 128 cases, with 84% utilization. Forty-eight (38%) of 128 patients received IP, 17 (13%) had DD, and 63 (49%) SC. Median age for IP was 60 years (range, 34–76 years) compared with

66 years for SC (range, 38–86 years) and 64 years for DD (range, 36–80 years) ($P \leq .001$). Twelve (25%) of 48 IP patients had stage IV disease compared with 39 (62%) of 63 SC patients and 9 (53%) of 17 DD patients ($P \leq .001$). Median CA-125 at the time of diagnosis was 927 U/mL (range, 12–8,143 U/L) in IP patients, 1,410 U/mL (range, 98–10,514 U/L) in DD patients, and 370 U/mL (range, 6–16,923 U/L) in SC patients ($P \leq .001$). The median number of IP cycles after IDS was 3. Three (5.3%) of 57 ports developed problems that required a regimen switch. There were no differences in neuropathy or platinum hypersensitivity rates between IP, DD, and SC. With follow-up of 45.3 months (range, 12.5–71.9 months), median PFS was 9.9 months (95% CI, 7.4–13.9 months) for IP patients, 7.3 months (95% CI, 3.6–11.2 months) for DD patients, and 7.2 months (95%CI, 4.3–12.6 months) for SC patients (landmark analysis starting at 3.4 months after IDS).

Conclusions: Thirty-eight percent of patients received IP after IDS, with a high rate of successful port utilization and few regimen switches because of port malfunction or treatment tolerability. Candidates for IP after IDS were younger, with fewer patients having stage IV disease. PFS and rates of optimal resection after IDS were comparable across all groups.

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67 - Scientific Plenary

Standard chemotherapy for ovarian cancer increases expression of cancer stem cell biomarkers which is predictive of survival

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Objectives: Many molecular mediators have been described to possess cancer stem cell (CSC) characteristics in ovarian cancer. It has been hypothesized that these mediators are potentiated by chemotherapy, which portends earlier recurrence and shorter survival. We aimed to explore the effect of chemotherapy on ovarian CSC-like mediators.

Methods: Matched pre- and post-chemotherapy tumor specimens from ovarian cancer patients were obtained. All patients underwent neoadjuvant chemotherapy with interval debulking surgery. Samples were analyzed for expression of 27 CSC markers via quantitative polymerase chain reaction (qPCR). Data were depicted as a fold change in gene expression between post- and pre-treatment samples and compared with clinical factors. Associated immunohistochemical stains were used to validate qPCR data. CSC markers were validated in a tumorsphere model and in vivo tumor-initiating studies.

Results: Specimens from 22 patients with stage IIIC/IV serous ovarian cancer were obtained. Twenty-seven CSC markers demonstrated an increase in gene expression after exposure to chemotherapy. A 3-fold or greater increase in gene expression after exposure to chemotherapy was seen in 9 (33%) of 27 markers: ABCG2 (5.8-fold), ALDH1A1 (4.0), CTGF (5.4), DPP4 (4.2), MYC (3.4), POSTN (6.7), CD133 (6.5), SOX2 (8.5), and VCAN (3.2). Only 3 markers demonstrated a significant fold increase that correlated with platinum resistance: POSTN 4.1-fold ($P = .04$), ALDH1A1 5-fold ($P = .037$), and SOX2 14.5-fold ($P = .004$). SOX2(hi) OVCAR8 ovarian cancer cells exhibited significantly higher levels of tumorsphere-forming potential ($P = .04$) than Sox2(lo) cells. SOX2(hi) OVCAR8 cells were more tumorigenic than SOX2(lo) cells when implanted in immunocompromised mice. “HIGH” gene expression (greater than mean fold increase) in these 3 markers demonstrated shorter progression-free survival compared with “LOW” expression: POSTN (5 vs 11 months, $P = .02$), ALDH1A1 (2 vs 11 months, $P = .01$), and SOX2 (6 vs 10 months, $P = .04$).

Conclusions: Chemotherapy increased gene expression of 27 CSC markers in ovarian cancer. POSTN, ALDH1A1, and SOX2 significantly correlated with platinum resistance and higher expression predicted shorter progression-free survivals. The correlation of elevated CSC markers with poor prognosis highlights the need for the use of a CSC-directed agent to potentially extend survival of patients with ovarian cancer.

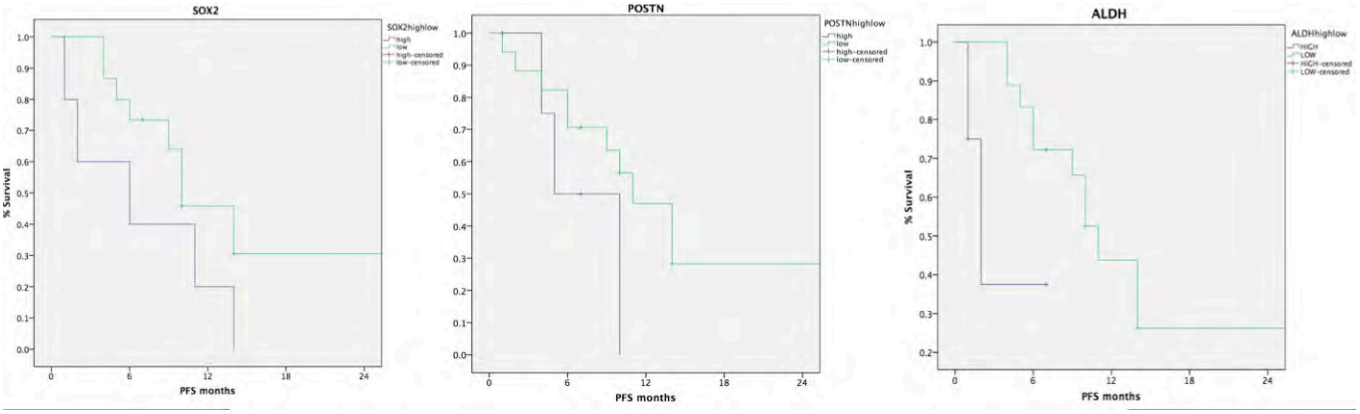

Fig. 1
Progression free survival (PFS) stratified by cancer stem cell gene expression.

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68 - Scientific Plenary
Primary cytoreductive surgery and adjuvant hormone therapy in women with advanced low-grade serous carcinoma: Reducing overtreatment without compromising survival?
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Objectives: Women with low-grade serous carcinoma (LGSC) of the ovary or peritoneum have low chemotherapy response rates and poor overall survival (OS) with advanced-stage disease. Most LGSC tumors overexpress hormone receptors, which represent a potential treatment target. Our study objective was to determine the safety and survival outcomes of patients with advanced-stage LGSC treated with cytoreductive surgery (CRS) and hormone therapy (HT) in the primary setting.

Methods: A retrospective study at two academic cancer centers was performed. Patients with stage II–IV LGSC underwent either primary or interval CRS, followed by adjuvant HT, between 2004 and 2014. Expert gynecologic pathologists reviewed all cases. Data on patient, surgical, and treatment variables were collected. Median progression-free survival (PFS) and OS were calculated. Outcomes were compared with those of an age- and stage-matched LGSC control group treated with CRS and chemotherapy.

Results: Twenty-six patients with LGSC were treated with CRS + HT. Primary CRS + HT was administered in 25 patients, and neoadjuvant chemotherapy followed by CRS + HT was administered in 1 patient. The median patient age was 46.5 years, and patients had stage II (n = 4), stage IIIA (n = 6), stage IIIC (n = 15), and stage IV (n = 1) disease. Optimal CRS to no apparent gross residual disease was achieved in 81.5%, optimal CRS less than 1 cm in 14.8%, and suboptimal CRS in 3.7%. The patient treated with neoadjuvant chemotherapy had extensive carcinomatosis and liver metastases (stage IV) that progressed with chemotherapy; after CRS, she has been progression-free for 15 months with shrinking liver implants on HT. Anastrozole was administered postoperatively in 55.6%, letrozole in 37.0%, and tamoxifen in 7.4%. The median time for HT was 18 months. After a median follow-up of 28 months (range, 10–126 months), 4 patients (14.8%) developed a recurrence. All initial abdominopelvic recurrences were salvaged with CRS with or without chemotherapy or HT. Three patients (11.5%) are alive with disease, and 23 (88.5%) have no evidence of disease. The median PFS was 22 months and median OS was not yet reached. Compared with a control group of 44 patients with LGSC treated with CRS + chemotherapy (median PFS: 21 months, median OS: 70 months), the survival of the HT-treated cohort was not significantly different.

Conclusions: Our series describes the initial experience with CRS and HT for primary advanced-stage LGSC. Although surgery remains the mainstay of therapy, cytotoxic chemotherapy may not be necessary in the primary setting. These results merit further investigation in a prospective trial.

Featured Poster Session: Meet the Professor: Connecting Minds for a Better Future

69 - Featured Poster Session
The relationship between endometrial cancer sentinel lymph node micro and macro metastases and uterine pathology features
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Objectives: The practice of selective lymphadenectomy based on uterine pathology risk factors has been popularized after risk factors for lymph node metastases were identified in large observational single institution and cooperative group studies. SLN biopsy is an alternative staging technique proposed to overcome the limitations of selective algorithms. The clinical validity of low-volume metastases identified in SLN specimens that have been ultrastaged has been questioned. The objective of this analysis is to identify whether patients with positive SLNs demonstrate the previously identified risk factors for lymph node metastases.

Methods: The FIRES trial is a multi-institution, prospective cohort study measuring the accuracy of SLN mapping in clinical stage I endometrial cancer (all histologies) in identifying metastatic disease. All patients received a standardized SLN mapping technique with cervical indocyanine green injection and robotic fluorescence imaging, followed by hysterectomy with pelvic and para-aortic lymphadenectomy. All H&E-negative SLN specimens were ultrastaged with immunohistochemistry (IHC) to cytokeratin. Pathologic results of the SLNs (including volume of disease: macro metastases versus micro metastases [<2 mm and isolated tumor cells]) were evaluated along with uterine tumor risk factors. Fisher exact test was used to compare dichotomous variables between groups.

Results: Among 308 patients, 37 (12%) had nodal metastases, 30 of whom mapped at least 1 SLN (81%). Twelve patients (32%) with nodal metastases were detected only with IHC (≤2 mm). Compared with patients with macro metastases, micro metastases were less likely to be associated with high grade or nonendometrioid histology (P = .02), para-aortic metastases (P = .05), and lymphovascular space invasion (P = .001). All but 1 node-positive patient (97%) (including all patients with SLN micro metastases) demonstrated at least 1 previously described uterine pathology risk factor for lymphatic spread (grade 3 histology, outer half myometrial invasion or tumor size >2 cm).

Conclusions: Micro metastases within SLNs appear to be associated with known uterine risk factors for nodal metastases. This supports the validity of metastatic disease identified in SLNs with ultrastaging techniques. The disease-specific outcomes of patients with low-volume disease have not yet been established.

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70 - Featured Poster Session
When does the sentinel lymph node mapping support a less radical surgery in the management of early stage cervical cancer? A single institutional prospective study
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Objectives: Lymph node (LN) metastasis is considered an important prognostic factor for recurrence in cervical cancer (CaCx). Therefore, we aim to develop a single algorithm detecting the sentinel lymph nodes (SLNs) and combining their status with other individual prognostic factors for metastasis, to avoid lymphadenectomy and radical parametriectomy in the surgical management of early-stage CaCx.

Methods: Our prospective study included patients with CaCx, stage IA1-IIA1 (tumor size, 0.5-3 cm). Intracervical injection of methylene blue was given after induction of anesthesia, followed by detection of LNs that are dyed and sent for frozen section biopsy. Bilateral pelvic lymphadenectomy and radical hysterectomy was then performed and correlated with final histopathology.

Results: Thirty-four patients were recruited. At least 1 SLN (range 0-6) was identified in 79.4% (27/34), whereas bilateral involvement was detected in 80% (20/25). SLNs were located at the external (53.8%) or internal iliac region (15.4%), obturator fossa (19.2%), and ventral to the hypogastric vessels (11.6%), whereas 9.1% were found in unexpected areas (parametrium) in cases with tumor sizes (TS) of 2.2 cm or more, positive lymphovascular space invasion, and depth of invasion of 0.5 cm or more. Parametrial involvement was not detected when SLNs were negative. False-negative SLNs and micrometastasis were identified in only 2 cases (TS ≥2.2 cm). Frozen section biopsy was positive in 4 cases (11.7%) and the procedure was aborted. SLN sensitivity in detection of metastasis was 100%

for TS less than 2.2 cm, negative lymphovascular space involvement (LVSI), and DOI <5 mm. Median follow-up was 11.2 months (range 1-24) and all patients remain without evidence of disease.

Conclusions: Our findings confirm the clinical significance of SLN mapping in minimizing systematic lymphadenectomy and support less radical surgery of the parametrium with greater safety in cases with small tumors. However, this study establishes our technique as feasible and adequate in early-stage cervical cancer.

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71 - Featured Poster Session

Obesity significantly reduces the sentinel lymph node detection rate in women with endometrial cancer

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Objectives: The role of sentinel lymph node (SLN) mapping continues to evolve in the surgical management of endometrial cancer. The reported overall detection rate of any SLN is 80%, with a bilateral SLN detection rate of nearly 60%. The purpose of this study was to determine if patient-specific factors affect the ability to identify SLNs in women with newly diagnosed endometrial cancer.

Methods: Prospective data collected as part of 2 ongoing clinical trials evaluating SLN in endometrial cancer were reviewed. Clinical characteristics such as age, body mass index (BMI), previous abdominal surgery, uterine size, presence of fibroids, adenomyosis, grade, and depth of invasion were collected. Identification of SLN was classified as any, unilateral, or bilateral. Univariate logistic regression was used to calculate odds ratios.

Results: Two hundred and forty-six patients underwent attempted SLN mapping between April 2013 and August 2015. Median age and BMI were 60.5 years (range, 23.5–87.0) and 33.8 kg/m^2 (range, 15.8–68.3), respectively. At least 1 SLN was detected in 79.7% (194/246) of patients; of these, 59.8% (116) were bilateral, 39.2% (76) were unilateral, and 1% (2) were paraaortic only. Indocyanine green was the most common dye used (n = 169, 68.7%), followed by blue dye (n = 63, 25.6%) and blue dye + technetium (n = 12, 4.9%). Surgical approach varied with 39.4% (97) robotic, 50.0% (123) laparoscopy, and 10.6% (26) laparotomy. Compared with normal weight women, obese women were significantly less likely to have an SLN (odds ratio [OR] 0.07, 95% CI 0.01–0.56, P = 0.01). With each increase in BMI by 1 kg/m^2, there was a 5% decrease in SLN detection (OR 0.95, 95% CI 0.92–0.99, P = .004). There was no difference in SLN detection rates based on age, previous surgery, uterine size, fibroids, adenomyosis, grade, or depth of invasion.

Conclusions: Overall SLN detection rate was 79.7%. Obesity was the only patient-specific factor that decreased the likelihood of identifying a SLN. This should be considered when counseling patients about SLN biopsy for endometrial cancer.

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72 - Featured Poster Session

Feasibility study of indocyanine green for sentinel lymph node mapping in early-stage cervical cancer

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Objectives: Standard techniques for sentinel lymph node (SLN) mapping in cervical cancer remain unclear, with limited data on the use of indocyanine green (ICG). We sought to determine the feasibility and mapping rate of SLNs with intracervical injection of ICG in patients with cervical cancer.

Methods: Women with early-stage cervical cancer (stage IA1–IB2) underwent SLN mapping with ICG during initial surgical management, either with robotic-assisted radical hysterectomy (RA-RH) or fertility-sparing surgery at 2 high-volume centers from October 2012 to August 2015. ICG was injected peritumorally at the 3 and 9 o'clock positions of the cervical stroma. Bilateral pelvic lymphadenectomy was concurrently performed for all patients, except in cases in which extracervical disease was identified intraoperatively. All clinically enlarged lymph nodes were removed.

Results: Twenty-three women with a median age of 47 years and body mass index of 28.4 were included: 17 (74%) had squamous cell carcinoma and 6 (26%) had adenocarcinoma. Most patients (74%) had stage IB disease. Most patients (91%) underwent RA-RH, 1 patient underwent cold knife cone for fertility preservation, and in 1 case, the RH

was aborted. Clinical tumor size ranged from microscopic to 4.5 cm, with a median of 1.5 cm. SLN mapping was successfully performed in 22 cases (96%), of which 91% demonstrated successful bilateral mapping. Seven tumors were 2 cm or greater, and 100% had successful bilateral mapping. A median of 2 SLNs were removed from each hemi-pelvis. SLNs were most commonly identified in the hypogastric (48%), external iliac (20%), obturator (14%), common iliac (8%), and para-aortic (8%) regions. In 2 cases, lymph node metastasis was identified. In 1, bilateral SLN mapping was successful, and frozen section of the sentinel nodes was positive at the time of surgery. In another, bilateral SLN mapping was successful and the SLNs were negative; however, enlarged nodes were removed because of their suspicious appearance at the time of surgery and found to have metastasis.

Conclusions: SLN mapping with ICG is feasible and has high detection rates in early-stage cervical cancer. Removal of clinically suspicious nodes is critical regardless of SLN mapping success. Further studies are needed to determine if SLN alone can replace lymphadenectomy in women with early-stage cervical cancers in the absence of clinically suspicious lymph nodes.

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73 - Featured Poster Session
Single-port laparoscopy and PINPOINT mapping of sentinel lymph nodes with indocyanine green (ICG) in endometrial carcinoma
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Objectives: To present the first report and feasibility of single port laparoscopy (SPL) for sentinel lymph node (SLN) mapping using indocyanine green (ICG) in women with endometrial carcinoma (EC).

Methods: Women with EC were prospectively followed under an institutional review board–approved protocol for SLN mapping as part of their initial surgical management. An injection of 0.5 mL of a 500 µg/ mL solution was given superficially, then 1-cm deep at the 3 and 9 o'clock positions of the cervix. All patients subsequently underwent SPL with SLN mapping and hysterectomy with additional lymphadenectomy as indicated based on Mayo Clinic criteria for staging.

Results: Seven women with a median age of 59 years underwent SPL with hysterectomy/salpingo-oophorectomy and SLN mapping. Median body mass index and prior surgeries were 28.7 and 1, respectively. Thirteen (92.9%) of 14 hemi-pelvises were mapped with ICG and a median of 1 SLN was removed per hemi-pelvis (range 0–5). The most common SLN sites were inferior and medial to the common iliac bifurcation and the obturator space. Median operative (op) time, estimated blood loss, and length of stay were 184 minutes, 60 mL, and 1 day, respectively. Operative time declined significantly with additional cases (range, 134–201 minutes; $R^2 = 0.80$). There were no conversions to either standard laparoscopy or laparotomy and no intraoperative or 30-day postoperative complications were noted.

Two (28.6%) of seven women had at least 1 positive SLN. One had a grade 2 tumor with 15% myoinvasion and + lymph-vascular space invasion (LVSI), and 1 of 1 right and 1 of 2 left SLNs were positive, only on ultra-staging. The other patient had a grade 2 tumor with 7% myoinvasion, + LVSI, and 0 of 2 right and 1 of 1 left SLNs were positive on standard microscopy. Given low-risk features at surgery, neither underwent full lymphadenectomy. Overall, 3 (42.9%) of 7 women had LVSI: 2 with positive SLNs and another with microscopic spread to her ovary, but negative SLNs and pelvic lymph nodes. All 3 women received adjuvant treatment with a combination of radiation and systemic therapy.

Conclusions: SPL can be successfully used for consistent SLN identification using ICG and a fluorescence-based laparoscopic laser in patients undergoing hysterectomy for EC. Evidence is accumulating to help identify the true usefulness of and the most appropriate patients for SLN detection in women with EC.

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74 - Featured Poster Session
Comparison of single incision surgery to other laparoscopic modalities of endometrial cancer staging
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Objectives: There are no published data comparing surgical outcomes for single incision laparoscopy with other more widely performed surgical modalities in gynecologic oncology. Our goal was to directly compare single incision endometrial cancer staging with both robotic assisted and multiple port laparoscopy.

Methods: All surgical encounters at a single institution with the preoperative diagnosis of endometrial cancer from January 2012 to May 2015 were identified. Planned laparoscopic endometrial cancer staging cases via a robotic, single incision, or multiple port approach were included in the analysis. There were 4 participating surgeons. Preoperative demographics, surgical outcomes, pathology and readmissions were compared.

Results: A total of 220 laparoscopic endometrial cancer staging surgeries were identified, 144 (65.5%) robotic, 48 (21.8%) single incision, and 28 (12.7%) multiple port. Patients did not differ significantly in age, body mass index, race, or medical comorbidities across the 3 groups. Operative time was similar between the 3 laparoscopic approaches (robotic: 248 minutes, single incision: 238 minutes, multiple port: 235 minutes; $P = .78$). The average blood loss was 130 mL, 150 mL, and 231 mL for robotic, single incision, and multiple port, respectively ($P = .25$). Pathology results showed similar lymph node counts, tumor size, and stage. Single incision surgery had a statistically significant increased rate of readmission within 30 days of surgery (6.3%, $P = .021$) compared with robotic (0.7%) but not multiple ports (7.1%).

Conclusions: Single incision laparoscopic endometrial cancer staging has comparable outcomes to other modalities of laparoscopic staging. Further investigation is warranted in the causes for readmission rate found after single incision surgery. Because of a similar safety profile, it would be acceptable to consider incorporating single incision surgery into gynecologic oncology practice.

Table 1
Preoperative Characteristics.

	Robotic surgery	Single port surgery	Multiple ports surgery	P value
N	144	48	28	
Age	65 (36-91)	62 (21-45)	62 (37-88)	0.21
BMI	33 (18-60)	31 (21-45)	29(19-45)	0.14
RACE				0.78
Caucasian	141(98%)	45 (93%)	27(96%)	
African American	2 (1.3%)	2 (4%)	0	
Others	1 (0.7%)	1 (3%)	1 (4%)	
MEDICAL COMORBIDITES				0.45
DM	30(21%)	9(19%)	4(14%)	
HTN	58(53%)	24(49%)	13(46%)	
Previous surgery	93(65%)	34(71%)	17(60%)	0.54
GRADE				0.24
G1	84(58%)	16(33%)	17(60%)	
G2	28(16%)	13(25%)	5(17%)	
G3	10(7%)	4(8%)	2(7%)	
Papillary serous	11(7.5%)	4(8%)	1(3.5%)	
Clear cell	8(6%)	4(8%)	3(11%)	
Sarcoma	6(4%)	0	0	
Other	2(1.4%)	0	0	

Table 2
Postoperative Outcomes.

	Robotic surgery	Single port surgery	Multiple ports surgery	P value
N	144	48	28	
Surgery				
Length of surgery	248 (163-402)	238(175-338)	235(169-327)	0.78
EBL	130(0-1800)	150(0-1500)	231(0-2500)	0.25
Hospital stay	1.6(1-15)	2.1(1-8)	1.5(1-8)	0.32
ICU admission	3(2%)	1(2%)	0	0.64
Complications				
Acute				0.45
No	137(95%)	45(84%)	21(75%)	0.21
Total complications	7(5%)	3(6%)	7(25%)	0.06
Pulmonary embolus	1(0.7%)	0	0	0.04
Pulmonary edema	2(1.3%)	1(2%)	1(3.5%)	0.47
AKI	2(1.3%)	1(2%)	3(11%)	0.03
Obturator N. injury	1(0.7%)	0	0	0.01
Ileus	2(1.3%)	0	1(3.5%)	0.52
Blood transfusion	2(1.3%)	1(2%)	3(11%)	0.001
Long term				
Readmission (< 30 days)	1(0.7%)	3(6.3%)	2(7.1%)	0.021
Pathology outcome				
Staging				0.32
IA	86(60%)	21(43%)	19(67%)	
IB	31(21%)	18(37%)	5(18%)	
II	5(3.5%)	3(6%)	1(3.5%)	
IIIA	3(2%)	1(2%)	2(7.1%)	
IIIB	2(1.3%)	0	0	
IIIC1	5(3.5%)	2(4%)	1(3.5%)	
IIIC2	10(7%)	3(6.2%)	0	
IV	2(1.3%)	0	0	
LN counts				0.24
Pelvic LN	16.4(2-41)	17.3(5-52)	13(0-33)	
Para aortic LN	7.3(1-50)	7.1(1-13)	6(0-16)	
Tumor greatest dimension (cm)	3.3	3.8	3.0	0.31
LVSI (+)	34(23%)	16(33%)	5(18%)	0.45

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75 - Featured Poster Session
National Cancer Data Base report of associations, patterns, and survival benefit of lymphadenectomy in endometrial cancer
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Objectives: The aim of this study was to describe contemporary treatment patterns of comprehensive surgical staging with lymph node dissection (LND) in uterine carcinoma, identify factors that may influence management, and quantify the survival benefit of LND using a large tumor registry.

Methods: The National Cancer Data Base was queried for patients undergoing hysterectomy for endometrioid and serous uterine carcinoma from 2003 to 2012. X^2, Cochran-Armitage trend test, multivariate logistic regression, and Cox proportional hazards model were used to identify relationships, trends, and predictive factors of outcome.

Results: A total of 200,989 patients were identified with 193,069 (96.1%) endometrioid and 7,920 (3.9%) serous carcinomas. Of these, 157,891 patients had stage I, 14,074 had stage II, 21,658 had stage III, and 7,366 had stage IV disease. From 2003 to 2012, utilization of LND increased from 58.7% to 64.9%. Factors associated with receipt of LND included more than 50% myometrial invasion (OR 1.61, 95% CI 1.55–1.68), grade 2–3 (OR 2.06, 95% CI 1.99–2.14), tumor size greater than 2 cm (OR 1.53, 95% CI 1.47–1.60), and serous histology (OR 1.24, 95% CI 1.16–1.32). Of the 161,422 patients who met criteria for comprehensive staging, only 114,267 (70.8%) underwent LND. Patients of African-American race (OR 0.87, 95% CI 0.83–0.90), Medicaid insurance status (OR 0.80, 95% CI 0.76–0.84), care received at a community program (OR 0.43, 95% CI 0.37–0.50), and West South Central (AR, LA, OK, TX) geographic location (OR 0.6, 95% CI 0.49–0.75) were less likely to receive LND. After adjusting for clinicopathologic factors, LND was associated with a substantial improvement in survival (HR 0.6, 95% CI 0.58–0.62, $P < .001$).

Conclusions: Nationally, LND has increased since 2003; however, a significant number of patients with greater than 50% myometrial invasion, grade 2–3, or tumor size greater than 2 cm did not undergo LND. While our observed differences in survival require validation, our study promotes LND and perhaps centralizing cancer treatment in comprehensive cancer centers.

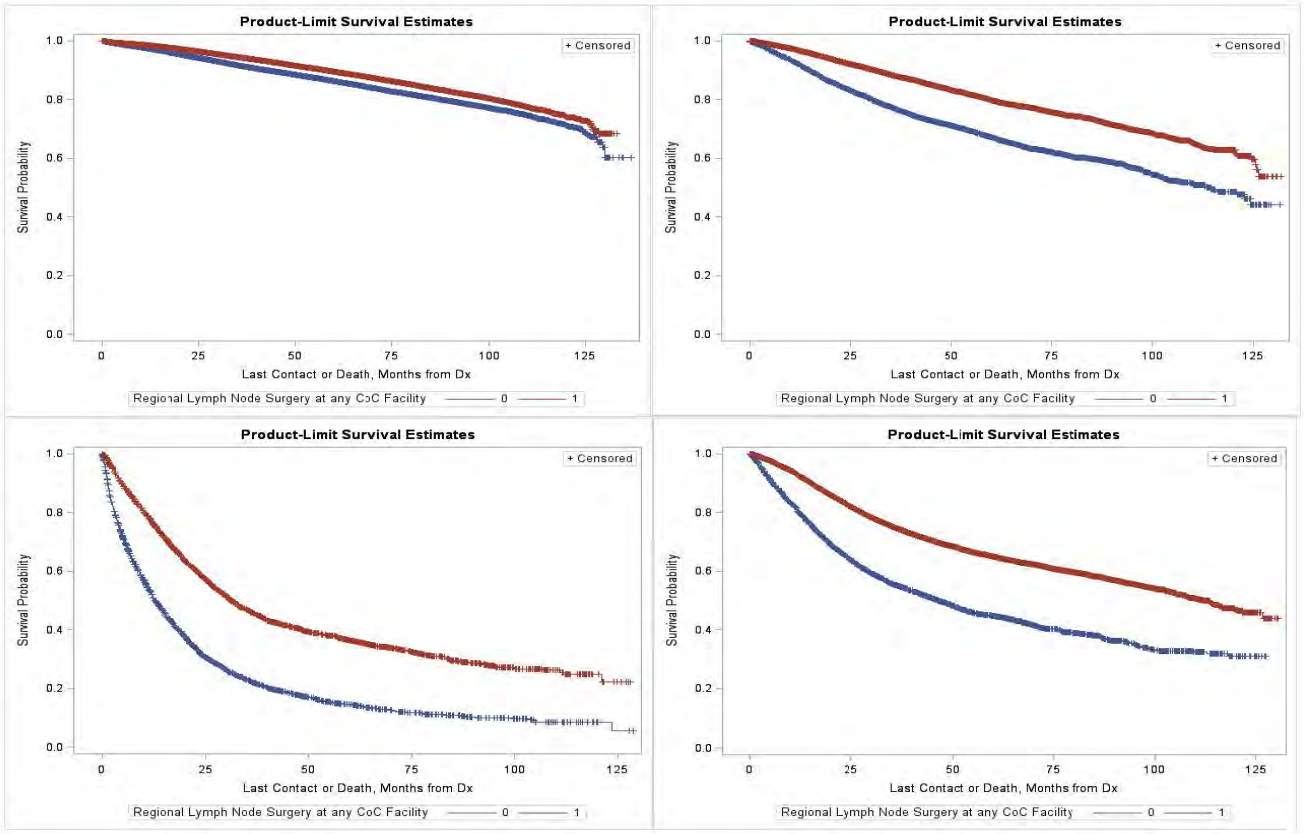

Fig. 1
Product-limit Survival Estimates.

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76 - Featured Poster Session
High-risk cancer, unequal care: Disparities in the complete surgical staging of high-grade endometrial cancer in the Southeastern United States
J.R. Foote[a], S. Gaillard[b], G. Broadwater[a], J. Sosa[b], B.A. Davidson[a], M. Adam[b], A.A. Secord[a], M.B. Jones[c], J. Chino[a] and L.J. Havrilesky[a]. *[a]Duke University Medical Center, Durham, NC, USA, [b]Duke Cancer Institute, Durham, NC, USA, [c]Duke Cancer Center Macon Pond, Raleigh, NC, USA*

Objectives: To determine whether receipt of full surgical staging for high-grade endometrial cancer is associated with socioeconomic factors, distance traveled to obtain care, and type of cancer treatment program.

Methods: The National Cancer Data Base (NCDB) was searched for patients who underwent surgical treatment for grade 3 endometrioid, clear cell, and serous endometrial cancer from 1998 to 2012 in the Southeastern United States. Rates of NCCN guideline–based surgical staging and overall survival (OS) were the main outcome measures. Categorical variables were compared using chi-square tests. Multivariate logistic regression was used to examine

differences in receipt of lymph node staging based on race (Caucasian [C] vs African American [AA]), income, type of cancer program (academic vs other), and distance to care (≤25 or >25 miles), controlling for Charlson comorbidity score. Multivariate Cox proportional hazards regression modeling was used to assess OS based on stage (I/II vs III/IV), race (C vs AA), income, and distance traveled (≤25 or >25 miles) controlling for age.

Results: A total of 10,767 patients were identified who underwent surgery for high-grade endometrial cancer: 77% were Caucasian, 38% were privately insured, 35% traveled more than 25 miles for cancer treatment, and 37% had stage III/IV disease. Lymph node staging was more common among Caucasians (75% vs 70%, $P < .0001$), patients who traveled more than 25 miles (77% vs 72%, $P < .0001$), had higher income (76% vs 72%, $P < .0001$), or were treated at an academic center (77% vs 72%, $P < .0001$). In multivariate analysis, C race, higher income, academic/research program, Charlson score, and distance traveled to care were all significant predictors of lymph node staging. In Cox analysis, stage III/IV disease (HR 3.2, 95% CI 3.1–3.5), AA race (HR 1.4, 95% CI 1.2–1.5), lowest income quartile (HR 1.2, 95% CI 1.1–1.3) and traveling more than 25 miles to care (HR 1.1, 95% CI 1.0–1.2) were significant predictors of lower survival.

Conclusions: Women with high-grade endometrial cancer in the Southeast do not receive uniform surgical care, with travel distance, race, income, and academic treatment center each strongly associated with receipt of guideline-consistent staging. Community-based patient navigation systems are needed as an interface between the highest-risk patients and high-quality care.

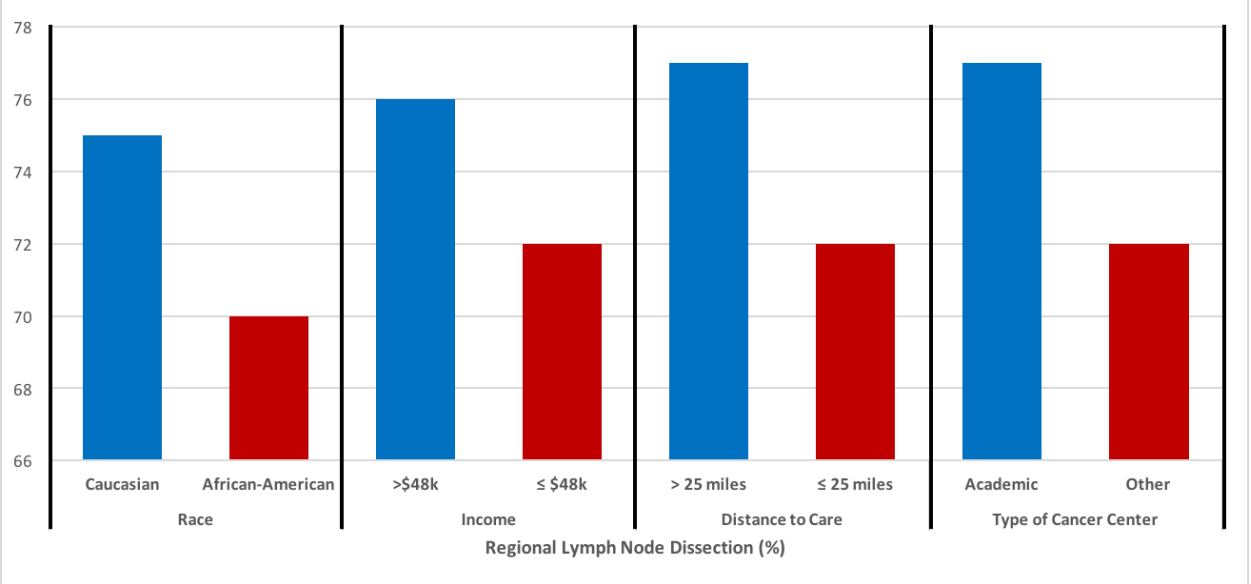

Fig. 1
Receipt of Guidance-Centered Staging in High-Risk Endometrial Cancer.

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77 - Featured Poster Session
Magnitude of risk for nodal disease in women with endometrial cancer and lymphovascular space invasion
S. Jorge[a], Y. Huang[a], A.I. Tergas[b], W.M. Burke[a], J.Y. Hou[a] and J.D. Wright[a]. *[a]Columbia University College of Physicians and Surgeons, New York, NY, USA, [b]NYP/Columbia University Medical Center, New York, NY, USA*

Objectives: The most important predictor of outcome in women with endometrial cancer is tumor stage. Lymphovascular space invasion (LVSI) is a commonly identified risk for lymph node (LN) metastases, and thus advanced stage, though the magnitude of this risk is difficult to quantify. We performed a large, population-based analysis to determine the risk of lymph node metastasis from LVSI in women with early-stage primary tumors of the endometrium.

Methods: Patients with surgically staged, T1A (<50% myoinvasion) and T1B (>50% myoinvasion) endometrioid adenocarcinomas of the endometrium from 2010 to 2012 were identified from the National Cancer Data Base (NCDB). The association between LVSI and LN metastases stratified by depth of uterine invasion and grade are reported. Multivariable regression models were developed to estimate the association between LVSI and LN metastases while accounting for other clinical and demographic characteristics.

Results: We identified 25,907 patients including 18,713 (72.2%) with T1A and 7,194 (27.8%) with T1B tumors. Overall, 3,928 patients (15.2%) had LVSI, and 1,290 patients (5.0%) had positive lymph nodes. Among patients with positive LVSI, 21.0% had positive lymph nodes, compared with 2.1% in patients without LVSI ($P < .0001$). In analyses stratified by stage and grade, LVSI increased the risk of LN metastasis by a magnitude of 3- to more than 10-fold (Table). In a multivariable model controlling for clinical and demographic characteristics, the RR of nodal disease with LVSI was 9.29 (95% CI 7.29–11.84) for T1A tumors and 4.64 (95% CI 3.99–5.39) for T1B tumors. The strength of association between LVSI and nodal disease was stronger than for any variable analyzed including tumor grade.

Conclusions: The presence of lymphovascular space involvement in endometrial cancer is significantly and independently associated with an increased risk of pelvic lymph node metastases. The magnitude of lymph node positivity in the presence of LVSI in this population-based study is higher than previously reported.

Table 1

Stage	Grade	LVSI	Regional Node Status				*P* value
			Negativ		Positiv		
			n	% (95% CI)	n	% (95% CI)	
T1A	Well	Not present	9307	99.3 (99.1, 99.5)	65	0.7 (0.5, 0.9)	<.0001
		Present	459	88.6 (85.6, 91.1)	59	11.4 (8.9, 14.4)	
	Moderate	Not present	6004	98.7 (98.4, 99.0)	78	1.3 (1.0, 1.6)	<.0001
		Present	559	86.8 (84.0, 89.2)	85	13.2 (10.8, 16.0)	
	Poorly	Not present	1627	96.4 (95.4, 97.2)	60	3.6 (2.8, 4.6)	<.0001
		Present	353	86.1 (82.4, 89.1)	57	13.9 (10.9, 17.6)	
T1B	Well	Not present	1993	96.0 (95.1, 96.8)	83	4.0 (3.2, 4.9)	<.0001
		Present	377	74.7 (70.7, 78.3)	128	25.4 (21.7, 29.3)	
	Moderate	Not present	1918	94.0 (92.9, 95.0)	122	6.0 (5.0, 7.1)	<.0001
		Present	751	71.3 (68.4, 73.9)	303	28.8 (26.1, 31.6)	
	Poorly	Not present	663	91.8 (89.6, 93.6)	59	8.2 (6.4, 10.4)	<.0001
		Present	606	76.0 (73.0, 78.9)	191	24.0 (21.1, 27.0)	

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78 - Featured Poster Session

Treatment outcomes in FIGO stage IB-IIA cervical cancer patients with disruption of cervical stromal ring on magnetic resonance imaging: A propensity score matching study

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Objectives: The aim of this study was to compare treatment outcomes of radical hysterectomy (RH) followed by adjuvant chemoradiation and primary concurrent chemoradiation therapy (CCRT) for patients with FIGO stage IB-IIA cervical cancer with disruption of cervical stromal ring on MRI.

Methods: Among 162 patients with FIGO stage IB-IIA cervical cancer with disruption of the cervical stromal ring on MRI, treatment outcomes were compared between RH plus adjuvant CCRT (RH-based group, n = 59) and primary CCRT (RT-based group, n = 59) after propensity score matching for each of the patients using a logistic regression model including the following variables: age, tumor size on MRI, pelvic lymph node enlargement, and histology. Recurrence rates, disease-free survival (DFS), overall survival (OS), and treatment-related complications were compared for these 2 groups.

Results: The 5-year DFS was 85.3% for the RT-based group and 75.7% for the RH-based group ($P = .057$). The 5-year OS was 76.6% for the RT-based group and 80.0% for the RH-based group ($P = .210$). The incidence of acute grade 3 genitourinary, gastrointestinal, hematologic adverse reactions, and late grade 1-2 lower limb lymphedema were significantly higher for the RH-based group, compared with the RT-based group. Among 18 patients with grade 2–3 genitourinary adverse events, 7 patients received urologic interventions.

Conclusions: Primary CCRT was associated with fewer treatment-related complications and achieved comparable survival outcomes for patients with FIGO stage IB-IIA cervical cancer with cervical stromal invasion on MRI, compared with RH plus adjuvant CCRT.

79 - Featured Poster Session
Preoperative nomogram for individualized prediction of parametrial invasion in patients with FIGO stage IB cervical cancer treated with radical hysterectomy
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Objectives: This study aimed to establish a nomogram predicting parametrial invasion (PMI) by combining preoperative clinicopathologic factors in patients with FIGO stage IB cervical cancer treated with radical hysterectomy (RH) with retroperitoneal lymphadenectomy.

Methods: We retrospectively analyzed clinicopathologic data of 298 patients with FIGO stage IB cervical cancer treated with RH with retroperitoneal lymphadenectomy between February 2000 and March 2015. The nomogram was developed based on multivariate logistic regression analysis of preoperative clinicopathologic data. The accuracy and discriminative ability of the nomogram were evaluated by concordance index and calibration curve. The low-risk group was defined as having a predicted probability of less than 5% of having PMI.

Results: Multivariate analysis identified diameter-based tumor volume and disruption of the cervical stromal ring on MRI, squamous cell carcinoma-antigen level, and menopausal status as independent prognostic factors associated with PMI. These factors were incorporated for construction of the nomogram. The concordance index of the nomogram was 0.940 (95% CI 0.908–0.967), and calibration plots revealed good agreement between the observed probabilities and nomogram-predicted probabilities. The nomogram classified 134 (45.0%) of 298 patients as low risk. In the low-risk group, the predicted probability of PMI was 1.90% and the actual PMI rate was 0.74% (1 of 134).

Conclusions: We developed a preoperative nomogram predicting PMI in patients with surgically treated FIGO stage IB cervical cancer. More comprehensive information based on this nomogram may provide valuable guidance for physicians on the primary management of FIGO stage IB cervical cancer cases.

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80 - Featured Poster Session
Does the robotic platform reduce the morbidity associated with combined radical surgery and adjuvant radiation for early cervical cancer?
L.H. Clark, E.L. Barber, P.A. Gehrig, J.F. Boggess, J.T. Soper and K.H. Kim. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: Open radical hysterectomy (RH) followed by adjuvant radiation (XRT) for cervical cancer has been associated with high morbidity; however, RHs are now often performed robotically. We examined if the robotic platform decreases the morbidity associated with radical surgery followed by adjuvant XRT.

Methods: A retrospective cohort study of patients with cervical cancer undergoing RH from 1995-2013 was performed. Clinical and pathologic data were obtained from the medical record. Long-term (LT) complications were defined as urinary and/or bowel complications, and lymphedema presenting more than 30 days after completion of therapy. Complications were graded. Grade 1 was mild symptoms and easily treated. Grade 2 was symptoms resolving with long-term medical therapy. Grade 3 was major symptoms requiring surgery or invasive procedures. The X^2 and student *t* tests were used for analysis.

Results: Overall, 243 patients underwent RH for cervical cancer. The open surgical approach was used in 43% (n = 104) and the robotic approach was used in 57% (n = 139). Eighty-three patients (34.2%) required adjuvant XRT. XRT was associated with increased risk of LT complication (28.9% vs 7.0% $P < .001$). LT complications included lymphedema (n = 18), bowel-associated complications (enteritis/proctitis n=8, obstruction n=2), and urinary complications (hemorrhagic cystitis n = 1, neurogenic bladder n = 2, fistula n = 1, and ureteral stricture n = 3). Among patients who received adjuvant XRT, the open surgical approach was used in 48% (n = 40) and the robotic approach in 52% (n = 43). There was no difference in time to initiation of XRT between the 2 surgical groups (43.2 ± 15.6 vs 47.3 ± 19.6 days, $P = .33$). There was no difference in grade 2/3 LT complications in patients receiving adjuvant XRT between the groups (27.5% vs 27.9%, $P = .97$). However, patients undergoing open surgery experienced a trend toward increased adhesion-related complications, such as bowel obstruction and ureteral stricture (10% vs 2.3%, $P = .19$).

Conclusions: We found no difference in LT complications between patients who underwent robotic and those who underwent open RH and adjuvant XRT. Fewer adhesion-related LT complications may be seen with robotic surgery.

However, because many XRT-related complications occur at later time points, continued follow-up is needed to evaluate for potential differences between the 2 groups.

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81 - Featured Poster Session
Association between hypoalbuminemia and surgical site infection in vulvar cancers
S.A. Sullivan, L. Van Le, A. Liberty, J.T. Soper and E.L. Barber. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: Preoperative albumin has been associated with poor surgical outcomes in gynecologic cancers. Postoperative wound complications after vulvar surgery are common, however, variables affecting this rate are heterogeneous. We sought to determine if preoperative albumin affects postoperative wound complications for vulvar malignancy.

Methods: The National Surgical Quality Improvement Project (NSQIP) database was queried for cases of vulvar cancer in which vulvectomy was performed with or without lymph node dissection from 2008 to 2013. The primary outcome was major wound complication defined as deep surgical site infection (SSI), organ space SSI, wound dehiscence, or graft/flap failure. The secondary outcome was minor wound complication defined as superficial SSI. Hypoalbuminemia was defined as an albumin level less than 3.5 g/dL. Descriptive statistics and multivariable logistic regression were used for analysis. Covariates for the multivariable model were selected based on published risk factors for vulvar wound complication.

Results: Of 777 vulvar cancer patients, 514 (66.2%) had vulvar surgery alone and 263 (30.3%) had a lymph node dissection. Median age was 66.0 years (range, 20-90 years) and median body mass index (BMI) was 28.9 kg/m^2(range, 14.3–65.5). The wound complication rate was 10.4% (81/777) with 48 minor and 39 major complications. There was no difference in wound complications between patients who underwent an inguinal lymph node dissection and those who did not (P = .17). Preoperative albumin was recorded in 429 patients (55.2%). Patients with hypoalbuminemia were more likely to have a major wound complication (relative risk 2.9, 95% CI 1.1–7.3, P = .02). Preoperative hematocrit of less than 38 was associated with increased wound complications (13.7% vs 7.6%; P = .01). In bivariable analysis, age, diabetes, and BMI were not associated with wound complication. In a multivariable logistic regression model adjusting for BMI, age, preoperative hematocrit, and diabetes, the relationship between hypoalbuminemia and major wound complication persisted (adjusted odds ratio 2.7, 95% CI 1.1–7.1, P = .04).

Conclusions: Low preoperative albumin is associated with major postoperative wound complications among women with vulvar cancer. This provides a target for intervention to optimize patients before surgery.

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82 - Featured Poster Session
Five year survival surgical outcome for clinic stage I cervical cancer: Comparison of robotic vs. laparoscopic or laparotomy radical hysterectomy
P.C. Lim. *Center of Hope, Reno, NV, USA*

Objectives: To determine if there is a difference in 5-year survival between robotic versus laparoscopic versus open radical hysterectomy in the treatment of clinical stage I cervical cancer.

Methods: Retrospective case-matched cohort study was undertaken from 1999 to 2014. Age, subset of stage I, histology and tumor grade in the cohort, and robotic, laparoscopic, and open radical hysterectomy were analyzed. Overall survival for surgical treatment for stage I cervical cancer was analyzed. The 5-year survival for each respective surgical treatment was analyzed to determine if there was difference among robotic, laparoscopic and radical hysterectomy.

Results: During the period 1999 to 2014, 110 patients underwent radical hysterectomy with bilateral pelvic lymphadenectomy (RHBPLND) for clinical stage I cervical cancer. From 1999 to 2008, 28 (25.5%) patients underwent open RHBPLND (ORHBPLND), and (30.9%) patients underwent laparoscopic radical hysterectomy with pelvic lymphadenectomy (LRHBPLND). From 2008 to 2015, 48 (43.6%) patients underwent robotic radical hysterectomy with bilateral pelvic lymphadenectomy (RoRHBPLND). Of those who underwent robotic surgery, 25% were stage 1a2, 47.9 % were stage 1B1, and 10.4% stage IB2. The overall 5-year survival was 87.5%. The 5-year survival for robotic, laparoscopic, and open surgical cohorts were 87.5%, 96.9%, and 82.1%, respectively. There was no difference in 5 -ear survival for stage IA2, IB1, and IB2 for all 3 surgical procedures. We also reviewed histology, grade, and parametrial as well as vaginal cuff measurements in all 3 groups.

Conclusions: The overall 5-year survival for RoRHBPLND for treatment of clinical stage I cervical is 87.5%. There was no difference in 5-year survival among RoRHBPLND, LRHBPLND, and ORHBPLND.

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83 - Featured Poster Session
Evaluating the trend of minimally invasive surgery for cervical cancer: An NSQIP database analysis
J.B. Szender, P.C. Mayor, K.O. Odunsi, S.B. Lele, E. Zsiros and P.J. Frederick. *Roswell Park Cancer Institute, Buffalo, NY, USA*

Objectives: Determine the impact of more minimally invasive surgery (MIS) on postoperative outcomes in cervical cancer patients.

Methods: We evaluated the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective surgery for cervical cancer. Patients were categorized as undergoing hysterectomy through an MIS approach (CPT code 58500-58599) or laparotomy. Analyses were also stratified by year of surgery. Postoperative outcomes including venous thromboembolism (VTE), surgical site infection (SSI), pneumonia, urinary tract infection (UTI), sepsis, return to the operating room (ROR), and death were recorded. Outcomes were compared using χ^2 test of independence or Mann-Whitney U test, as appropriate. The Mantel-Haenszel method was used for adjustments. The threshold of significance was $P < .05$.

Results: We identified 1,320 patients with complete data who underwent elective hysterectomy for cervical cancer; 608 were minimally invasive surgeries. The frequency of MIS increased from 18.2% in 2007 to 54.9% in 2013. Operative times did not differ between open and MIS approaches (208 min vs 206 min, $P = .6425$); however, length of stay for MIS patients was significantly shorter (1.7 vs 5.0 days, $P < .0001$). MIS patients had a 56% lower risk of postoperative complications compared with laparotomy patients (RR 0.44, 95% CI 0.35–0.55), the relative risk of SSI was 0.33 (95% CI 0.18–0.59). Risk of pneumonia (RR 0.29, 95% CI 0.06–1.37) and UTI (RR: 0.92, 95% CI 0.61–1.40) did not differ between approaches. There were also no significant differences in risk of VTE ($P = .09$), ROR ($P = .33$), or death ($P = .91$). Complications tended to be more common in MIS before 2010 (127.7 per 1,000 MIS surgeries vs 69.2 per 1,000 open surgeries), but starting in 2010, the risk of complications was more than 60% lower for MIS patients (RR 0.37, 95% CI 0.29–0.48).

Conclusions: Treatment of cervical cancer with MIS significantly reduces the risk of postoperative complications and length of hospitalization. Although there was no difference in rate of perioperative deaths, improved patient outcomes without a significant change in operative time may lead to cost savings to the health system. MIS should be considered for patients undergoing surgical treatment of cervical cancer.

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84 - Featured Poster Session
Adding bevacizumab to single-agent chemotherapy for the treatment of platinum-resistant recurrent ovarian cancer: A cost-effectiveness analysis of the AURELIA trial
W.Z. Wysham, E.M. Schaffer, T.M. Coles, D.R. Roque, S.B. Wheeler and K.H. Kim. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: AURELIA was a randomized phase III trial of adding bevacizumab to single-agent chemotherapy for the treatment of platinum-resistant recurrent ovarian cancer that demonstrated improved progression-free survival (PFS) in the bevacizumab + chemotherapy arm compared with chemotherapy alone. The goal of this study was to evaluate the cost-effectiveness of adding bevacizumab to single-agent chemotherapy in the treatment of platinum-resistant recurrent ovarian cancer.

Methods: A decision tree model was constructed to evaluate the cost-effectiveness of adding bevacizumab to standard treatment with single-agent chemotherapy based on the arms of the AURELIA trial. Costs, quality-adjusted life years (QALYs), and PFS were modeled over a 15-month period. All model inputs were extracted from published peer-reviewed literature and public sources. Costs and QALYs were discounted at an annual 3% rate. All costs were adjusted to 2015 US dollars. Incremental cost-effectiveness ratios (ICERs) per QALY gained and ICERs per progression-free life year saved (PF-LYS) were calculated. Probabilistic sensitivity analyses were performed to evaluate the robustness of results.

Results: The ICER associated with bevacizumab + chemotherapy is $285,624 per QALY gained and $151,059 per PF-LYS. At a willingness-to-pay (WTP) threshold of $50,000/QALY, adding bevacizumab to single-agent chemotherapy is

not cost-effective in this patient population. Even at a WTP threshold of $100,000/QALY, bevacizumab + chemotherapy is not cost-effective. These findings are robust to deterministic and probabilistic sensitivity analyses.

Conclusions: Despite gains in QALY and PFS, the addition of bevacizumab to single-agent chemotherapy for treatment of platinum-resistant recurrent ovarian cancer is not cost-effective at a WTP threshold of $50,000/QALY. Benefits, risks, and costs associated with treatment should be taken into consideration when prescribing chemotherapy for this population of patients.

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85 - Featured Poster Session

A cost-effectiveness analysis of the AURELIA trial: Bevacizumab and paclitaxel offer a promising clinical and economic combination for platinum-resistant ovarian cancer

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Objectives: To evaluate the cost-effectiveness of bevacizumab use in platinum resistant-ovarian cancer (PR-OC).

Methods: Decision-analysis models were constructed to evaluate each of the treatment arms of the AURELIA trial. Arm 1 of each model included the standard chemotherapy regimen: liposomal doxorubicin, topotecan, or paclitaxel. Arm 2 included the standard regimen with the addition of bevacizumab (doxorubicin + bevacizumab, topotecan + bevacizumab, or paclitaxel + bevacizumab). Overall survival (OS), rates of adverse events (AEs), and rates of salvage bevacizumab in each arm were obtained from the AURELIA trial. Table 1 lists these rates as well as costs for each treatment arm, based on average number of chemotherapy cycles. Treatment strategies were compared using an incremental cost-effectiveness ratio (ICER) and a standard willingness to pay threshold of $100,000/year of life saved (YLS). Sensitivity analyses were performed to account for uncertainty in assumptions.

Results: The paclitaxel arm with a median OS of 13.2 months was the least costly arm with an average cost of $10,386. The paclitaxel + bevacizumab arm had an average cost of $62,814 and a median OS of 22.4 months. The 9.2-month improvement in OS came at an ICER of $68,088/QALY (Table 1). With little improvement in OS in the topotecan + bevacizumab and doxorubicin + bevacizumab arms, the ICERs were not cost-effective (Table 1). Sensitivity analyses demonstrated the results to be not sensitive to changes in the percentage or costs of AEs within a clinically reasonable range or the number of cycles of salvage bevacizumab administered.

Conclusions: This study demonstrates that bevacizumab may be cost-effective in recurrent, platinum-resistant ovarian cancer. This model does not incorporate the improvement in abdominal/gastrointestinal symptoms observed during treatment with bevacizumab; this would likely translate to an improvement in quality of life and further reduce the ICER. The addition of bevacizumab to paclitaxel appears to be cost-effective in the treatment of PR-OC.

Table 1

	Standard treatment	Standard Treatment + bevacizumab	Mean costs (in US dollars)
Rate of AE's (range)			
Hypertension	6.6% (3.3-9.9)	20.1% (10-30)	$5,153
Gastrointestinal Perforation	0% (0-2)	2.2% (1-3)	$31,079
Gastrointestinal or Genitourinary Fistula	0% (0-2)	2.2% (1-3)	$20,187
Thromboembolism	0% (0-2)	2.2% (1-3)	$10,657
Salvage bevacizumab	3 cycles (0-6)	0 cycles	$23,106
	paclitaxel	paclitaxel + bevacizumab	
OS (mo)	13.2	22.4	
Proportion receiving salvage bevacizumab	38%	0%	
Mean cost of treatment	$1,468	$61,403	
ICER	$68,088/YLS		
	liposomal doxorubicin	liposomal doxorubicin + bevacizumab	
OS (mo)	14.1	13.7	
Proportion receiving salvage bevacizumab	40%	0%	
Mean cost of treatment	$11,858	$82,180	
ICER	Dominated		
	topotecan	topotecan + bevacizumab	
OS (mo)	13.3	13.8	
Proportion receiving salvage bevacizumab	40%	0%	
Mean cost of treatment	$1,585	$47,020	
ICER	$938,871/YLS		

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86 - Featured Poster Session

Risk factors for surgical treatment delay in women with endometrial cancer

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Objectives: Delays in cancer treatment and improving quality of cancer care delivery are targets for treatment of gynecologic malignancies. This study aims to identify risk factors for surgical treatment delays in women with endometrial cancer (EC).

Methods: This study investigated women in The Health Improvement Network presenting with abnormal uterine bleeding (AUB) who then developed EC. This U.K. population-based cohort received universal access to care through a general practitioner–centered health system. Baseline demographic and clinical factors were reported, and appropriate tests of difference were used to compare time from cancer diagnosis to surgery. A log-transformation was performed on time to surgery to allow a multivariable linear regression to identify risk factors for surgical delay using a standard backward elimination method. All tests were performed using Stata 12.1 software (College Station, TX) with 2-sided test of difference and P =.05.

Results: A total of 537,650 women with AUB were observed from August 1995 to July 2010 for 0.30 to 13.6 years, at ages 27 to 100 years (mean, 66 years). Among these women, 1,472 developed EC, and 1,198 underwent hysterectomy after 0 to 13 years; 761 women had their cancer reliably documented before surgery and were included in this analysis. Time to surgery from EC diagnosis ranged from 1 to 3,462 days (median, 25 years, interquartile range, 14–40). In univariable analyses, age, hypertension, smoking status, and Townsend index of socioeconomic deprivation emerged as statistically significant factors, as reported in Table 1. Coronary artery disease, history of polycystic ovary

syndrome, smoking, and Townsend index of socioeconomic deprivation emerged as independent risk factors in the multivariable model for increased time to surgery.

Conclusions: Clinical, social, and economic risk factors were associated with an increased time to surgery, but obesity and diabetes were not. Despite receiving care in a socialized medical system with universal access and standardized wait time, patients' socioeconomic status remained an independent factor for delay. This study identifies potential targets for decreasing delays and improving quality of oncologic care for EC patients in all nations. Additional studies are planned to investigate whether surgical delays correlate with poorer outcomes in EC.

Table 1
Risk Factors for Surgical Delays.

Total n =761	n (%)	Median days to surgery (affected v. not)	Univariable p-value	RR/day in multivariable linear regression (p-value)
Obesity[1]	467 (44.06%)	25 v. 24	0.268	-
BMI[2] (kg/m[2])	30.3 (18.9-50.9)	-	0.051	-
BMI[3] (Class):			0.551	-
Underweight,	9 (0.85%)	24.5		
Normal weight,	244 (23.0%)	22		
Overweight	340 (32.1%)	24		
Class I obese	239 (22.6%)	24		
Class II obese	118 (11.1%)	23		
Class III obese	11 (10.4%)	29		
Age[2] (mean years)	64 (36-88)	-	0.021	-
Diabetes Mellitus[4]	153 (12.8%)	23.5 v. 25	0.484	-
Prior cancer history[4]	118 (15.5%)	24 v. 15	0.507	-
Hypertension[4]	325 (42.6%)	27 v. 23	0.011	-
Coronary artery disease[4]	13 (1.7%)	35 v. 24	0.082	1.75 (0.039)
Prior MI[4]	12 (1.6%)	31 v. 24	0.802	-
Observed pregnancy[4]	29 (3.8%)	23 v. 25	0.572	-
PCOS[5,4]	2 (0.3%)	187 v. 24	0.091	4.33 (0.027)
Anemia[4]	105 (13.8%)	24 v. 25	0.809	-
Ever Smoker[4]	218 (30.2%)	21 v. 26	0.004	0.79 (0.003)
Townsend index of socioeconomic depravity[2], *(median of 1-10 scale)*	2 (IQR 1-4)	-	0.002	1.09 (0.002)

Legend: [1]T-test, [2]Spearman's correlation, [3]ANOVA, [4]Wilcoxon rank-sum, [5]Polycystic ovary syndrome

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87 - Featured Poster Session
Surgical wait time: A new health indicator in women with endometrial cancer
A.E. Strohl, J.M. Feinglass, S. Shahabi and M.A. Simon. *Feinberg School of Medicine of Northwestern University, Chicago, IL, USA*

Objectives: Evaluate trends between sociodemographic and clinical characteristics and the likelihood of delayed surgical treatment and all-cause mortality among women diagnosed with endometrial cancer.

Methods: Using the National Cancer Data Base, we analyzed time to first surgery for AJCC stage 0–IV epithelial endometrial cancer patients who underwent surgical treatment from 2003 to 2011. X^2 tests and Poisson regression were used to examine factors associated with delays of more than 6 weeks between diagnosis and surgery. Survival for women diagnosed between 2003 and 2006 with timely versus delayed surgery was compared using the log rank test and a Cox proportional hazards model.

Results: The final study population included 112,041 women diagnosed at 1,108 continuously reporting NCDB hospitals. Survival follow-up through 2011 was available for 40,184 women. All patients underwent hysterectomy for surgical staging. Twenty-eight percent of patients underwent surgery more than 6 weeks after initial diagnosis. Poisson regression estimates indicated that patients younger than 40 years old, groups of black or Hispanic race/ethnicity, those with Medicaid or no insurance, patients from the lowest education zipcode quartiles, and those with comorbid conditions all had a significantly higher likelihood of a surgical wait time of more than 6 weeks. Patients diagnosed in 2010 to 2011 were 32.5% more likely (interrater reliability 1.32, 95% CI 1.24–1.40) to undergo surgery more than 6 weeks after diagnosis compared with patients treated in 2003. Survival for women with surgical wait times longer than 6 weeks was significantly worse compared with patients who were surgically treated within 6 weeks of diagnosis (HR 1.14, 95% CI 1.09–1.20).

Conclusions: This large study demonstrates that wait times greater than 6 weeks from diagnosis of endometrial cancer to definitive surgery may have a negative impact on overall survival and that race and ethnicity, socioeconomic factors, and insurance coverage are all associated with increased likelihood of delayed surgical treatment.

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88 - Featured Poster Session
Herniation formation in women undergoing surgery for endometrial cancer
M.B. Schiavone, M. Bielen, G.J. Gardner, O. Zivanovic, E. Jewell, Y. Sonoda, R.R. Barakat, D.S. Chi, N.R. Abu-Rustum and M.M. Leitao. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: To determine the incidence of trocar site herniation in women who have undergone robotically assisted laparoscopic surgery (RBT) for endometrial cancer staging, and compare this with rates of ventral hernia formation in patients who underwent laparotomy (LAP) for the same indication.

Methods: We retrospectively identified all patients who underwent surgical staging for endometrial cancer via RBT or LAP between 2009 and 2012, in order to have a minimum of 2 years of follow-up for all cases. Various clinicopathologic data were abstracted and analyzed. Appropriate statistical tests were used.

Results: A total of 738 patients with endometrial cancer undergoing staging through RBT or LAP were identified. Of these, 567 patients underwent staging with RBT compared with 171 patients via LAP. Median age in both cohorts was 61 (RBT range 33–90; LAP range 28–86; $P = .4$). Median body mass index was 29.5 kg/m^2 (range 17.9–66) and 30.3 kg/m^2 (range 16.8–67.2), respectively ($P = 1.0$). No statistically significant difference was noted in rates of hypertension, diabetes, or smoking history between the cohorts. Trocar site herniation was noted in 11 (2%) of 567 patients in the RBT cohort, whereas ventral hernias were found in 11 (6%) of 171 patients in the LAP cohort ($P = .002$). Median time to diagnosis was 18 months (range 3–49 months) and 17 months (range 7-30 months), respectively ($P = .7$). Of the 11 patients with trocar site herniations in the RBT group, 10 (91%) were classified as midline defects and 1 (9%) was a lateral defect of a prior inferior epigastric port site. There were no instances of emergent surgery to correct postoperative trocar herniation. All midline camera ports were closed primarily at the time of surgery; lateral ports with robotic trocars were not. Four (0.7%) of 567 RBT patients underwent surgical hernia repair after diagnosis compared with 2 (1.2%) of 171 patients with ventral hernias after LAP ($P = .4$).

Conclusions: Trocar site herniation associated with RBT for endometrial cancer staging is rare and is significantly less common than ventral hernia formation associated with LAP. Diagnosis of trocar site herniation can take many months to manifest, but overall rates of surgical revision are low.

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89 - Featured Poster Session
Approach to hysterectomy for endometrial cancer in Washington State, 2008-2013: A cost analysis
T.L. Beck, M.A. Schiff, B.A. Goff and R.R. Urban. *University of Washington Medical Center, Seattle, WA, USA*

Objectives: Many studies have evaluated operative costs for hysterectomy by surgical route, but few include readmission costs. Our aim was to determine if the total cost of care differs based on surgical approach among women with endometrial cancer (EC).

Methods: We performed a population-based retrospective cohort study of endometrial cancer patients who underwent hysterectomy with robot-assisted surgery (RAS), laparoscopy (LS), or laparotomy (XLAP) in Washington State from 2008 to 2013. We identified patients using the Comprehensive Hospital Abstract Reporting System (CHARS) and compared patient characteristics and cost of care including any costs related to readmissions within 30 days of initial hospital discharge. Costs were derived using hospital-specific charge-to-cost ratios and adjusted for inflation using the Consumer Price Index for Medical Care. Differences in mean cost of care were analyzed using multivariable linear regression. All analyses were adjusted for year of surgery, patient's Charlson Comorbidity Index score (CCI), and performance of a lymph node dissection (LND).

Results: We identified 3,712 patients who underwent surgery for EC: 1,687 RAS, 400 LS, and 1,625 XLAP procedures. Patients undergoing XLAP had more comorbidities (11.3%) than the RAS (8.9%) or LS (7.3%) groups as indicated by a CCI of 2 or greater. Obesity prevalence varied by group, with the highest proportion of obese patients undergoing RAS (35.3%), followed by LS (33.8%), then XLAP (27.5%) ($P < .001$). Mean length of stay was shorter (1.5 days) for RA and LS versus XLAP (4 days). LND was performed more often in the XLAP (54%) and RAS (51%) group than the LS group (43%) ($P < .001$). More patients undergoing XLAP experienced a major perioperative complication (15.6%) compared with the RAS (8.2%) and LS (9.0%) groups ($P < .01$). Readmissions were least frequent in the RAS group (4.2%) compared with the XLAP (8.1%) and LS (6.3%) groups ($P < .01$). Mean total cost of care was greatest for XLAP, followed by RAS, then LS, while the adjusted difference in mean cost was $1,183.93 less for LS and $2,329.23 less for RAS compared with XLAP. RAS was also $1,145.30 less than LS when compared directly (Table).

Conclusions: In our cohort, RAS delivered the lowest adjusted total cost of care, followed by LS and then XLAP. When considering the cost-effectiveness of a therapeutic strategy, inclusion of patient outcomes and readmissions provides an important perspective.

Table 1
Analysis of Total Cost of Care by Surgical Approach.

Analysis of total cost of care by surgical approach.								
	Mean Cost	(Range)	Adjusted Difference in Mean Cost*	[95% CI]	p	Adjusted Difference in Mean Cost*	[95% CI]	p
Laparotomy	$14,841.45	($273.53 - 287,984.80)	-ref-	---	---	---		
Laparoscopy	$12,427.30	($3,339.26 - $59,383.20)	-$1,183.93	[$230.96, $2,136.90]	0.015	-ref-	---	---
Robotic	$13,891.10	($1,383.18 - $94,399.23)	-$2329.23	[$1,246.76,$3,411.71]	<0.001	-$1,145.30	[$212.26, $2,078.35]	0.016
*Adjusted for year, CCI, and LND								

90 - Featured Poster Session
Is intraoperative gross evaluation of the uterus in patients with complex atypical hyperplasia and endometrial adenocarcinoma reliable?
B.Q. Smith, J.D. Boone, E.D. Thomas, T.B. Turner, G. McGwin, C.A. Leath III and W.K. Huh. *University of Alabama at Birmingham, Birmingham, AL, USA*

Objectives: Initial treatment of endometrial cancer (EC) involves surgical resection including removal of pelvic and para-aortic lymph nodes. Attempts have been made to identify preoperative and intraoperative markers to determine which patients are at an increased risk of lymph node metastasis and thus need surgical staging. The goal of this study is to assess the reliability of intraoperative uterine evaluation compared with final pathologic measurements in patients with EC.

Methods: After obtaining institutional review board approval, a prospective study was conducted of women who underwent surgery for biopsy-proven complex atypical hyperplasia (CAH) or EC between March 2015 and September 2015. Demographics, preoperative biopsy results, procedure, intraoperative and final pathologic evaluation of lesion size, myometrial invasion, and lower uterine segment/cervical involvement were abstracted. The level of agreement between intraoperative and final pathologic evaluation of tumor involvement of the uterus was determined using κ statistics and intraclass correlation coefficients (ICC).

Results: Eighty-six patients with a preoperative diagnosis of CAH or EC were included—29 (33.7%) with CAH and 57 (66.3%) with EC. Mean age was 62 ± 10.5 years, and mean body mass index (BMI) was 38 ± 10.7. The majority of women were white (69%). Seventy (81.4%) patients underwent a laparoscopic or robotic hysterectomy, and 16 (18.6%) underwent an exploratory laparotomy. Seventy-one (82.6%) patients had EC and 15 (17.4%) patients had CAH on final pathology. There was a strong correlation between the intraoperative estimated size of the lesion and the final pathologic assessment (ICC 0.85, mean 3.8 cm, range 0–20 cm, $P < .0001$). However, there was fair

correlation between intraoperative estimation of myometrial invasion and moderate correlation between lower uterine segment/cervical involvement compared with final pathologic evaluation (κ = 0.37 and 0.51, respectively).

Conclusions: Estimated intraoperative evaluation of tumor size correlated strongly with final pathology whereas myometrial invasion and lower uterine segment/cervical involvement had moderate agreement at best. Therefore, intraoperative evaluation is inconsistent when determining the extent of disease and may not be an acceptable method for determining the need for surgical staging.

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91 - Featured Poster Session
A quick and inexpensive alternative to frozen section for diagnosing myometrial invasion in endometrial cancer
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Objectives: Depth of myometrial invasion is an important determinant for performing lymphadenectomy in endometrial cancer. Frozen section of the uterus correlates with final pathology 87% to 92% of the time but is associated with increased time and expense. We have developed a technique that can be used in the operating room immediately after the uterus is removed, which accurately predicts the depth of endometrial cancer invasion.

Methods: Fifteen women with endometrial cancer who were undergoing hysterectomy and bilateral salpingo-oophorectomy with possible lymphadenectomy were recruited for this study. Each patient received intravenous fluorescein dye approximately 5 minutes before uterine artery ligation. After the hysterectomy, the uterus was taken to pathology, bivalved, and the most suspicious areas excised as a transverse section incorporating the endometrium and myometrium. Using a Wood lamp, a measurement of the tumor specimen (nonfluorescent) was compared with the full-thickness specimen. Frozen section analysis of the most suspicious area and gross inspection were conducted, values of which were compared with the final pathology finding. Pearson correlation coefficient was used to compare results between the groups.

Results: The correlation between depth of invasion predicted by fluorescein and final pathology findings was high (r = 0.8765; P < .05) and was comparable to the frozen section correlation with final pathology (r = .8707; P < .05). When patients were categorized as having either less than 50% or more than 50% invasion, X^2 analysis revealed fluorescein to be significantly predictive of final pathology (P = .01).

Conclusions: These results suggest that a rapid and inexpensive test in the operating room can help identify patients who require lymphadenectomy for EC.

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92 - Featured Poster Session
Hybrid models of care between high and low volume centers and associations with uterine cancer treatment and survival
K.M. Doll, K. Meng, W.R. Brewster, P.A. Gehrig and A.M. Meyer. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: High-risk uterine cancer (UC) rates are increasing, and centralization is key to alleviating disparities in care. As cancer care is centralized in high-volume (HV) centers, patients may interact with HV centers for all (HV-All), a portion (HV-Hybrid), or none (LV) of their care. Neither the frequency of these referral care models nor their impact on outcomes is known.

Methods: The North Carolina Central Cancer Registry (NCCCR) was used to identify all UC cases from 2004 to 2009, which were linked to insurance claims using the Integrated Information Cancer Surveillance System. Sites of care were defined by UC surgery volume (HV ≥ 50). Demographic and histologic data were obtained from the NCCCR and clinical data from claims, using ICD-9 and CPT codes. Bivariate statistics were used to compare care model groups, modified Poisson regression to evaluate the receipt of surgical staging and chemotherapy, and Cox models and KM curves to explore crude survival differences.

Results: A total of 1,964 women had UC linked to insurance claims. Mean age was 67 (±12) years, 328 (17%) were racial/ethnic minorities, and 618 (31%) resided in nonmetropolitan counties. Stage was 73% (n = 1,473) localized, 19% (n=378) regional, 5% (n = 105) distant, and less than 1% (n=8) unknown, with 66% (n = 1,287) low-risk and 34% (n = 677) grade 3 histology. For initial surgery, 73% (n = 1,519) were performed at HV centers.

Lymphadenectomy was performed in 71% (n = 1,388) of all cases, and in 498 (74%) of 677 patients with grade 3. In adjusted models, LV centers were less likely to perform lymphadenectomy (RR 0.73, 95% CI 0.66–0.80) with a trend toward decreased chemotherapy for type 2 patients (RR 0.73, 95% CI 0.51–1.05). Among type 2 patients receiving chemotherapy, 62% (n = 92) were in HV-All, 27% (n=40) HV-Hybrid, and 11% LV (n = 17) models. HV-All patients experienced lowest mortality (Figure) while a 50% greater risk of mortality was seen in both HV-Hybrid (RR 1.5, 95% CI 0.9–2.6) and LV (RR 1.5, 95% CI 0.7–3.2) patients.

Conclusions: Nearly a third of high-risk UC patients split care between HV and LV centers. Although further research is needed, these hybrid models appear to have outcomes similar to those with no HV care. Given the importance of adjuvant therapy in improving survival in high-risk UC, surgical centralization alone may be inadequate to combat disparities in care.

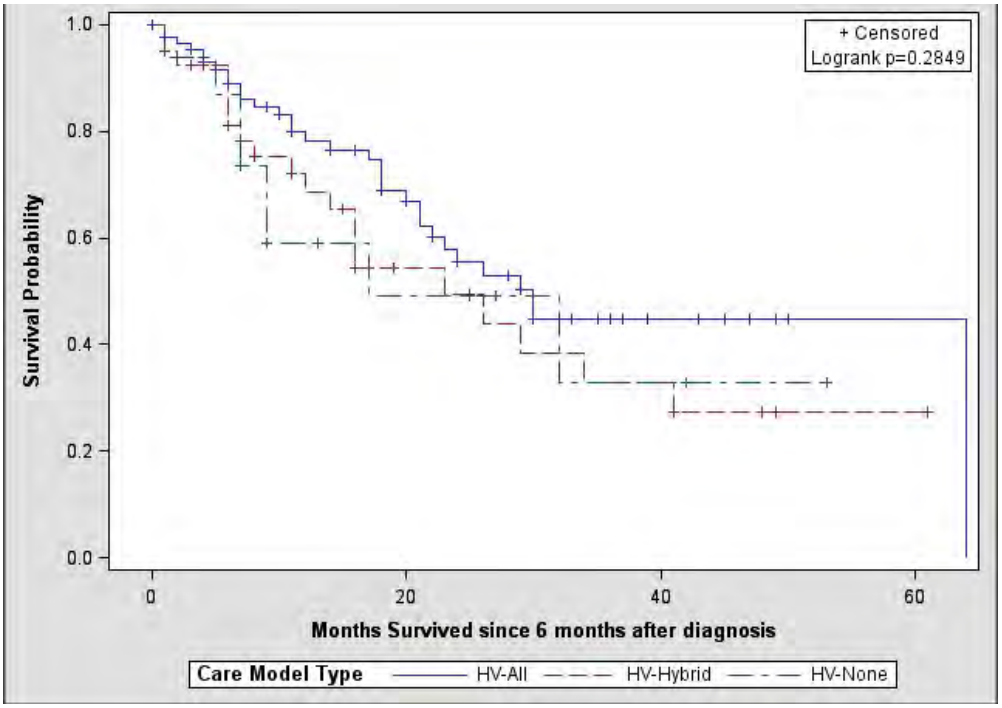

Fig. 1
Kaplan-Meier Survival Curve by Care Model Type: Product-Limit Survival Estimates.

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Phase 3 trial of APF530 vs. ondansetron, each with a neurokinin 1 antagonist and corticosteroid, for prevention of chemotherapy-induced nausea and vomiting in highly emetogenic chemotherapy regimens (MAGIC Trial): Outcomes in cisplatin-based regimen

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Objectives: In the randomized, double-blind, multicenter MAGIC trial, APF530, an extended-release formulation of granisetron providing therapeutic levels for 5 or more days, demonstrated superior complete response (CR; no emesis + no rescue medication) during delayed (>24–120 h) CINV after highly emetogenic chemotherapy (HEC) vs ondansetron (OND) (65% vs 57%, respectively; *P* = .014) in a recommended 3-drug combination regimen with a neurokinin 1 antagonist + dexamethasone (DEX) (NCT02106494), the first phase 3 prospective comparison of this 3-drug regimen. Here we present outcomes in patients who had cisplatin (CIS)-based regimens.

Methods: Patients scheduled to receive single-day HEC were stratified by CIS 50 mg/m^{2}or more (yes/no) and randomized 1:1 to APF530 500 mg SC (10 mg granisetron) or OND 0.15 mg/kg intravenously (IV). Patients were to receive concomitant fosaprepitant 150 mg IV + DEX 12 mg IV on day 1 and oral DEX 8 mg daily on day 2 and twice daily on days 3 to 4. The primary endpoint was delayed-phase CR in cycle 1. Secondary and other endpoints were CR in overall (0–120 h) and acute (<24 h) phases, and complete control (CC; CR and no more than mild nausea) and total response (TR; CR and no nausea) in delayed, overall, and acute phases, all in cycle 1. Response rates were compared using 95% CIs for treatment difference, because this subset analysis was not powered for statistical tests. Safety assessments included adverse events (AEs), injection-site reactions (ISRs), and vital signs.

Results: Of 902 patients in the modified intent-to-treat population (450 APF530, 452 OND), 251 (28%) had CIS-based HEC (125 APF530, 126 OND). Baseline demographics were similar between arms. The most common regimen was CIS + gemcitabine (27%). Delayed-phase CR was 8.5% (95% CI 3.6–20.5) higher with APF530 than OND in the CIS-based subgroup (Table). Although this CI contains 0, the result is consistent with APF530 benefit in the overall population (8.0% higher; 95% CI 1.7–14.4, *P* = .014). Similar trends favoring APF530 were found across overall- and acute-phase CR, and all CINV phases for CC and TR. APF530 was generally well tolerated; most AEs were ISRs of mild or moderate intensity.

Conclusions: Consistent with the overall study, APF530 showed clinical benefit in delayed-phase CR in patients receiving CIS-based HEC, usually difficult to manage.

Table 1
MAGIC Trial CIS Stratum Data.

Phase, n (%)	APF530 N=125	Ondansetron N=126	Treatment Difference %, (95% CI)
Complete response			
Delayed	81 (65)	71 (56)	8.5 (-3.6, 20.5)
Overall	76 (61)	69 (55)	6.0 (-6.2, 18.2)
Acute	105 (84)	101 (80)	3.8 (-5.6, 13.3)
Complete control			
Delayed	77 (62)	67 (53)	8.4 (-3.8, 20.6)
Overall	73 (58)	64 (51)	7.6 (-4.7, 19.9)
Acute	105 (84)	96 (76)	7.8 (-2.0, 17.6)
Total response			
Delayed	60 (48)	57 (45)	2.8 (-9.6, 15.1)
Overall	60 (48)	56 (44)	3.6 (-8.8, 15.9)
Acute	102 (82)	93 (74)	7.8 (-2.5, 18.0)

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Effective outpatient management of carboplatin hypersensitivity reactions in gynecologic oncology patients
L.R. Daily, C.L. Walters Haygood, C.J. Mitchell, K.P. Crump, W.K. Huh, R.D. Alvarez and J.M. Straughn Jr. *University of Alabama at Birmingham, Birmingham, AL, USA*

Objectives: Hypersensitivity reactions (HRs) to carboplatin often prompt permanent discontinuation. We evaluated the safety and effectiveness of an outpatient protocol for treating mild, moderate, and severe HRs.

Methods: Gynecologic oncology patients who experienced an HR to carboplatin were classified as having a mild, moderate, or severe reaction. No skin tests were performed. Patients with a mild HR were treated in the following cycle with enhanced prophylaxis consisting of oral steroids, ranitidine, and loratadine on the day before and day after chemotherapy. Standard premedications included 100 mg of hydrocortisone on the day on chemotherapy. Patients with a moderate HR were treated with a 3-hour desensitization protocol in the outpatient infusion clinic. The carboplatin dose was calculated using the Calvert formula and the total dose was divided into 3 bags; 1st bag – 1% of dose in 250 mL over 1 hour, 2nd bag – 9% of dose in 250 mL over 1 hour, and 3rd bag – 90% of dose in 500 mL over 2 hours. Patients with a severe HR were switched to cisplatin prepared in a 235-mL bag for the next cycle of chemotherapy. All breakthrough HRs were treated with suspension of infusion, antihistamines, and steroids.

Results: From January 2011 to July 2015, 48 patients were identified with a HR to carboplatin. Of these, 79.2% had ovarian cancer, 93.8% experienced the HR in the recurrent setting, 91.7% (44/48) received further platinum chemotherapy, and 22.9% (11/48) had a mild HR and were treated with enhanced prophylaxis on subsequent cycles. All patients completed their planned chemotherapy with 6 or more cycles of carboplatin given. Twenty (41.7%) of 48 had a moderate HR and were treated with desensitization on subsequent cycles. The median number of desensitizations was 3 per patient (range 1–8). Sixty-six (94.3%) of 70 desensitization cycles were completed. Of patients treated with desensitization, 86.7% completed the prescribed number of carboplatin cycles, 27.1% (13/48) had a severe HR and received cisplatin on subsequent cycles, and 92.3% completed their planned chemotherapy with 1 to 12 cycles of cisplatin. No patient developed life-threatening symptoms during retreatment with platinum therapy.

Conclusions: This 3-tier outpatient protocol for carboplatin HRs was effective and safe, with 85.4% of patients successfully completing their planned chemotherapy cycles.

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Safety and efficacy of a 4-step outpatient platinum desensitization protocol in heavily pretreated gynecologic oncology patients

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Objectives: The incidence of hypersensitivity reactions (HSRs) to platinum chemotherapy increases to more than 25% after 7 cycles. This results in discontinuation of therapy potentially limiting the utility of further platinum therapy. The goal of this study was to evaluate the safety and efficacy of an outpatient platinum desensitization protocol.

Methods: This is a single-institution retrospective analysis of patients with a documented platinum hypersensitivity reaction challenged with an outpatient desensitization protocol from 2005 to 2015. The 4-step, 6-hour protocol consisted of increasing platinum treatment by 10-fold increments, each administered over 90 minutes. Patients were premedicated with dexamethasone, diphenhydramine, famotidine, and ondansetron before treatment. Additional diphenhydramine and hydrocortisone were given before the final infusion.

Results: A total of 53 patients who previously developed mild (51%), moderate (41.2%), or severe (7.8%) HSRs underwent desensitization. The median number of platinum infusions before a HSR was 12 (range, 4–37). Of 316 platinum desensitization infusions, 308 were successfully completed (97.5%). Forty-eight (90.5%) of 53 women completed a full course of treatment as planned. The median number of desensitization cycles administered was 4 (range, 1–26), with 7 women completing 15 or more cycles. No patient with a mild hypersensitivity reaction failed the protocol. Breakthrough reactions were encountered in 11% of all cycles: 74% were mild cutaneous reactions, 20.6% moderate reactions, and 5.8% severe reactions with gastrointestinal and respiratory symptoms. There were no anaphylactic reactions. Approximately 76.5% of these cycles were completed after additional medical support. Women with a more severe initial HSR were more likely to experience breakthrough reactions.

Conclusions: This case series represent results from the largest outpatient 4-step 6-hour desensitization protocol reported in the literature. The protocol was effective and well tolerated, allowing most women with platinum HSR to continue treatment and reach their full target dose.

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Does frequency of laboratory testing impact clinically important outcomes in patients undergoing platinum-based chemotherapy?

C. Garcia, L. Montemorano, E. Saks, L. Duska and L.A. Cantrell. *University of Virginia School of Medicine, Charlottesville, VA, USA*

Objectives: To evaluate whether incidence of grade 3 or 4 toxicities, dose reduction or delays, hospital admissions, or neutropenic fevers were affected by frequency of complete blood count (CBC) testing in patients undergoing chemotherapy for ovarian or endometrial cancer.

Methods: Patients with endometrial or ovarian cancer who received platinum-based chemotherapy (upfront or recurrent) from January 2005 to December 2014 were identified from a clinical database. Patients were excluded if they received chemotherapy more frequently than every 21 days. Electronic charts were reviewed to collect demographic characteristics and chemotherapy regimens, laboratory results, toxicities, dosing changes, complications, and hospital admissions. SPSS software was used for data analysis with a significance level of $P < .05$.

Results: A total of 219 patients were identified, 67 (30.6%) with endometrial cancer and 152 (69.4%) with ovarian cancer. In the majority of patients, CBCs were checked multiple times per cycle (62.6%), and they were treated with a platinum-based doublet (71.7%). Chemotherapy regimen was significantly associated with more laboratory testing per cycle as the number of agents increased ($P = .001$). Chemotherapy was delayed 45% of the time, whereas only 36% required a dose reduction. Both dose delay and dose reduction were significantly associated with more laboratory testing per cycle as were the rates of grade 3 or 4 hematopoietic complications. Dose delays occurred more commonly for laboratory results (50.0%) than for symptoms (29.8%). Similarly, the majority of dose reductions (57.5%) were for abnormal laboratory tests. However, when a laboratory result was the cause of the treatment change, it was most often because of a day 21 laboratory result rather than a midcycle result (90.1% vs 9.9%). There was no difference in rates of neutropenic fever or hospital admission by frequency of CBC evaluation (Table 1).

Conclusions: More frequent laboratory testing detected more cases of grade 3 or 4 hematopoietic toxicities and was associated with more dose reductions and delays. However, these decisions were most frequently made based on laboratory results on the day of chemotherapy. There were no differences in number of hospitalization or cases of neutropenic fever depending on frequency of laboratory testing, suggesting that it may be safe and more cost-effective to space out routine laboratory tests for select patients.

Table 1
Demographic and Clinical Characteristics Study Participants.

	Multiple labs per cycle N = 137 (62.6%)	1 lab test per cycle 82 (37.4%)	*P* value
Mean Age	62.6 ± 11.2yrs	61.7 ± 13.1yrs	0.121
Race			0.927
Caucasian	116 (84.7)	66 (80.5)	
African American	16 (11.7)	12 (14.6%)	
Asian	1 (0.7)	1 (1.2)	
Hispanic	2 (1.5)	1 (1.2)	
Other	2 (1.5)	2 (2.4)	
Type of cancer			0.782
Endometrial	41 (29.9)	26 (31.7)	
Ovarian	96 (70.1)	56 (68.3)	
Stage			0.208
1	18 (13.1)	19 (23.5)	
2	19 (8.7)	8 (9.9)	
3	75 (34.4)	43 (53.1)	
4	25 (11.5)	11 (13.6)	
Chemotherapy Regimen			**<0.001**
Single agent platinum	5 (3.6)	16 (19.5)	
Platinum based doublet	95 (69.3)	62 (75.6)	
Platinum based doublet +bevacizumab	15 (10.9)	3 (3.7)	
Platinum based doublet +bevacizumab + PARP inhibitor	19 (13.9)	1 (1.2)	
Other	3 (2.2)	0 (0)	
Line of chemotherapy			0.296
First	114 (83.8)	64 (78.0)	
Second	17 (12.5)	11 (13.4)	
Third or greater	5 (3.7)	7 (8.5)	
Concurrent radiation	18 (13.1)	10 (12.2)	0.840
Dose reduction	54 (39.4)	19 (23.2)	**0.014**
Dose delay	66 (48.2)	28 (34.1)	**0.042**
G3/4 toxicity			
Anemia	40 (29.2)	9 (11.0)	**0.002**
Thrombocytopenia	8 (5.8)	0 (0)	**0.022**
Neutropenia	18 (22.0)	101 (73.1)	**<0.001**
Neutropenic fever	6 (4.4)	3 (3.7)	0.547
Hospital Admission	30 (21.9)	18 (22)	0.993

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Metabolic impact of progestin therapy for complex atypical hyperplasia and grade 1 endometrial cancer

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Objectives: Progestin therapy is used in patients with complex atypical hyperplasia (CAH) and grade 1 endometrial cancer as a means to preserve fertility and in those in whom medical comorbidities are felt to confer increased surgical risk. The morbidity of progestin therapy in this population has yet to be assessed and is critically important for an informed discussion of risks and benefits of medical versus surgical therapy.

Methods: Clinical, pathologic, and demographic data were abstracted for patients with CAH or grade 1 endometrial cancer who were treated between January 1, 2009, and August 1, 2015, at a university-affiliated county hospital. Outcome measures tracked over time included weight, blood pressure, and hemoglobin A1c (HgbA1c).

Results: A total 109 patients were identified: 49 patients were treated with hysterectomy (HYST group), 43 with megestrol acetate +/- LNG-IUD (MEG group), and 17 with LNG-IUD only (IUD group). Median follow-up was 14.7 months (range, 1.4–76.9 months). At the time of initial diagnosis, median body mass index (BMI) was higher (P = .04) in patients who were medically managed (MEG group + IUD group) (median; IQR 29.1–40.3). The proportion of patients with HgbA1C greater than 6.5 at the time of initial diagnosis was significantly different among the 3 groups (HYST group: 12.2%, MEG group: 23.3%, IUD group: 41.2%; P = .04). The median changes in BMI in the 3 groups are listed in the table. There was no significant difference between treatment modalities in the proportion of at-risk patients who developed hypertension or HgbA1c greater than 6.5 during the follow-up period. Resolution rate was 53% for the MEG group and 47% for IUD group (P = NS).

Conclusions: Treatment with megestrol acetate was associated with significant weight gain, which is a known driver in both the metabolic syndrome pathway and in the development of CAH and endometrial cancer. Weight gain was not observed with the use of the LNG-IUD alone and resolution rates were comparable. The IUD may thus offer an equally efficacious therapy with less metabolic impact.

Table 1
Observed change in BMI during treatment.

	HYST **n = 49**	**MEG** **n = 43**	**IUD** **n = 17**
Median change in BMI from diagnosis to maximum during follow-up	+0.4 kg/m^2 referent	+1.8 kg/m^2 P = .02	+0.10 kg/m^2 P = NS
Median change in BMI from diagnosis to end of follow-up	0.0 kg/m^2 referent	+1.0 kg/m^2 P = .04	-0.4 kg/m2 P < .01

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Use of whole pelvic radiotherapy for high-intermediate risk endometrial cancer
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Objectives: For women with endometrial cancer, radiation decreases the risk of local recurrence but does not influence survival. For those with high intermediate risk (HIR) tumors, the PORTEC2 trial, published in 2010, demonstrated similar tumor control with vaginal brachytherapy and whole pelvic radiation therapy (WPRT) despite substantially greater toxicity with WPRT. We analyzed the use of WPRT in women with HIR endometrial cancer before and after PORTEC2.

Methods: The National Cancer Database (NCDB) was used to identify women with HIR endometrial cancer based on the previously reported criteria: age more than 60 years, stage IA/grade 3, or stage IB grade 1 or 2 tumors. Multivariable generalized estimating equations were developed to estimate use of WPRT while controlling for clinical and demographic characteristics. Separate models were analyzed based on performance of lymphadenectomy (LND).

Results: Among 8,242 women with HIR endometrial cancer, 915 (11.1%) received WPRT and 2,614 (31.7%) received brachytherapy. Use of WPRT decreased over time from 18.1% in 2008 to 8.5% in 2010 and 8.6% in 2012 (P < .0001). Among women who underwent LND, WPRT decreased from 17.2% in 2008 to 7.6% in 2012 (P < .0001). For women who did not undergo LND, the rate of WPRT declined from 26.2% in 2008 but only to 20.8% in 2012 (P = .35). In a multivariable model, use of WPRT was more common in patients who had not undergone LND, eastern US residents, those treated at community cancer centers, younger women, and those with stage IB/grade 2 tumors (P < .05 for all). Compared with women who underwent LND, not having undergone LND was associated with an RR of 2.32 (95% CI 1.99–2.72) for receiving WPRT.

Conclusions: Despite randomized clinical trial data, use of whole pelvic radiotherapy remains common for women with HIR endometrial cancer. Knowledge of the status of the regional lymph nodes appears to decrease the use of pelvic radiation.

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Adjuvant therapy for grade 3, deeply invasive endometrioid adenocarcinoma of the uterus
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Objectives: Although patients with grade 3 deeply invasive endometrioid adenocarcinoma are typically managed with primary surgery, the type of adjuvant therapy used is controversial. This subgroup was excluded from PORTEC-1 and -2 because they were felt to have a high risk of recurrence. Although they were included in GOG99, only 38 patients fell into this category. The purpose of this study was to evaluate the role of adjuvant radiation and/or chemotherapy in women with deeply invasive grade 3 endometrioid tumors.

Methods: A multicenter retrospective chart review was performed at 3 large medical institutions in the United States. Patients with grade 3 endometrioid adenocarcinoma invading more than 50% of the myometrium were included. Medical records were queried to evaluate whether lymph node assessment was performed, the status of the lymph nodes, and adjuvant treatment strategy used. Overall survival (OS) was calculated from the date of primary surgery to date of last follow-up or death. Log-rank tests were performed to compare management strategies. A multivariable Cox proportional hazards model was then conducted, controlling for age and body mass index.

Results: Between 1984 and 2012, 257 patients were identified with a median follow-up of 3.08 years. Most patients (n = 215, 84.7%) underwent evaluation of pelvic and/or para-aortic lymph node status and 92 (43%) had positive lymph nodes. For node-negative patients, there was no difference in 5 year survival between those who received adjuvant pelvic radiation +/- vaginal brachytherapy (n = 52) versus brachytherapy alone (n = 46) (0.73 vs 0.70, P = .729). Among patients with positive lymph nodes (n = 92), 16 patients received radiation alone versus 50 who received combination of chemotherapy +/- radiation. Chemotherapy did not improve 5-year overall survival compared with radiation alone (0.48 vs 0.50, P = .761).

Conclusions: Among women with grade 3 deeply invasive endometrioid adenocarcinoma, vaginal cuff brachytherapy alone resulted in similar survival compared with pelvic radiation in node-negative patients. The addition of chemotherapy did not show clear benefit compared with radiation therapy alone in women with positive nodes.

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100 - Featured Poster Session
The role of adjuvant radiation in lymph node-positive endometrial adenocarcinoma
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Objectives: The role of adjuvant radiation in patients with locally advanced endometrial adenocarcinoma is controversial. The purpose of this study was to examine the impact of adjuvant radiation on overall survival (OS) and cause-specific survival (CSS) in patients with lymph node–positive endometrial cancer.

Methods: We analyzed all women diagnosed with FIGO stage IIIC endometrial adenocarcinoma in the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2012 (n = 2,177). SEER does include details regarding chemotherapy utilization. Patients not undergoing surgery or with missing treatment information were excluded. X^2 tests were used to compare predictors of treatment received. Cox proportional hazards model and Kaplan-Meier method were used to assess OS and CSS.

Results: The median age was 61 years (range 27–84 years) and the median follow-up was 34 months (6–107 mo). Adjuvant radiation was administered to 1,255 (58%) patients, and therapy consisted of external beam radiation alone (59%), brachytherapy alone (29%), or external beam radiation with brachytherapy (11%). The 3-year actuarial CSS was 80.8% in patients receiving radiation versus 71.9% in patients without radiation (P < .001). The 3-year actuarial OS was 83.6% in patients receiving radiation versus 76.4% in patients without radiation (P < .001). On multivariable analysis, radiation was associated with an improved OS (HR 0.538, 95% CI =0.428–0.676, P < .001) and CSS (HR 0.548, 95% CI 0.425–0.706, P < .001). Of those receiving radiation, brachytherapy use was not associated with OS (HR 0.552, 95% CI 0.776–1.609, P = .552) or CSS (HR 0.776, 95% CI 0.706–1.593, P = .776). On multivariable analysis, increased number of lymph nodes (continuous) examined (P < .001), younger age (P < .001), and lower grade (P < .001) also were associated with improved OS while increased number of lymph nodes examined (P < .001) and lower grade (P < .001) were associated with improved CSS.

Conclusions: In this large population registry analysis, adjuvant radiation was associated with improved OS and CSS in patients with lymph node–positive endometrial cancer. Prospective data are needed to confirm these findings.

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From identification of therapeutic targets to clinical strategies
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Objectives: shRNA-mediated lethality screening is a useful tool to identify essential targets using functional genomics. Ovarian cancer (OC) has a high response rate initially, but becomes resistant to standard chemotherapy. We analyzed 4 shRNA screens in an unbiased manner to identify druggable molecular targets.

Methods: We selected a total of 55 genes from shRNA screens across 4 OC cell lines. After validating by siRNAs in an expanded set of 6 OC cell lines, 6 candidates were identified for further investigation. Their clinical relevance was examined in The Cancer Genome Atlas (TCGA) OC dataset. To move these findings toward the clinic and to recapitulate the siRNA results, we used pharmacologic inhibitors including oxozeaenol (for MAP3K7/TAK1), BI6727 (PLK1), MK1775 (WEE1), and lapatinib (ERBB2). The cytotoxic effects were measured by XTT assay, as single agents and in 2-way combinations. Cotreatments were evaluated in either sequential or simultaneous exposure to the drug.

Results: Essential targets were identified independent of OC subtype or p53 status. Candidate genes were dysregulated in a subset of TCGA OCs, though their alterations showed no significant correlation to overall survival. Oxozeaenol, BI6727, and MK1775 showed cytotoxic effects on OC cell lines regardless of cisplatin responsiveness, whereas all OC cells tested were resistant to lapatinib. Furthermore, the addition of cisplatin did not increase the cytotoxicity of BI6727 in cisplatin-resistant OC cells. Importantly, the combined treatment of BI6727 and MK1775 at their sublethal concentrations was more potent than single drug exposure. However, in an extended period of treatment, BI6727 alone was equally potent as the cotreatment with BI6727 and MK1775, suggesting the coinhibition may not be more efficacious than monotherapy.

Conclusions: Loss-of-function screen followed by in vitro target validation using chemical inhibitors identified clinically relevant essential targets. This approach has the potential to systematically refine therapeutic strategies in OC. These molecular target-driven strategies may provide additional therapeutic options for women whose tumors have become refractory to standard chemotherapy.

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102 - Featured Poster Session
Objective response rate is a possible surrogate endpoint for survival in patients with advanced, recurrent ovarian cancer
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Objectives: To evaluate published literature to determine if response rate could be a suitable surrogate endpoint of survival in patients with ovarian cancer.

Methods: A systematic review, consistent with PRISMA criteria, was undertaken to identify randomized controlled trials reporting overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) in patients with recurrent ovarian cancer. The MEDLINE® and Embase® databases were searched (year 2000–March 23, 2015), augmented by bibliographic screening. Data from trials meeting predefined eligibility were extracted by a single reviewer and reviewed by a second. Proposed surrogate measures (independent variables) were ORR (complete response [CR] + partial response [PR]) and disease control rate (DCR; CR + PR + stable disease). True clinical outcomes (TCO, dependent variables) were median OS and PFS. Units of analysis were treatment arms across studies and trial (preserving randomization). Analyses were performed on unweighted and weighted data using correlation analysis, linear regression, and the surrogate threshold effect (STE; the minimum effect on a surrogate predicting a nonzero, statistically significant effect on the TCO). The smaller the STE, the greater the predictive precision with the magnitude of STE dependent on the variance of prediction.

Results: From 1,386 references, 87 publications representing results of 39 studies comprising 86 treatment arms and 13,848 platinum-sensitive and resistant patients were included. Main results (treatment level) are in the Table. ORR was a better predictor than DCR and was strongly correlated with OS and PFS. Weighted-regression analysis showed that for each 10% increase in ORR, PFS increased by 1.20 months, and OS increased by 2.83 months. Regression analysis based on treatment effects (odds ratio of response, hazard ratio [HR] of survival) suggested that a 10% increase in the odds ratio of ORR would result in 2.5% reduction in HR of OS. Based on weighted data, the STE indicated that an ORR of 1% or more is needed to achieve a nonzero OS benefit.

Conclusions: Data analyzed in this systematic review support ORR as a possible surrogate endpoint for OS in patients with recurrent ovarian cancer who have received at least second-line therapy. Results should be interpreted in the context of existing literature.

Table 1. Summary of results of correlation, regression analysis, and STE for the relationship of OS/PFS with ORR/DCR (treatment arms as unit of analysis).

Relationship	Unweighted				Weighted			
	N	Correlation coefficient (*P* value)	R^2	STE, %	N	Correlation coefficient (*P* value)	R^2	STE, %
ORR with OS	60	0.70563 (<0.0001)	0.4979	<1	58	0.81737 (<0.0001)	0.6681	1
ORR with PFS	86	0.75637 (<0.0001)	0.5721	11	84	0.84825 (<0.0001)	0.7195	13
DCR with OS	41	0.553 (0.0001)	0.3058	30	41	0.57687 (<0.0001)	0.3328	36
DCR with PFS	55	0.64225 (<0.0001)	0.4125	52	55	0.72542 (<0.0001)	0.5262	56

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Toxicity and response to pemetrexed in persistent and recurrent ovarian, primary peritoneal and fallopian tube cancers: A retrospective chart review

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Objectives: To evaluate the toxicities, response, and progression-free survival in heavily pretreated women with recurrent, progressive, platinum-resistant epithelial ovarian, fallopian tube (FT), and primary peritoneal (PP) cancer treated with a regimen of single-agent pemetrexed.

Methods: A retrospective chart review of 73 patients who received pemetrexed with a median dose of 900 mg/m^2 on day 1 of a 21-day cycle between January 1, 2014, and January 1, 2015, was performed after institutional review board approval. Patients with recurrent, progressive, platinum-resistant epithelial ovarian, FT, and PP cancer were eligible for review. Statistical evaluation was performed with STATA 13.1, paired *t*tests, and Cox proportional hazards were used for statistical significance.

Results: A total of 73 patients were evaluated, the majority of whom (67%) had stage IIIC ovarian cancer. The median number of chemotherapy regimens received before treatment with pemetrexed was 6.8 (range, 1–16), with at least 1 being a platinum-containing regimen. During treatment, patients received a median of 3.2 cycles of pemetrexed (range, 1–8) over 47.8 days (median) (range, 1–148 days). Treatment was well tolerated; the most common side effects (grade 2 or less) were nausea (32.9%), rash and mucositis (16.4% each), and fatigue (27.4%). Four patients (6%) required hospital admission for toxicities including cytopenic fever, intractable nausea, and failure to thrive. Initial response was noted in 33 patients (45%) but was sustained in only 11 patients (15%), with 1 patient (1%) having a complete response and 10 patients (14%) having a partial response. Stable disease was not observed, and progression of disease occurred in 62 patients (85%).The median progression-free survival of partial responders was 5.8 months (range, 0.7–20). One patient who had a complete response is currently free of disease 47 months after diagnosis of disease. Patients were followed for a mean of 10.4 (±10) months after stopping pemetrexed.

Conclusions: With a response rate of 15% and a low rate of grade 3 and 4 toxicities, pemetrexed is a well-tolerated regimen for recurrent platinum-resistant ovarian, FT and PP cancer in patients who desire ongoing chemotherapeutic options.

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CRISPR-CAS9-negative selection screen identifies genes that sensitize high-grade serous ovarian cancer cell lines to carboplatin, paclitaxel, and olaparib

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Objectives: The development of therapeutic resistance remains one of the greatest challenges in treating high-grade serous ovarian cancer (HGSOC). In this study, we used CRISPR-CAS9 technology to identify genes that may sensitize HGSOC cell lines to the most commonly used therapeutic agents: carboplatin, paclitaxel, and olaparib.

Methods: The CRISPR-CAS9 system is used to introduce targeted loss of function mutations at specific sites in the genome through a synthetic single guide RNA (sgRNA) using associated nuclease CAS9. Genes related to survival, metabolic, and oncogenic pathways were selected as targets for the sgRNA library. Three HGSOC cell lines (OVSAHO, TYKNU, and JHOS 2) were infected with lentiviruses containing the sgRNA library at a low multiplicity of infection, delivering, on average, only 1 CRISPR/cell and a puromycin selection marker. Deep sequencing of cellular DNA preparations was performed before treatment and after 4 weeks. Scatterplots were used to depict the genes in the library with their depletion metric (DM) calculated in *R* for both replicates. Because this is a negative selection screen, increased depletion of a gene (DM < 1) at the end of 4 weeks indicates increased sensitivity to the drug condition.

Results: DM scores were ranked and genes with the lowest scores for both replicates were selected for validation. The Table shows selected genes, screen conditions under which they identified, along with DM values for both replicates. In this pilot screen, genes involved in histone modification and regulation of apoptosis were identified to have the lowest DM values. Histone modification genes included histone acetyltransferases *KATA6A*, *EP300*, and *CREBBP*, and histone deacetylase, *HDAC3*. Antiapoptosis genes included *MCL1* and *BCL2L2* and were preferentially identified in the olaparib screen.

Conclusions: This is the first large negative selection screen of its kind in ovarian cancer. Validation of target genes within the histone modification and antiapoptotic gene families in sensitizing HGSOC to carboplatin, paclitaxel, and olaparib is ongoing. These results will serve to focus the search for potential therapeutic targets to improve sensitivity to current therapies.

Table 1
Selected Genes from CRISPR-CAS9 Negative Selection Screen.

Functional group	Gene	Cell line	Treatment	DM values	Targetable
Histone modification	KATA6A	TYKNU	paclitaxel	0.90, 0.56	Unknown
	HDAC3	TYKNU	paclitaxel	0.67, 0.90	Yes
		JHOS2	carboplatin	0.86, 0.69	
		OVSAHO	paclitaxel	0.67, 0.77	
	EP300	JHOS2	carboplatin	0.28, 0.36	Yes
			olaparib	0.47, 0.38	
	CREBBP	JHOS2	carboplatin	0.47, 0.37	Yes
Anti-apoptosis	MCL1	TYKNU	olaparib	0.69, 0.80	Yes
	BCL2L2	TYKNU	olaparib	0.89, 0.70	Yes

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Off-target effects of erythropoietin stimulate ovarian cancer via EphB4

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Objectives: While recombinant human erythropoietin (rhEpo) has been widely used to treat anemia in cancer patients, concerns about its adverse effects on patient survival have emerged. A lack of correlation between expression of the canonical EpoR and rhEpo's effects on cancer cells prompted us to consider the existence of an alternative Epo receptor.

Methods: We used a multitude of methods including in silico modeling, bioinformatics, in vitro binding studies, and in vivo genetically engineered mouse models to determine the potential role of EphB4 as an Epo receptor. We also analyzed EpoR and EphB4 expression in relation to clinical outcomes based on rhEpo use by cancer patients (n = 175).

Results: In silico modeling identified EphB4 as a candidate Epo receptor. Binding studies revealed that Epo bound to EphB4 with low affinity. After development of stable clones in which either EpoR or EphB4 was silenced, exposure of shEpoR cells to soluble EpoR showed noncompetitive inhibition; however, exposure to soluble EphB4 competitively inhibited ^{125}I-Epo binding demonstrating the specificity of Epo binding to the EphB4 receptor. Overexpression of EpoR and EphB4 was noted in 79% and 39% of tumors, respectively. Kaplan-Meier analyses indicate that high EphB4 was related to high mortality rate (3 vs 6.69 years, $P < .001$). rhEpo treatment was related to higher mortality among patients with EphB4 overexpressing tumors (2.18 vs 4.52 years, $P = .0004$), but not in patients with high tumoral levels of EpoR (4.38 vs 5.28 years, $P = .19$). In vivo treatment with rhEpo resulted in increased tumor growth compared with untreated animals ($P < .01$). EpoR siRNA did not result in significant decreases in Epo-stimulated tumor growth, but EphB4 silencing completely blocked Epo-stimulated tumor growth.

Conclusions: These results identify EphB4 as a critical mediator of erythropoietin-induced tumor progression and further provide clinically significant dimension to the biology of erythropoietin.

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Obesity is associated with altered angiogenic gene expression in high-grade serous ovarian cancer

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Objectives: Obesity has been associated with increased risk and worse outcomes in ovarian cancer (OC). In addition, we found obesity to be associated with increased tumor aggressiveness in a genetically engineered mouse model of serous OC. We sought to evaluate the association between obesity and angiogenesis to determine if obesity alters the tumor microenvironment in high-grade serous OCs in mice and women.

Methods: We used the K18-gT$_{121}^{+/-}$; p53$^{fl/fl}$;*Brca*1$^{fl/fl}$ (KpB) OC mouse model. KpB mice were subjected to 60% calories derived from fat in a high-fat diet (HFD) to mimic diet-induced obesity versus 10% calories from fat in a low-fat diet (LFD). Tumors from obese and lean KpB mice were analyzed using custom Agilent 244K chip arrays for differential expression of angiogenic genes and validated using qualitative polymerase chain reaction (qPCR). Confirmation of findings in human OCs was performed using institutionally derived patient specimens (IDB) and TCGA database.

Results: As previously reported, diet-induced obesity resulted in a tripling of tumor size in KpB mice compared with those fed a LFD. Fourteen angiogenic-related genes were differentially expressed in the obese versus lean mice ($P <$ 0.01). After adjusting for multiple comparisons, *thrombospondin4* (*THBS4*) and *eregulin (EREG)* demonstrated 2- and 1.6-fold higher expression in lean compared with obese mice (adjusted P value (q) < .01). In contrast, *natriuretic peptide receptor 1* (*NPR1*) and *MMP12* demonstrated 1.9- and 2.7-fold higher expression in obese compared with lean mice ($q < .005$). Alterations in gene expression were confirmed in 57% (8/14) by PCR. Body mass index (BMI) data were available for 209 patients of 412 patients (IDB [41/51]; TCGA [168/361]). High BMI was associated with low *EREG* expression ($P = .03$).

Conclusions: Obesity may alter the tumor microenvironment and promote tumor progression via differential modulation of angiogenic pathways. Differentially expressed angiogenic genes may serve as novel therapeutic targets unique to obesity-driven OCs.

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Therapeutic potential of ruxolitinib in human ovarian cancer

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Objectives: STAT3 activation leads to tumorigenesis and has been demonstrated to be a potential novel target in ovarian cancer therapy. Ruxolitinib is a US Food and Drug Administration–approved inhibitor of JAK/STAT signaling pathway used in the treatment of polycythemia vera. Our objective is to test the therapeutic potential of ruxolitinib in human ovarian cancer.

Methods: The in vitro antitumor activity of ruxolitinib was studied in several human ovarian cancer cell lines (OVCAR8, SKOV3, and MDAH 2774). The effect of ruxolitinib on phosphorylation of STAT3 was tested with Western blot analysis. The effect of ruxolitinib on cell viability was examined using a standard MTS assay or the acid phosphatase assay, either alone or in combination with chemotherapy. Chou-Talalay method was used to assess synergy between ruxolitinib and other anticancer agents. The in vivo antitumor activity of ruxolitinib was evaluated in mice bearing peritoneal OVCAR8-ip human ovarian cancer cells. This cell line was derived from OVCAR8 human ovarian cancer cells by selecting for a peritoneal metastatic phenotype in the mice. Comparisons between 2 groups were determined with the Student *t* test. $P < .05$ was considered statistically significant.

Results: Ruxolitinib was found to effectively inhibit the phosphorylation of STAT3 in OVCAR8, SKOV3, and MDAH2774 cells, and reduced cell viability with IC50 value in the range of 10 to 17 mM in these cells. In addition, ruxolitinib synergistically increased antitumor activity of cisplatin, carboplatin, paclitaxel, doxorubicin, and topotecan. The IC50 of these anticancer agents decreased two- to threefolds in the presence of ruxolitinib. Finally, ruxolitinib reduced the tumor burden of OVCAR8 in a peritoneal ovarian cancer mouse model when these mice were treated with ruxolitinib by oral gavage at 60 mg/kg twice a day.

Conclusions: Our results demonstrate that ruxolitinib inhibits activation of STAT3, reduces cell viability, enhances sensitivity of ovarian cancer cells to other anticancer agents, and suppresses ovarian tumor growth in mice. These results may provide a foundation for clinical investigation of ruxolitinib in ovarian cancer patients.

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Preclinical data supporting the flavone baicalein as a novel mTOR inhibitor with potent activity against endometrial cancer cells
E.S. Han, Q. Xing, J. Yan, W. Wen, T. Dellinger, M.T. Wakabayashi and J.H. Yim. *City of Hope, Duarte, CA, USA*

Objectives: The mTOR pathway is a promising target for endometrial cancer therapy commonly because of the loss of PTEN expression. Metformin has been shown to inhibit endometrial cancer cell proliferation and is currently in phase II/III clinical trial testing. We have identified a natural flavone, baicalein, which markedly upregulates DNA Damage Induced Transcript 4 (DDIT4), suppresses breast and ovarian cancer cell growth, and alters mTOR pathway. We examined the activity of baicalein in endometrial cancer cells.

Methods: The endometrial cancer cell line HEC1a was treated with baicalein (5–80 μM) or metformin (5–10,000 μM) and growth was assessed at 24 to 72 hours with the MTT assay. Total protein lysates were obtained for Western blot analysis to evaluate mTOR pathway mediators and DDIT4 levels. In vivo studies were performed with an HEC1a mouse model. Mice received either control or baicalein (80 mg/kg) treatment by oral gavage daily. Tumor volumes were measured over time.

Results: Baicalein inhibited growth of HEC1a cell line in a dose-dependent fashion (IC_{50} ~10 μM). In contrast, higher millimolar concentrations (>1,000-fold) were required to inhibit growth with metformin. The observed growth inhibition with baicalein was associated with decreased PS6K1 and PS6 levels and increased DDIT4 levels. We tested baicalein (80 mg/kg) in an endometrial cancer cell mouse model. We observed significant tumor growth inhibition in the HEC1A mouse model compared with control mice (Figure).

Conclusions: Both in vitro and in vivo studies support baicalein as a potent inhibitor of endometrial cancer cell proliferation. The inhibitory effect correlates with mTOR pathway inhibition and increase in DDIT4 expression. This preclinical study supports the use of baicalein as a novel treatment for endometrial cancer.

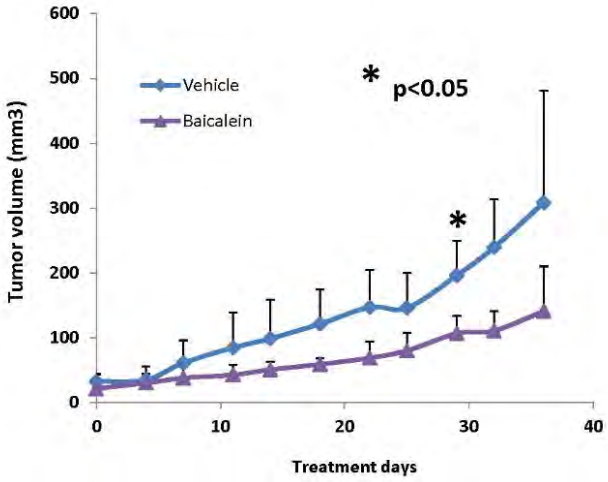

Fig. 1

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Micro-RNAs associated with ovarian cancer in vitro cisplatin resistance regulate epithelial-mesenchymal transition

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Objectives: The central role of micro-RNAs (miRNAs) in biologic processes make them appealing candidates as cancer biomarkers and therapeutic targets. We sought to define the miRNAs associated with the development of ovarian cancer (OVCA) in vitro cisplatin resistance and the biologic processes they regulate.

Methods: Serial OVCA cell cisplatin treatments were performed in parallel with measurements of miRNA expression changes. Pearson correlation was used to identify miRNA with expression that correlated with increasing cisplatin resistance (IC_{50}). The MiRanda database was used to identify predicted target genes of miRNAs associated with cisplatin resistance. GeneGo Metacore analysis identified the representation of molecular signaling pathways associated with the differentially expressed genes.

Results: Correlation analysis identified 9 miRNAs that were significantly ($P < 0.01$) associated with the $IC_{50}$of 4 OVCA cell lines with acquired resistance to cisplatin: miR-496, miR-485-5p, let-7g, miR-152 (positive correlation), and miR-422b, miR-17-3p, miR-520h, miR-27b, and miR-432* (negative correlation). Target gene information was available for 5 of 9 cisplatin resistance–associated miRNA. Metacore analysis identified 15 molecular signaling pathways (FDR < 0.05) common to 3 or more of the resistance-associated miRNAs. Eleven of 15 signaling pathways are involved in epithelial-mesenchymal transition (EMT).

Conclusions: miRNAs associated with the evolution of OVCA in vitro cisplatin resistance regulate the expression of genes and signaling pathways involved in EMT. Our data suggest that EMT processes influence the development of chemoresistance and may provide a new avenue for therapeutic intervention.

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Identification of distinct ADP-ribosylation patterns in ovarian cancer: A novel biomarker for therapy response

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Objectives: Poly(ADP-ribose) polymerases (PARPs) function in several essential cellular processes, including DNA repair, transcriptional regulation, modulation of chromatin structure, and stress response. It is unknown what molecular mechanisms and which of the 17 PARP proteins encoded in the human genome drive the diversity of ADP-ribosylation in normal and malignant cells. The goal of our current work is to identify a molecular signature of ADP-ribosylation and PARP expression that may predict clinical outcome in ovarian cancer.

Methods: Tissues specimens were obtained from primary or metastatic sites of 23 patients with stage II-IV serous ovarian cancer at the time of primary cytoreductive surgery. Protein extracts from each tissue specimen were prepared and analyzed with Western blotting for PARPs 1 and 3, as well as for mono- and poly(ADP-ribose). Imaging software was used to determine band intensity and variations in expression patterns. Clinical data collected for each patient included demographics, preoperative laboratory values, stage, histology, presence of germline mutation, cytoreductive status, adjuvant and salvage treatments, and survival outcomes.

Results: We identified 4 subtypes of ovarian cancers based on band intensity of mono- and poly(ADP-ribosyl)ation and the expression of PARPs 1 and 3. Subtype 1 had the highest levels of mono-(ADP-ribose) (MAR) and poly-(ADP-ribose) (PAR) as well as high PARP-1 and -3 levels. Subtype 2 had high levels of PAR and MAR and increased PARP-1 but decreased PARP-3 levels. Subtype 3 had the lowest levels of PAR with decreased PARP-1 levels but higher levels of MAR and increased PARP-3 levels. Subtype 4 had the lowest levels of MAR and PARP-3 but increased PAR and decreased PARP-1 levels. Subtype 3 had the highest median progression-free survival (PFS) at 13 months, and subtype 4 had the worst median PFS at 6 months, which was independent of *BRCA* status.

Conclusions: We have demonstrated that our novel ADP-ribose detection reagents bind to proteins with different forms of ADP-ribosylation that differ across a panel of serous ovarian cancers. To further characterize these distinctions, we are performing RNA-seq to characterize the transcriptomes of the tumor specimens. In addition, we will be using tumor-matched cell lines to identify sensitivity to PARP-inhibitors based on the elucidated molecular subtypes.

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Targeting of free fatty acid receptor 1 in EOC: A novel strategy to restrict the adipocyte-EOC dependence

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Objectives: Adipocyte-derived free fatty acids (FFAs) promote epithelial ovarian cancer (EOC) by acting as a fuel source to support the energy requirement of the cancer cells. FFAs may also exert biological effects through signaling pathways. Recently, a family of FFA-activated G-protein–coupled receptors (FFAR/GPCRs) was identified. Our objective was to investigate the role of FFAR/GPCRs in EOC and assess their potential as therapeutic targets.

Methods: The mRNA (RT-PCR) expression of FFAR/GPCR family members (FFAR1/GPR40; FFAR2/GPR42, FFAR3/GPR41, FFAR4/GPR120 and GPR84) was examined in: (1) a syngeneic mouse model of EOC fed high-energy diet (60% fat) or regular diet (30% fat), (2) EOC cell lines exposed to FFAs and (3) specimens from 13 histologically normal ovaries and 28 high-grade ovarian serous carcinomas. The GPR 40 antagonist, GW1100, was used to inhibit FFAR1/GPR40 and cell survival was assayed using MTT in various cell lines.

Results: High-grade serous carcinoma specimens expressed significantly increased GPR40 compared with normal ovaries ($P = .0020$). Higher expression was observed to be stage specific and noted to be significant in advanced-stage disease (X^2 $P = .04$). ID8 ovarian tumors from mice fed with high fat diet showed higher GPR40 expression. Exposing EOC cells to FFAs increased GPR40 expression. Treatment of EOC cell lines with GW100 resulted in growth inhibition and was associated with an alteration in their energy metabolism

Conclusions: FFA-induced cancer cell growth may be partly mediated through FFAR1/GPR40. Targeting of FFAR1/GPR40 may be an attractive treatment strategy in EOC, and possibly offers a targeted treatment for a subset of EOC patients.

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Examining selection for resistant clones in high-grade serous ovarian cancer after neoadjuvant chemotherapy

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Objectives: We examine the mutational landscape of ovarian high-grade serous carcinoma (HGSC) from patients with platinum-sensitive and resistant disease before and after neoadjuvant chemotherapy (NACT). Our objective is to identify changes in clonality following NACT and to determine whether these changes reflect emergence of new

clones or enrichment of existing clones. We also aim to identify molecular mechanisms associated with intrinsic or acquired platinum resistance.

Methods: Patients with advanced HGSC with a documented response to platinum-based NACT who have donated a blood sample to the Princess Margaret Gynecologic Oncology BioBank and have banked tumor before and after NACT were identified. Whole exome sequencing was performed in normal and pre/post-treatment tumor samples to identify somatic nonsynonymous mutations.

Results: Three resistant and 2 sensitive cases (mean 4.2 and 20.2 months to recurrence, respectively) were selected for DNA extraction and exome sequencing. Preliminary analysis of a single tumor specimen from each time point revealed that an average of 35% (range 1%–63%) of somatic, exonic, nonsynonymous mutations were shared between pre- and post-treatment samples from the same patient, suggesting a significant impact of NACT irrespective of time to recurrence. Mutations in *CSPG4* and *TUBA3D* were detected in pretreatment samples from 2 of 3 resistant cases, while both sensitive cases contained mutations in *CYP2D6* and *DNAH5*. Post-treatment samples from 2 of 3 resistant cases contained mutations in *ABP1, GPR98, MTMR11, OR52N5, and TMEM14B*; ultra-deep targeted sequencing will determine if they are present at a low allelic fraction before NACT and enriched by treatment.

Conclusions: This is the first systematic examination of the impact of NACT on the mutational landscapes of platinum-sensitive and resistant HGSC. Preliminary exome analysis from 5 retrospective cases reveals a significant impact of NACT on somatic mutation status and has identified candidate markers for prediction of response. Further experiments will assess spatial heterogeneity and allelic fraction of candidate mutations. These data will provide insights into the molecular mechanisms of platinum-resistance, and could lead to new treatments for platinum-resistant HGSC.

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Does the initial management of high-grade serous ovarian cancer predict recurrence?
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Objectives: To determine if the primary mode of treatment influences the number and site of recurrence in patients with advanced high-grade serous ovarian cancer.

Methods: We identified women with FIGO 3C/IV recurrent high-grade serous ovarian cancer treated between 2007 and 2013 who had undergone high-resolution CT imaging before the initiation of treatment and at diagnosis of first recurrence. Patients were grouped based on initial treatment (primary cytoreduction surgery vs neoadjuvant chemotherapy plus interval cytoreduction surgery) and degree of cytoreduction (microscopic, optimal, suboptimal) based on synoptic OR notes. Blinded radiologists read the CT scans, recording the number and site of initial and recurrent disease based on an established mapping system. Statistical significance (P =.05) was reported using the Fisher exact and nonparametric Wilcoxon rank-sum tests.

Results: A total of 178 patients were identified, of whom 65 met inclusion criteria. Thirty-eight (58%) were treated with PDS and 27 (42%) with NACT. In the PDS group, cytoreduction rates were as follows: 20 (52%) experienced microscopic, 9 (24%) optimal, and 9 (24%) suboptimal cytoreduction. In the NACT group, the cytoreduction rates were 15 (55%), 8 (30%), and 4 (15%), respectively. When all patients independent of cytoreductive status or when patients with optimal or suboptimal cytoreduction were analyzed, no significant difference was seen in the number of sites of disease at recurrence or overlap percentage – defined as number of original sites with recurrence over the number of sites at diagnosis. However, when patients with microscopic cytoreduction were analyzed, there were significantly fewer sites of disease at recurrence (4.9 vs 8.0, $P = .021$) in the PDS group with no difference in number of initial sites of disease. A significant difference was also found in the percentage overlap, with 20.3% of original sites recurring in the PDS group versus 39.4% in the NACT group ($P = .0394$).

Conclusions: Primary cytoreductive surgery with microscopic resection for advanced high-grade serous ovarian cancer results in fewer sites of recurrence and less recurrence at initial anatomic sites of disease compared with treatment with neoadjuvant chemotherapy. These results suggest that the effect of surgical clearance may be more complex than simply tumor load reduction in this predominantly peritoneal-based cancer.

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Optimal according to whom? Interobserver variability in surgical cytoreduction for advanced ovarian carcinoma

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Objectives: Although presumed to be an objective variable, the extent of cytoreduction (no residual disease [NRD], optimal, suboptimal) is subject to the assessment and interpretation of the surgeon. This prospective quality improvement study assessed the interobserver agreement among surgeons regarding extent of surgical cytoreduction for advanced ovarian carcinoma (AOC).

Methods: After obtaining institutional review board approval, all patients undergoing cytoreductive surgery for AOC from June 2014 to May 2015 were included. Following surgery, the primary surgeon completed a survey assessing the extent of cytoreduction. A blinded second surgeon then assessed the extent of cytoreduction. Interobserver agreement was assessed with unweighted Cohen κ statistic.

Results: One hundred and eleven patients underwent laparotomy for AOC. Seventy-seven patients (69%) underwent a secondary surgical assessment and were included in the final analysis. The average operative time was 149 minutes (range 62–330) and average blood loss was 582 mL (range 50–2,000). Thirty-four patients (44%) received neoadjuvant chemotherapy. Based on the primary surgeon assessment, 34 patients were cytoreduced to NRD, 35 were optimal, and 8 were suboptimal. Of the NRD patients, 29 (85%) were considered NRD by the second surgeon and 5 (15%) were optimal. Of the optimal patients, 22 (63%) were considered optimal by the second surgeon, 8 (23%) were NRD, and 5 (14%) were suboptimal. Of the 8 suboptimal patients, 7 (88%) were considered suboptimal by the second surgeon and 1 (12%) was optimal. This yielded a κ of 0.59 (95% CI 0.43–0.75).

Conclusions: Although often considered an objective variable, we found only moderate agreement among surgeons regarding the extent of surgical cytoreduction. This variability calls into question the current approach to treatment, prognosis, and clinical trial enrollment based on cytoreductive status.

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Morbidity and mortality risk assessment in gynecologic oncology surgery using the ACS NSQIP database

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Objectives: Gynecologic oncology patients represent a unique population with specific surgical risks. The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database provides the opportunity to accurately analyze a large cohort of patients over a long period. Our goal was to develop a postoperative risk assessment calculator specific for gynecologic malignancies, thus providing a standardized, objective means of preoperatively identifying high-risk patients to maximize patient safety.

Methods: The ACS NSQIP database was queried for gynecologic oncology patients from 2005 to 2013. Using similar methodology as previously published, NSQIP predictive models, multivariate logistic regression was performed to generate predictive models specific for 30-day postoperative mortality and major morbidity, defined as the occurrence of any of the following postoperative events: surgical site infection, wound dehiscence, pneumonia, reintubation, failure to wean from ventilator, pulmonary embolism, deep venous thrombosis, septic shock, re-operation.

Results: A total of 12,832 patients with a primary gynecologic malignancy were identified: 7,847 uterine, 1,051 cervical, 3,366 adnexal, and 567 perineal cancers. In this cohort, 125 patients died within 30 days of their surgery, and 784 major morbidity events were recorded. For 30-day mortality, the mean calculated predictive probability was 0.128 (standard deviation [SD] 0.219) compared with 0.009 (SD 0.027) in patients who were alive 30 days postoperatively ($P < .0001$). Mean calculated predictive probability of major morbidity was 0.097 (SD 0.095) compared with 0.059 (SD 0.043) in patients who did not experience major morbidity 30 days postoperatively ($P < .0001$).

Conclusions: Using NSQIP data, this predictive model will help to determine patients at risk for 30-day mortality and major morbidity. Clinically this may be useful in identifying patients who may benefit from neoadjuvant procedures (chemotherapy, radiation therapy, etc.). Further clinical validation of this model is required.

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Prognostic impact of the time interval from surgery to chemotherapy in patients with advanced ovarian cancer
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Objectives: Surgery followed by platinum-taxane chemotherapy is the current standard approach to treat advanced ovarian cancer. A major unproven concern is whether a long postoperative delay reduces the benefits of an extensive procedure and leads to disease progression. Our objectives were to evaluate the correlation between clinical and pathologic variables and to evaluate the effect of the "time to chemotherapy" (TTC) interval on survival.

Methods: We retrospectively studied data from 276 patients with FIGO stage III or IV ovarian cancer who were consecutively treated between January 2006 and 2013. TTC was analyzed and correlated with outcome.

Results: Median age at diagnosis was 54 years (range 20–80 years), and 258 patients received postoperative platinum-based chemotherapy. The 25%, 50%, and 75% quartiles of intervals from surgery to start of chemotherapy were 18, 22, and 28 days, respectively. TTC (≤28 vs >28 days; HR 1.578, 95% CI 1.057–2.355), $P = .026$), complete debulking with no gross residual disease (HR=0.419, 95% CI=0.274–0.640, $P < .05$), and preoperative albumin level (HR 0.549, 95% CI 0.382–0.791, $P = .001$) were significant prognostic factors for progression-free survival in multivariate analysis. Although delayed TTC (>28 days) did not possess prognostic significance in patients without postoperative residual disease (n = 94), it significantly correlated with progression-free survival in patients with postoperative residual disease (n = 164, HR 1.893, 95% CI 1.209–2.962, $P = .005$).

Conclusions: Our findings suggest that delayed initiation of chemotherapy might compromise progression-free survival in patients with advanced serous ovarian cancer, especially in cases of gross residual disease. A prospective study randomizing patients to different time intervals could clarify the definitive relevance of the time between surgery and chemotherapy.

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Epidemiologic profile of preoperative differences between patients undergoing benign versus oncologic gynecologic surgeries: Illustrating the need for risk adjustment in different gynecologic surgical populations
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Objectives: To demonstrate differences in preoperative health status of patients undergoing benign gynecologic surgery compared with gynecologic cancer surgery (and among gynecologic cancer types), to document components important for baseline risk adjustment when measuring perioperative outcomes and surgical complications.

Methods: All cases of benign and malignant gynecologic surgeries in the National Surgery Quality Improvement Program (NSQIP) database between 2006 and 2012 were identified. Gynecologic cancers were grouped by site: uterus (UtCa), ovary (OvCa), cervix (CvCa), and "other" (OtherCa) including labia, vulva, vagina, pelvis, peritoneum, and retroperitoneum. Preoperative comorbidities were captured. Descriptive analyses were performed using nonparametric tests.

Results: A total of 36,736 patients underwent gynecologic surgery: 64.4% benign and 35.6% oncologic. Median age for women with benign surgery was significantly lower (46 years, interquartile range [IQR] 41–51) than those with oncologic surgery (60 years, IQR 50–68). Racial differences were significant: nearly one-quarter of benign surgical patients were African American, compared with only 7%, 6%, 9%, and 6% among those with UtCa, OvCa, CvCa and OtherCa, respectively ($P < .001$). Less than one-third (31%) of benign surgical patients had any comorbidity. Conversely, more than 50% of cancer patients had 1 or more comorbidities and 20% had 2 or more ($P <.001$). The prevalence of morbid obesity, diabetes, hypertension, pulmonary disease, cardiovascular and peripheral vascular

disease all individually differed between the benign and oncologic groups ($P < .001$). Most notably, comparing UtCa to benign, 56% versus 26% had hypertension, 18% versus 5% had diabetes, and 25% versus 10% had morbid obesity. Cancer patients had more than double the rate of pulmonary (9.1 % vs 4.0%) and cardiac disease (2.3% vs 0.6%) compared with benign surgical patients.

Conclusions: Consistent with our clinical impression that significant differences exist between patients undergoing benign versus oncologic gynecologic surgery, we demonstrated that gynecologic cancer patients are significantly older and heavier, with different racial profile, and have far more comorbidities than patients undergoing benign surgery. Perioperative outcomes and surgical complication rates for women undergoing gynecologic surgery must account for these baseline differences.

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Diverting ileostomy during primary cytoreductive surgery for ovarian cancer: Associated factors and postoperative outcomes
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Objectives: To investigate the associated factors and postoperative outcomes of diverting loop ileostomy (DI) at the time of primary cytoreductive surgery (CRS) for ovarian cancer.

Methods: All patients with stage II–IV ovarian, tubal, or peritoneal carcinoma who underwent colon resection during primary CRS at our institution from January 2005 to December 2013 were identified. Demographics and clinical data were collected. Statistical analysis was performed using SPSS v22 software.

Results: Among 331 patients, 231 (70%) had stage III disease and 292 (88.2%) had high-grade serous histology. Median age was 61 years (range 26–91 years) and median serum albumin was 4.1 g/dL (2.5–4.9 g/dL). Optimal debulking was achieved in 91% of cases. One bowel resection was performed in 72.8% of patients and more than 1 bowel resection was performed in 27.2%. Eighty-five percent underwent rectosigmoid (RS) resection; 35.6% underwent other colon resection. Median length of stay (LOS) was 11 days (3–69 days). Eighty patients (24.2%) had 1 or more grade 3–4 postoperative complication. Sixty-day readmission rate was 23%. Median time from surgery to adjuvant chemotherapy was 40 days. Forty-four (13.3%) patients underwent DI. There were no significant differences in age, body mass index, comorbidity index, smoking status, serum albumin, attending surgeon, or rate of intraoperative complications between patients who underwent DI and those who did not (non-DI). Diabetes (13.6% vs 4.2%; OR 3.41, 95% CI 1.12–10.39; P =.031), operative time (8.1 vs 6.2 hours; OR 1.23, 95% CI 1.04–1.44; P =.013), and length of RS resection (20.5 vs 15.5 cm; OR 1.04, 95% CI 1.01–1.08; P =.005) were significant predictors of DI on multivariate analysis. There was no significant difference in 30-day complications, hospital LOS, readmission rate, or interval to adjuvant chemotherapy between patients with DI and those without (non-DI). Median follow-up time was 52.6 months. Between the DI and non-DI groups, there was no difference in median progression-free (17.9 vs 18.6 mo, P =.881) or overall survival (48.7 vs 63.8 mo, P =.249).

Conclusions: In patients undergoing primary cytoreductive surgery, those with diabetes, longer operative time, and greater length of rectosigmoid resection more commonly underwent DI. DI does not appear to compromise postoperative outcomes or long-term survival.

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Oncologic outcome of robotic and open cytoreductive surgery in combination with hyperthermic intraperitoneal chemotherapy (HIPEC) in the management of recurrent ovarian carcinoma
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Objectives: We aimed to evaluate the oncologic outcomes of hyperthermic intraperitoneal chemotherapy (HIPEC) after robotic or open cytoreduction for recurrent ovarian cancer.

Methods: In a single-institution pilot study, patients underwent optimal cytoreductive surgery in combination with HIPEC followed by consolidation chemotherapy from September 2011 to September 2015. Optimal cytoreduction was defined as no lesion greater than 0.5 cm. Adverse and oncologic outcomes were measured. Standard statistical analysis was used.

Results: Thirty patients with a median age of 57 years (range, 20–86 years) were identified. The median number of chemotherapy regimens before HIPEC was 3 (range, 1–12 prior regimens). A median of 2 platinum-containing regimens was administered before HIPEC (range, 0–5 regimens). Median CA-125 at time of HIPEC was 218 U/mL (range, 4–8,543 U/mL). Nineteen patients (63%) underwent a robotic optimal cytoreductive surgery. The following cytotoxic agents were used during HIPEC: carboplatin, 16 (53%); mitomycin, 7 (23%); cisplatin and paclitaxel, 4 (13%); paclitaxel, 2 (7%); cisplatin, 1 (3%). All patients received consolidation chemotherapy after cytoreduction and HIPEC. At a median follow-up of 11.8 months (range, 1–32 months), the median progression-free survival time was 11.3 months. The 5 year-overall survival rate was 73%.

Conclusions: In select patients, robotic and open cytoreductive surgery in combination with HIPEC resulted in encouraging survival outcomes. The optimal candidate and chemotherapy regimen have yet to be defined.

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The therapeutic and prognostic significance of systematic lymphadenectomy in patients with advanced ovarian cancer at the time of interval debulking surgery after neoadjuvant chemotherapy

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Objectives: The therapeutic role of systematic lymphadenectomy remains unclear in advanced ovarian cancer (AOC), especially in interval debulking surgery (IDS) after neoadjuvant chemotherapy (NAC). We analyzed the therapeutic and prognostic role of systematic lymphadenectomy (LND) in AOC patients.

Methods: From January 2009 to April 2015, the records of patients with epithelial ovarian cancer admitted to Severance hospital, Seoul (n = 347) were retrospectively analyzed. Among 217 consecutive patients with FIGO stage IIIB+ ovarian cancer, 74 patients underwent NAC followed by IDS. Patients were classified into 2 groups— patients who underwent systematic pelvic and para-aortic LND (lymph node count retrieved >10) and those who did not. Progression-free survival (PFS) and overall survival (OSA) were analyzed using the Kaplan-Meier method and log-rank test.

Results: Systemic LND was performed in 61 (82.4%) of 74 patients. After an overall median follow-up of 20 months (range, 3∼75), patients who underwent systematic LND had improved PFS (12 vs 8 months; *P* = .01) and OS (14 vs 11 months; *P* = .15). Twenty-four and 7 recurrences (39.3 vs 53.8 %; *P* = NS) and 6 and 4 deaths due to disease (9.8 vs 30.8%; *P* = NS) were observed in the LND and no-LND group, respectively. The performance of LND was a statistically significant predictor of improved PFS (HR 0.56, 95% CI 0.26–1.18) and OS (HR 0.16, 95% CI 0.04–0.67]) in univariate analysis but not in the multivariate analysis. The status of residual disease and the number of chemotherapy cycles were independent prognostic factors affecting survival. Values for median operating time, percentage of patients requiring blood transfusions, and percentage of patients requiring intensive care unit admission were higher for the no-LND group than the LND group (380 vs 237 min, *P* = .614; 69.2% vs 49.2%, *P* = .313; and 53.8 vs 26.2 %, *P* = .105, respectively).

Conclusions: Systematic LND may have a therapeutic value in AOC patients treated with NAC and IDS. Risk and benefit assessment would be necessitated.

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Ultrasound-guided laparoscopic ovarian resection: A novel surgical approach in the treatment of recurrent borderline ovarian tumours

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Objectives: To present a novel surgical method in the treatment of recurrent serous borderline ovarian tumors (rsBOTs) involving the use of intraoperative transvaginal ultrasound (TVUS).

Methods: This observational case series was performed in 2015 in a regional cancer center. Patients presenting with a primary rsBOT in which intraoperative identification was likely to be difficult and who desired fertility preservation were offered a TVUS-guided laparoscopic ovarian cystectomy. The suitability of this novel procedure was based on patient anatomy, previous surgery for borderline ovarian tumors, and ultrasound characteristics.

Results: Main outcome measures were histologic diagnosis of rsBOT, recurrence, fertility, and survival. Three patients (ages 28-40 years) presented with a suspected rsBOT measuring <2 cm on TVUS. Two had previous contralateral unilateral salpingo-oophorectomy (USO) and all highlighted future fertility as being of primary concern. They were thus inclined toward a conservative surgical option, and so underwent a TVUS-guided laparoscopic wedge resection of the suspected recurrence. Histologic examination confirmed a diagnosis of borderline ovarian tumors in all. No operative complications were noted. No significant reduction in ovarian size was seen on postoperative TVUS. To date (follow-up range, 6-12 mo), none have presented with recurrence or reported menopausal symptoms. Only 1 patient has attempted to conceive during follow-up.

Conclusions: rsBOTs affect women in their reproductive years. They present as small unilocular cysts (usually <2 cm) filled with a solid papillary projection. This presentation makes conventional surgical treatment challenging because of the difficulty in identifying the disease site, risk of intraoperative rupture, and previous USO. Furthermore, management involves a radical step, ie, adnexectomy and therefore reduction in fertility potential. The novel surgical technique described herein opens a new treatment door, resulting in complete tumor clearance and preservation of healthy ovarian tissue. Importantly, it can be readily implemented with widely available equipment at no additional cost. We encourage TVUS-guided laparoscopic management of all ovarian cysts that cannot be macroscopically visualized during laparoscopy in patients opting for a more cautious, fertility-sparing approach.

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Implementation of an enhanced recovery program at a tertiary cancer center
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Objectives: To implement a multidisciplinary enhanced recovery program (ERP) for all patients undergoing exploratory laparotomy for gynecologic indications at a tertiary cancer center.

Methods: All consecutive patients managed under an ERP undergoing exploratory laparotomy between November 3, 2014, and May 31, 2015 were compared with historical controls (May to October 2014). Interventions included, but were not limited to, allowing oral intake of fluids up to 2 hours before induction of anesthesia; pre-, intra-, and postoperative euvolemia as well as opioid-sparing analgesia (total intravenous anesthesia); and ambulation and regular diet on the day of surgery. Wilcoxon rank-sum and Fisher exact tests were used for comparisons.

Results: A total of 153 ERP women in the case group were compared with 74 women in the control group. ERP resulted in a 77% reduction in opioid intake (median morphine equivalents) during the first 3 days after surgery with no significant difference in mean pain scores between the pre- and post-ERP cohorts. Thus far, ERP has resulted in a 1-day reduction in hospital stay (median length of stay before implementation: 4 days [2–29] vs after implementation: 3 days [1–57], $P < .0001$) with stable readmission rates (pre-ERP: 13.2% vs post-ERP: 14.7%, $P = .8374$). No differences were observed in rates of pre- and post-ERP complications (GI: pre-ERP 29.7% vs post-ERP 19.05%, $P = .0706$; GU: pre-ERP 9.5% vs post-ERP 16.1%, $P = .1810$; hematologic: pre-ERP 16.2% vs post-ERP 10.7%, $P = 0.2193$).

Conclusions: Implementation of an ERP at a tertiary cancer center is feasible and resulted in substantial decrease in opioid use with no change in pain scores. Early evaluation has revealed a significant reduced length of stay with stable readmission and morbidity rates. Further study is warranted to determine impact on progression-free survival.

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123 - Featured Poster Session
Decreased intraoperative opioid consumption following institution of enhanced recovery program in open gynecologic surgery
J.D. Lasala, A.M. Nick, P.T. Ramirez, L.A. Meyer, K.E. Cain, M.F. Munsell, M.D. Iniesta, I.C. Ifeanyi, J. Singh, T. Moon Calderon, P. Kwater, J. Tsai, S. Vachhani, J.P. Cata and G. Mena. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To determine differences in morphine equivalents in the intraoperative period with an enhanced recovery program (ERP) after gynecologic surgery.

Methods: We examined 153 consecutive patients who underwent laparotomy after the implementation of our ERP program and compared these with 74 historical controls. A select group of anesthesiologists participated in the ERP and executed an anesthetic with multimodal pain management strategies and opioid sparing. If not contraindicated,

ERP patients received preoperative analgesia consisting of pregabalin, celecoxib, and tramadol in the holding area. Intraoperative narcotic sparing and multimodal pain management strategies with local anesthetic wound infiltration at the end of the case was performed on all 153 patients. Intraoperative regimens included all or some of the following regimens at the discretion of the anesthesiologist; IV propofol, IV acetaminophen, IV ketamine, IV dexmedetomidine, and IV lidocaine. The primary anesthetic management goal was a reduction in opioid administration. Intraoperative pain regimens for the historical controls varied. We used descriptive statistics to summarize morphine equivalent dose (MED) for pre- and postimplementation of ERP, and we used the Wilcoxon rank sum test to compare median MED between the pre-ERP and ERP groups.

Results: A total of 153 consecutive cases after implementation of our ERP were compared with 74 historical controls. Pre-ERP anesthesia techniques varied but did not include multimodal pain management or opioid-sparing strategies. Adoption of an intraoperative ERP resulted in a 61% reduction in morphine equivalents (median pre-ERP 102.5 mg [range, 0–544.5] vs median ERP 40 mg [range, 0–162.5], $P < .0001$) with no significant difference in mean pain scores between the pre- and post-ERP cohorts. Of these 153 patients, 18.3% (28/153) received no opioid medications.

Conclusions: Implementation of an ERP in open gynecologic oncologic surgeries resulted in a 61% reduction in intraoperative morphine equivalents, a substantial decrease, with no change in pain scores.

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124 - Featured Poster Session

Uterine leiomyosarcomas exhibit distinct drug resistance molecular profiles compared to extrauterine leiomyosarcomas: A comprehensive analysis of 1,023 leiomyosarcomas

S. Chatterjee[a], J. Xiu[b], S.K. Reddy[b], N.L. Jones[a], A. Buckley de Meritens[a], A.I. Tergas[c], W.M. Burke[c], J.D. Wright[c] and J.Y. Hou[c]. *[a]NYPH, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA, [b]Caris Life Sciences, Irving, TX, USA, [c]Columbia University College of Physicians and Surgeons, New York, NY, USA*

Objectives: Controversy exists as to whether uterine leiomyosarcomas (ULMS) and extrauterine leiomyosarcomas (ELMS) represent distinct pathological and molecular entities. We aim to evaluate molecular, genomic, and protein expression patterns in a large cohort of leiomyosarcomas (LMS) in hopes of identifying novel treatment strategies.

Methods: A total of 1,023 cases of LMS were submitted for molecular analysis from 2009 to 2015, including 635 ULMS and 388 ELMS. Testing included a combination of sequencing (Sanger or next-generation sequencing [NGS]), protein expression (immunohistochemistry), and gene amplification (fluorescence in situ hybridization [ISH]/chromogenic ISH).

Results: The mean age in the LMS cohort was 56.8 years, with 34% of ELMS occuring in men. Figure 1 summarizes molecular and sequencing alterations in ULMS and ELMS. Of the LMS samples evaluated using NGS, *TP53* was most commonly altered (41%), followed by *BRCA2* (6.3%) and *RB1* (4.5%). Evaluating markers of drug resistance, RRM1 expression, associated with gemcitabine resistance, was seen in 36% of ULMS and higher than in EMLS ($P <$ .0001). On subanalysis, RRM1-expressing LMS had higher expression of TOP2A ($P < .0001$) and TOPO1 ($P = .0039$), suggesting a potential role for anthracyclines and topotecan in these patients. Significantly more ULMS expressed TUBB3, a marker correlated with taxane resistance (33% ULMS vs 17% ELMS, $P < .0001$). Lower ERCC1 expression was seen in ULMS ($P =.0352$). Hormone receptor expression was frequent in LMS overall (45.2% ER, 34.2% PR and 24% AR), but much more common in ULMS than ELMS: AR ($P = .0014$), ER ($P < .0001$), PR ($P < .0001$). In ER/PR negative LMS, epidermal growth factor receptor overexpression, via immunohistochemistry and ISH, were significantly elevated ($P = .04$, $P = .001$, respectively). Of interest, 28.6% of LMS expressed PDL1 on tumor cells, and 48.6% PD1 protein on tumor-infiltrating lymphocytes. Table 1 summarizes statistically significant differences in biomarker expression profiles between ULMS and ELMS.

Conclusions: Our findings highlight the molecular heterogeneity in LMS, and distinct differences between ULMS and ELMS. Uterine LMS display significantly more biomarkers implicating drug resistance than extrauterine LMS. Of interest, one-third of ULMS expressed proteins associated with gemcitabine and docetaxel resistance. Alternate strategies such as anthracyclines, hormonal therapy, PD-1 inhibitors, and tyrosine kinase inhibitors may be considered as adjuvant therapy.

Table 1
Molecular Profile Distinctions between Leiomyosarcoma of Uterine and Extra-uterine Origin.

	Uterine LMS (n=635)	Extra-Uterine LMS (n=388)	*P*-values
IHC-ER	60.1%	18.2%	<0.0001
IHC-BCRP	43.0%	18.5%	0.0032
IHC-PR	41.8%	19.8%	<0.0001
IHC-ERCC1	40.0%	50.0%	0.0352
IHC-RRM1	36.2%	23.3%	<0.0001
IHC-TUBB3	33.3%	16.9%	<0.0001
IHC-TOPO1	32.5%	39.7%	0.0412
IHC-AR	29.1%	19.6%	0.0014

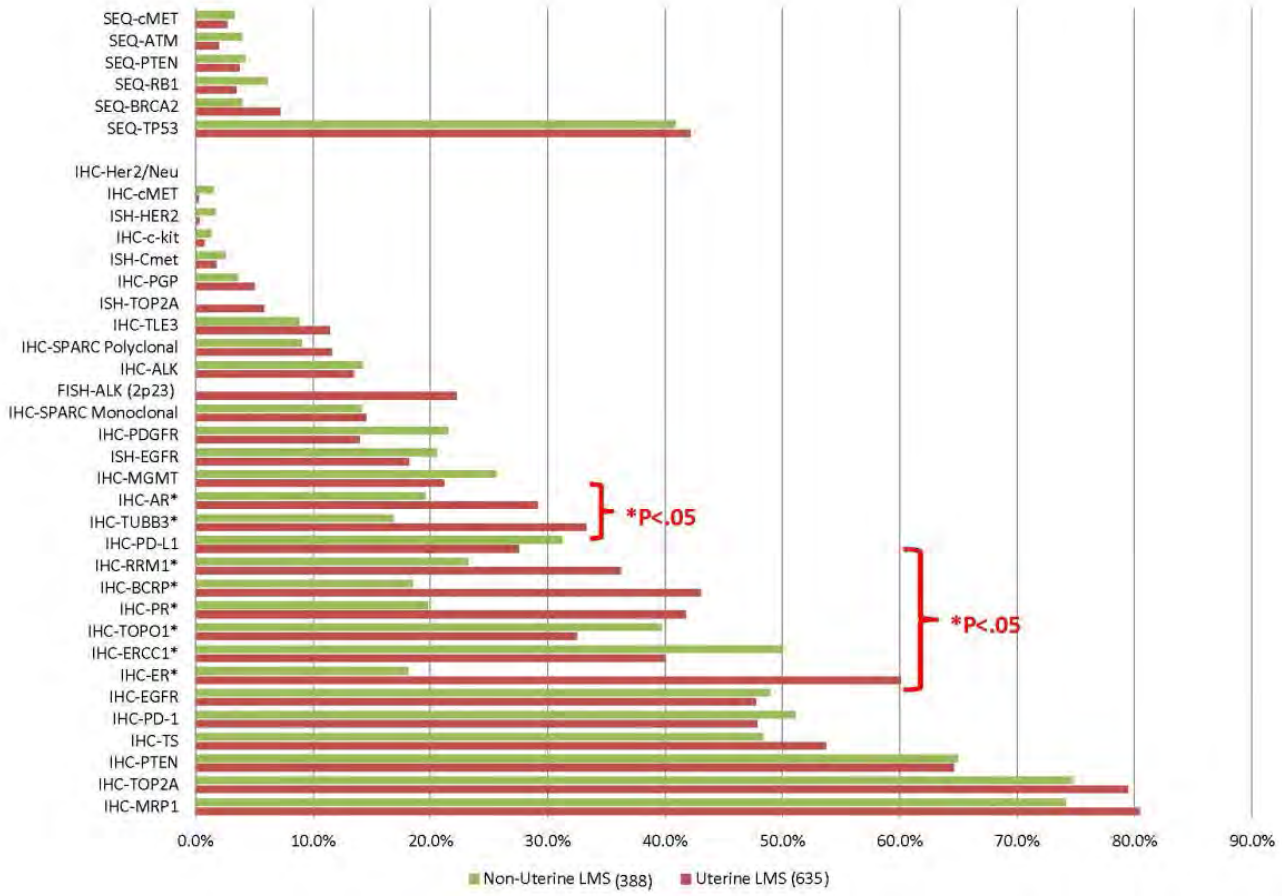

Fig. 1
Biomarkers and Sequence Alteration Frequencies.

125 - Featured Poster Session

Anaplastic lymphoma kinase (ALK) aberrations in gynecologic cancers: New treatment options?

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Objectives: Aberrations and overexpression of ALK are an important oncogenic factor in numerous cancers. Non–small cell lung cancer (NSCLC) is a well-known example benefiting from targeting ALK with promising inhibitor therapy, such as crizotinib and ceritinib. Several case reports have demonstrated diffuse ALK aberrations in gynecologic cancers associated with aggressive behaviors, such as metastatic uterine inflammatory myofibroblastic tumor and early-stage cervical cancer with unexpected pelvic lymph node metastases. A linear correlation of ALK expression from normal ovarian tissue to poorly differentiated epithelial ovarian carcinoma has also been recorded. These observations suggest possibly using ALK inhibitors as novel therapeutics in gynecologic cancers. Therefore, the incidence of ALK in gynecologic cancers should be evaluated.

Methods: We queried a prospective deidentified genomic database for ALK driver mutations across disease sites from a large tertiary cancer center of highly pretreated patients.

Results: The *ALK* gene was found in 1 of 168 ovarian cancers, 0 of 9 cervical, and 0 of 23 other uterine neoplasms, but in 5 of 9 uterine leiomyosarcoma (LMS) cases ($P < .05$ for all comparisons). All 5 LMSs were treated with ALK inhibitors. Four had clinical benefit and 1 had a near complete response. In comparison, using the same cohort, we found ALK in 1 of 356 colon adenocarcinoma cases, 1 of 1 penile cancer, 4.45% of lung adenocarcinoma, and 3.98% of all NSCLCs. Because of the unexpectedly high number of ALK abnormalities in our LMS cases, we conducted a broader analysis of all cases of LMS submitted to the same laboratory for genomic analysis from a larger sample cohort submitted from multiple providers across the country. Of 139 LMS cases, 5 ALK rearrangements were identified, for a frequency of 3.6%.

Conclusions: Our study demonstrated a higher than expected incidence of the *ALK* gene in aggressive uterine LMS cancers from a highly selected, heavily pretreated patient population. Using this genomic result, patients realized a clinical benefit. Uterine LMS, ALK findings may be comparable to that reported in lung cancers. Because of the relatively limited amount of cases, a multicenter study including a larger group of patients is needed to confirm the role of ALK inhibitors in this rare tumor.

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126 - Featured Poster Session

Racial disparities in incidence and survival of gynecologic sarcoma: An analysis of 19,797 women within the Surveillance, Epidemiology, and End Results database

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Objectives: Race has previously been shown to affect survival in soft tissue sarcoma and uterine sarcoma, but little is known about racial disparities in the survival of other gynecologic sarcomas. We explored the impact of race on gynecologic sarcoma incidence and survival in the United States.

Methods: Age-based incidence rates of gynecologic sarcoma were calculated for 2000 to 2012 from within the National Cancer Institute's Surveillance, Epidemiology, and End Results database catchment area. Primary and invasive cases diagnosed between 1973 and 2012 were then culled from the database. Demographic and clinicopathologic factors, including neighborhood socioeconomic status markers, were compared between white, black, and Asian/Pacific Islander (API) patients using parametric and nonparametric methods. Survival outcomes were compared with Kaplan-Meier methods and multivariable Cox proportional hazards modeling, with multiple sensitivity analyses.

Results: Compared with white women, black women demonstrated a 43% higher incidence rate of gynecologic sarcoma whereas API women demonstrated a 27% lower rate. In our final cohort, 15,061 women self-identified as white, 3,426 identified as black, and 1,310 as API. API women tended to be younger at diagnosis and had higher rates of grade I–II and lymph node–negative disease. Black women had greater uterine disease, higher lymph node positivity, and were less often treated surgically. They were also more likely to come from metropolitan areas with poor socioeconomic indicators. Black women had significantly worse 5-year cancer-specific survival compared with white and API women (46.0% vs 55.3% and 55.9%, respectively). After adjusting for clinicopathologic factors, black women still faced a 34% higher risk of cancer-specific death (95% CI 1.27–1.42) whereas API women had a 13% higher risk (95% CI 1.02–1.24). This disparity did not significantly change after adjusting for socioeconomic status, and persisted on multiple sensitivity analyses, including the exclusion of uterine cases.

Conclusions: Black and API patients diagnosed with gynecologic sarcoma have worse prognoses than white patients, with results suggesting minimal contribution of clinicopathologic and neighborhood socioeconomic factors. More research is needed on possible biologic etiologies of this disparity.

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127 - Featured Poster Session
The way of tumor removal with oncologic safety in uterine sarcoma: Macro- versus micro-seeding
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Objectives: Most recent studies on risk of tumor recurrence in uterine sarcoma have focused on power morcellation that is likely to cause tumor macro-seeding in abdominal cavity. The aim of this study is to evaluate the potential effect of various ways of tumor removal on tumor recurrence in patients with uterine sarcoma.

Methods: A total of 91 patients who underwent hysterectomy and had pathologic diagnosis of uterine carcinosarcoma or leiomyosarcoma were retrospectively reviewed on the way of tumor removal at the first surgery. Prognostic impact was compared among 3 ways of tumor removal in terms of the possibility of tumor seeding: (1) no seeding: open hysterectomy (n = 63) and laparoscopic hysterectomy with intact tumor (n = 18); (2) micro-seeding: open myomectomy (n = 3), laparoscopic myomectomy with vaginal removal of intact tumor (n = 1) and laparoscopic hysterectomy with vaginal tumor-cutting (n = 4); (3) macro-seeding: laparoscopic myomectomy with power morcellation (n = 2).

Results: Median follow up was 21 months (range 1–188 months). Seventy-one (78%) had stage I disease. Only 45.9% of the patients with leiomyosarcoma had a preoperative diagnosis of malignancy, whereas 90% of the patients with carcinosarcoma did ($P < .001$). All power morcellation happened in stage I leiomyosarcoma. Progression-free survival (PFS) of micro-seeding group was not different from that of no seeding group (5-year PFS 58.3% vs 52.5%; $P = .378$). However, the macro-seeding group had a significantly poor PFS compared with the no seeding group ($P = .019$). Without power morcellation, neither myomectomy followed by hysterectomy versus primary hysterectomy nor vaginal tumor-cutting had an association with poor PFS.

Conclusions: Power morcellation possibly causing tumor macro-seeding appears to be associated with early recurrence of uterine carcinosarcoma or leiomyosarcoma. However, vaginal removal with or without tumor-cutting from outside potentially causes tumor micro-seeding, and is not likely to worsen PFS.

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128 - Featured Poster Session
Safety of ovarian preservation in women with stage I epithelial ovarian cancer
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Objectives: Although ovarian preservation has been reported in small series of women with stage I ovarian cancer, the safety of the procedure remains uncertain. We examined utilization and safety of ovarian preservation in women with stage I epithelial ovarian cancer.

Methods: The National Cancer Data Base (NCDB) was used to identify women with stage I epithelial ovarian cancer, who were younger than 45 years and had undergone primary surgery from 1998 to 2012. Multivariable generalized estimating equations to adjust for facility-level clustering were used to determine predictors of unilateral salpingo-oophorectomy (USO) compared with bilateral salpingo-oophorectomy (BSO). Marginal Cox proportional hazards models were developed to examine the safety of ovarian conservation while controlling for other clinical and demographic variables.

Results: A total of 2,461 patients including 1,566 (63.6%) stage IA tumors, 129 (5.2%) stage IB tumors, and 766 (31.1%) stage IC tumors were identified. USO was performed in 48.5% of patients compared with BSO in 51.5% of patients. Use of USO increased over time from 44.2% in 1998 to 53.6% in 2012 ($P = .02$). USO was performed in 52.9% of women with stage IA cancers, 19.4% of those with IB cancers, and 44.4% of those with IC cancers ($P < .0001$). In a multivariable model, younger women and those with stage IA tumors were more likely to have a USO ($P < .05$ for both). There was no association between race, insurance status, grade, or histology and ovarian conservation.

In a multivariable model of survival, after adjusting for staging and adjuvant chemotherapy administration, ovarian conservation was not associated with survival (HR 1.16, 95% CI 0.86–1.57).

Conclusions: Ovarian preservation, after accounting for staging and adjuvant chemotherapy, is not associated with increased mortality among women with stage I ovarian cancer; therefore USO remains a surgical option in selected young women with early-stage ovarian cancer.

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129 - Featured Poster Session
No survival benefit with adjuvant chemotherapy in nonserous stage IB grade 2 epithelial ovarian cancer
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Objectives: Data on the utility of adjuvant chemotherapy in patients with stage IB grade 2 epithelial ovarian cancer (EOC) are scant. Because serous histology is now reported as low- or high-grade, without an intermediate grade, this study explored the use of adjuvant chemotherapy in mucinous or endometrioid ovarian cancer. Current National Comprehensive Cancer Network guidelines state that chemotherapy is optional. We sought to evaluate the efficacy of chemotherapy and to identify factors that may predict survival in this population.

Methods: The National Cancer Data Base was queried for all stage IB grade 2 EOC patients from 1998 to 2012. Only patients with mucinous or endometrioid histology and nodal dissection were analyzed. X^2 test, logistic regression analysis, log-rank test and multivariable Cox proportional regression were conducted to determine factors associated with utilization of chemotherapy and survival.

Results: A total of 227,499 patients had EOC during this period. Of these patients, 541 had stage IB grade 2 disease, with 401 having a nodal dissection. There were 226 endometrioid histology and 42 mucinous cases, for a total of 268 patients who were included. Chemotherapy was given in 60% of cases, with the majority (97%) receiving multiagent chemotherapy. There were no factors associated with the utilization of chemotherapy including histology, tumor size, age, race, facility location, or type. No association with histology or tumor size was seen with survival. Age, Charlson-Deyo Comorbidity index, and urban/rural location of patients were associated with survival on univariate analysis, but only age and location remained significant on multivariable analysis. The 5-year overall survival rates were 90% and 78% for patients who did and did not receive chemotherapy, respectively (P = .12).

Conclusions: Stage IB grade 2 nonserous EOC is exceedingly rare. Even in a very large dataset, there were very few patients with this stage, grade, and histology. Because chemotherapy does not demonstrate a survival benefit in this subgroup, we recommend against adjuvant administration, given unnecessary cost and potential side effects.

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130 - Featured Poster Session
Patterns of care and predictors of survival for ovarian dysgerminoma
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Objectives: Although rare, dysgerminomas comprise two-thirds of malignant ovarian neoplasms in women younger than 20 years. Fertility-sparing treatments are often used. Although the prognosis is good, little is known about predictors of outcome and long-term mortality. We examined patterns of care and overall survival.

Methods: The National Cancer Database (NCDB) was used to identify women with ovarian dysgerminoma diagnosed from 1998 to 2012. We compared factors influencing decision to administer chemotherapy and examined predictors of survival.

Results: A total of 997 women were identified, most diagnosed with stage I dysgerminoma (Table 1, column 2). Age distribution was as follows: 14.6% were 10 to 19 years of age, 52.8% were 20 to 29 years of age, 20.9% were 30 to 39 years of age, and 11.1% were older than 40 years. In total, 44.7% of women underwent USO. Among women with stage I tumors, 79.3% underwent USO, which decreased with increasing substage (Table 1, column 4). Overall, 50.2% received chemotherapy. In stage I and II disease, chemotherapy was used more often with increasing substage (Table 1, column 3). In a logistic regression model, chemotherapy use was associated with histologic grade (OR 5.26, 95% CI 1.04–26.65 for moderate, and OR 6.30, 95% CI 1.57–25.19 for poor) and stage (stage II: OR 10.83, 95% CI 5.69–20.59; stage III: OR 19.15, 95% CI 11.63–31.53; stage IV: OR 16.24, 95% CI 5.96–44.29). Patients older than 40 years were

less likely to receive chemotherapy (OR 0.44, 95% CI 0.21–0.92 for 40–49 year olds; OR 0.36, 95% CI 0.14–0.93 for ≥50 year olds). In a Cox proportional hazard model of survival, advanced-stage disease (stage II: HR 5.70, 95% CI 1.87–17.32; stage III: HR 9.62, 95% CI 4.15–22.26; stage IV: HR 36.98, 95% CI 13.73–99.59), Medicare insurance coverage (HR 4.33, 95% CI 1.21–15.49), and black race (HR 2.75, 95% CI 1.10–6.83) were associated with poor survival, while more recent year of diagnosis (HR 0.91, 95% CI 0.84–0.99) and receipt of chemotherapy (HR 0.27, 95% CI 0.13–0.55) were associated with improved survival. Survival was excellent for stage I–III disease, but stage IV disease had poor survival (Table 1, column 5).

Conclusions: Use of chemotherapy was frequent in high-grade histology and advanced-stage disease, and less common with increasing age. Improved survival was associated with chemotherapy and more recent diagnosis, whereas advanced-stage disease, black race, and Medicare insurance negatively affected survival.

Table 1
Predictors of survival by stage for ovarian dysgerminoma.

	Diagnosed %	Receiving Chemo %	Receiving USO %	Overall survival
Stage I	59.0%	31.70%	79.3%	96.9% (95% CI 94.8-98.2)
a		19.7%	65.8%	
b		46.7%	1.6%	
c		59.5%	22.6%	
Stage II	7.6%	80.3%		94.2% (95% CI 85.3-97.8)
a		66.7%		
b		76.2%		
c		91.3%		
Stage III	22.7%	87.2%		89.7% (95% CI 84.3-93.4)
Stage IV	4.0%	85.0%		58.4% (95% CI 40.5-72.6)

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131 - Featured Poster Session
Outcomes and national practice patterns in management of ovarian carcinosarcoma compared with high-grade papillary serous ovarian carcinoma: An NCDB analysis of 76,369 patients
S. Gaillard[a], G. Broadwater[b], J.R. Foote[b], M. Adam[a], A.A. Secord[b], M.B. Jones[c], J. Sosa[a], L.J. Havrilesky[b] and J. Chino[b]. [a]*Duke Cancer Institute, Durham, NC, USA,* [b]*Duke University Medical Center, Durham, NC, USA,* [c]*Duke Cancer Center Macon Pond, Raleigh, NC, USA*

Objectives: To compare outcomes and national practice patterns in the treatment of ovarian carcinosarcoma (OCS) versus high-grade serous ovarian carcinoma (HGSOC).

Methods: The National Cancer Data Base (NCDB) was reviewed to identify adult women diagnosed with OCS or HGSOC between 1998 and 2012. Demographic and clinical data were compared, and the impact of histology on overall survival (OS) was analyzed using the Kaplan-Meier method. The following tests were used: log-rank test to compare survival distributions, Wilcoxon rank-sum tests for continuous variables, and X^2tests for categorical variables. Multivariate Cox proportional hazard modeling was used to examine differences in OS based on age, stage, race, insurance status, and type of cancer program at which care was received.

Results: A total of 76,369 women met the inclusion criteria; 59,983 had complete data for inclusion in multivariate survival models. Of these, 1,450 (1.90%) were diagnosed with OCS, and 74,919 (98.1%) with HGSOC. Patients with OCS were more likely to be older (median age 68 vs 63 years, $P < .0001$), African-American (9.1% vs 6.3%, $P < .0001$), diagnosed with earlier-stage disease (stage I/II 26% vs 17%, $P < .0001$), and treated with radiation (3.0% vs 0.7%, $P < .0001$). They also had a higher 30-day and 90 day mortality after surgery (6.4% vs 2.4%, and 14.3% vs 5.3% respectively, both $P < .0001$) despite no significant difference in Charlson morbidity score (≥1, 19.9% vs 17.8%, $P = .08$). Women with OCS had compromised OS rates compared with HGSOC; this difference persisted when comparing 3-year survival for early-stage (OCS 57.2%, 95% CI 50.4%–64.9% vs HGSOC 84.4%, 95% CI 83.7%–85.2%) and late-stage disease (OCS 24.9%, 95% CI 21.4%–29.0% vs HGSOC 53.6% 95% CI 53.2%–54.2%) at diagnosis (Figure). After adjusting for age, stage, race, insurance status, and type of cancer program at which treatment was received, diagnosis with OCS was still associated with compromised OS (HR 2.0, 95% CI 1.8–2.2, $P < .0001$).

Conclusions: Compared with HGSOC, OCS is associated with compromised OS and an increase in short-term mortality after surgery. Interventions aimed at decreasing short-term mortality and improving long-term outcomes should be the focus of future trials. Ongoing trials focused on this histologic subtype (i.e., GOG261) may determine the optimal treatment regimen for this disease.

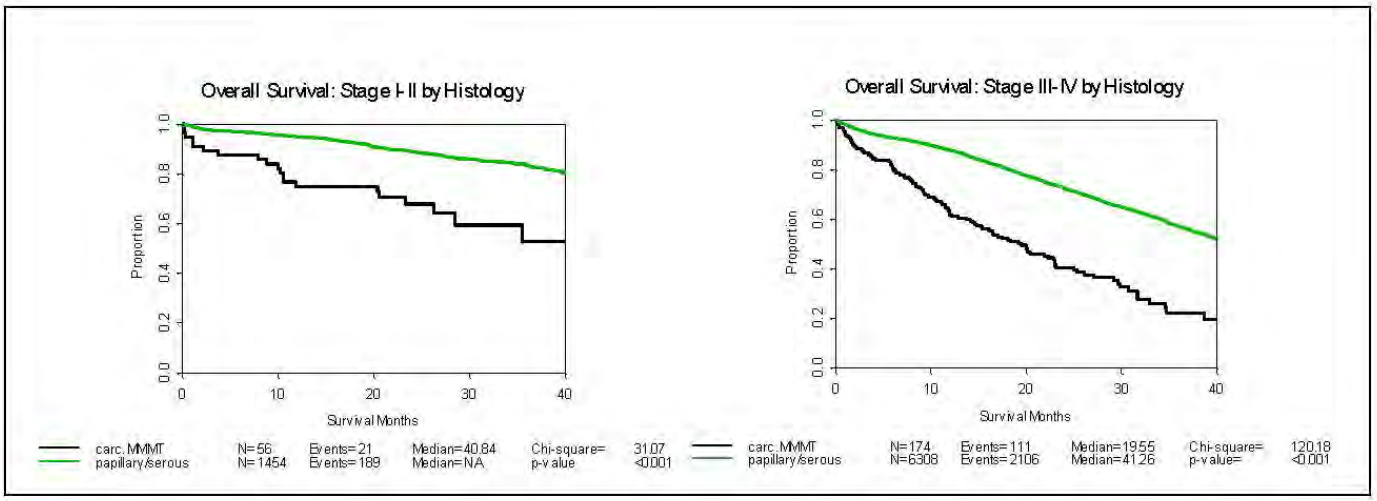

Fig. 1
Kaplan Meier Curve OCS vs. HGSOC by Stage.

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132 - Featured Poster Session
Outcomes among patients with advanced-stage low-grade serous ovarian cancer: Analysis of the National Cancer Data Base, 2003-2011

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Objectives: To identify factors associated with survival among patients with advanced-stage low-grade serous ovarian cancer.

Methods: Patients with stage III and IV ovarian cancer with grade 1 serous histology diagnosed between 2003 and 2011 were identified in the National Cancer Date Base. Demographic, socioeconomic, and clinical variables were abstracted and descriptive statistics were calculated. Extent of primary surgery was categorized as no surgery, pelvic surgery only, surgery that included upper abdominal debulking (including omentectomy), and exenterative procedures. Treatment factors associated with all-cause mortality were evaluated in a multivariate proportional hazards model adjusting for demographic, comorbid, socioeconomic, and treatment characteristics.

Results: A total of 1,159 patients with advanced-stage low-grade serous ovarian cancer were identified. Of these, 970 (83.7%) were diagnosed with stage III and 189 (16.3%) were diagnosed with stage IV disease. The median age at diagnosis was 54 years. Nearly all patients (96.9%) underwent surgery, and 73.4% received adjuvant chemotherapy. The median survival was 91 months (95% CI 84.5–104.3), and the 5-year survival rate was 63.9% (95% CI 60.8–67.2). Older age and stage IV disease were independent predictors of all-cause mortality. Compared with women who had pelvic surgery only, women who underwent upper abdominal (HR 1.5, 95% CI 2.1–2.0) and exenterative procedures (HR 3.8, 95% CI 1.8–8.5) had inferior survival. Conversely, undergoing lymphadectomy was an independent predictor of improved survival (HR 0.5, 95% CI 0.4–0.7). Receipt of chemotherapy was not associated with survival (HR 1.0, 95% CI 0.8–1.3).

Conclusions: Among women with advanced-stage low-grade serous cancer of the ovary, lymphadenectomy, but not receipt of adjuvant chemotherapy was associated with improved survival.

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133 - Featured Poster Session

Is it time to repurpose metformin for the treatment of low-grade ovarian cancer?

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Objectives: Low-grade ovarian cancer (LGOC) constitutes 10% of ovarian cancers and is refractory to chemotherapy. We and others have shown metformin to cause significant growth inhibition in high-grade ovarian cancer (HGOC) both in vitro and in vivo. In the current study, we aimed to analyze if metformin is equally effective in inhibiting proliferation of LGOC cell lines alone and in combination with MEK inhibitors.

Methods: LGOC lines; VOA1056, VOA1213 and VOA5646, and HGOS cell line CaOV3 were used for the experiments. Cells were treated with metformin (0–40 mM), tramatenib (0.1–10 μM) and combination of both. Proliferation was assayed with MTT assay. Western blotting was performed to estimate the activation of AMPK pathway.

Results: LGOC lines showed significant inhibition with the metformin in a dose-dependent manner. Metformin at 20 mM inhibited proliferation after 72-hour treatment by 56.5% in VOA1056 (P = .0007), by 36.2% in VOA1213 (P = .0004), and by 44.4% in VOA5646 (P = .0001), similar to high-grade cell line CaOV3 (P = .001). IC50 for VOA1056, VOA5646, and VOA1213 were 12.6, 24.1, and 45.4 mM, respectively. Long-term treatment on days 1,3, and 5 with lower dose of metformin (2.5 mM) was more effective than 72-hour treatment in inhibiting the growth of VOA1056 (P = .005) and VOA5646 (P = .001). Metformin treatment in LGOC cells activated AMPK and phosphorylated its immediate downstream target ACC. In addition, metformin treatment enhanced the cytotoxic effect of tramatenib synergistically at 0.1 μM (VOA1056, P = .09; VOA5646, P < .000.1) with a combination index of 0.3 for both cell lines.

Conclusions: Metformin alone or in combination with MEK inhibitors may be a potential therapy for LGOC, a cancer that is indolent but chemoresistant. Further work is being conducted to confirm these results in animal models.

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134 - Featured Poster Session

Clinicopathologic factors that influence the use and accuracy of frozen section diagnosis for mucinous ovarian tumors

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Objectives: To determine clinicopathologic factors that influence the use and accuracy of frozen section diagnosis (FS) for mucinous ovarian tumors, including all types of tumors (benign, borderline, and malignant).

Methods: A retrospective cohort analysis was conducted for 1,032 patients (662 benign, 272 borderline, and 98 malignant) from January 1997 to December 2010. Univariate and multivariate regression analyses were used to assess the influence of clinicopathologic factors on the possibility of misdiagnosis, especially underdiagnosis.

Results: We found that 1.0% (6/662) of benign tumors were overdiagnosed; 21.3% (58/272) and 4.0% (11/272) of borderline tumors were underdiagnosed and overdiagnosed, respectively, whereas 27.6% (27/98) of malignant tumors were underdiagnosed. In addition, 8.2% (85/1,032) of the total cases were underdiagnosed, and 1.6% (17/1032) of the total cases were overdiagnosed with FS. In univariate and multivariate analyses, the associated tumor and the predominant component (predominantly liquid tumors) were significant predictors for the underdiagnosis of mucinous borderline ovarian tumor (MBOT) with FS. In univariate and multivariate analyses, the mode of surgery (laparoscopic operation) and the predominant component (predominantly liquid tumors) were significant predictors for the underdiagnosis of mucinous ovarian carcinoma with FS.

Conclusions: FS was not as accurate as expected in the diagnosis of MBOT and mucinous ovarian carcinoma. Misdiagnosis, especially underdiagnosis, affects the surgical strategy for women with mucinous ovarian tumors because an underdiagnosis leads to inadequate conservative surgery and is a primary cause for problems with restaging; therefore, particular attention is required to minimize the risk of underdiagnosis, especially in mucinous ovarian tumors.

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STAT3/PIAS3 as 'early signature' gene pathways in the development of ovarian high-grade serous carcinoma from the fallopian tube

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Objectives: Our recent studies in human samples have demonstrated constitutive activation of STAT3 Tyr705 and loss of protein inhibitor of activated STAT3 (PIAS3) in STICs in the fallopian tubes and advanced HGSC tissues. The goal of this current study is to identify the molecular mechanisms leading to the development of HGSC through STAT3 activation and low levels or absence of PIAS3 in the fallopian tube (FT).

Methods: Human tissues—benign normal FTs, STICs (without ovarian cancer) and HGSC—were evaluated for expression of STAT3/PIAS3 (compared with their known TP53 signature) and their target proliferation genes. Isolated primary fallopian tubal serous epithelial carcinoma (FTSEC) cells from FT and immortalized FT cells were also used and were evaluated with real time polymerase chain reaction, immunohistochemistry, ICC, Western blotting, cloning, and orthotopic mouse models.

Results: We observed high-level expression of pSTAT3 Tyr705, and decreased levels of PIAS3 in dysplastic areas of FT obtained from patients with and without cancer and advanced-stage HGSC (compared with high PIAS3 low pSTAT3 expression in normal benign FT). In addition, FT cells transfected with a STAT3 overexpression construct showed translocation of pSTAT3 and c-Myc into the nucleus. Further, the in vivo experiments demonstrated that the overexpression of STAT3 in FTSECs promoted tumor progression and metastasis, mimicking the clinical disease behavior. In contrast, STAT3 knockdown in ovarian cancer cells was associated with reduced tumor growth and metastasis in vivo.

Conclusions: The STAT3 pathway may play a critical role in the development of STIC lesions and their progression to HGSC. In ongoing studies, we are screening additional FT samples and tissues from various stages of HGSC to determine expression levels of PIAS3 in HGSC and its precursor, and we are using a murine model of HGSC to establish the oncogenic role of STAT3 in initiating tumor growth. Our findings will provide important insights and potential targets that are critical for cancer prevention and early detection in deadly HGSC.

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Salpingectomy versus tubal occlusion for permanent contraception and ovarian cancer prevention: A cost-effectiveness analysis

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Objectives: Laparoscopic salpingectomy for permanent contraception is gaining favor because of data supporting ovarian cancer (OC) risk reduction with salpingectomy. Our objective was to compare the risks, benefits, and costs of salpingectomy versus tubal occlusive (TO) methods at the time of laparoscopic permanent contraception.

Methods: We built a decision analytic model to compare the cost-effectiveness of salpingectomy versus TO in preventing OC and unintended pregnancy. The hypothetical study population includes women of age 35 years with average OC risk who request laparoscopic permanent contraception. A Markov model accounts for the annual risk of developing OC over a 40-year time horizon, using data from the Surveillance, Epidemiology, and End Results (SEER) program. Contraceptive failure rates, utilities, and hospital costs associated with the procedures were obtained from the literature. OC risk reduction estimates were derived from Falconer et al, a Swedish case control study showing a hazard ratio of 0.35 with salpingectomy and 0.72 with sterilization procedures. To account for uncertainty, univariate and bivariate sensitivity analyses as well as Monte Carlo simulation were performed. We used a standard cost-effectiveness threshold of $100,000 per quality-adjusted life year (QALY) gained. We calculated incremental cost-effectiveness ratios (ICERs) that compared salpingectomy with TO.

Results: When applied to a theoretical cohort of 300,000 women (number of sterilizations annually), salpingectomy would result in 210 fewer unintended pregnancies, 1,020 fewer cases of OC, and 660 fewer deaths from OC over 40 years. Salpingectomy would also result in an additional 12,000 QALYs. This results in an ICER of $47,535 per QALY, showing that salpingectomy is cost-effective. Sensitivity analyses showed that the complication rate from salpingectomy would have to be almost double (to 3.1%) that of TO for it to not be the preferred strategy. However, if the cost of salpingectomy were to increase by $310 (from a baseline cost of $6,271 for salpingectomy vs $5,846 for TO) it would no longer be cost-effective.

Conclusions: Opportunistic salpingectomy for permanent contraception is a cost-effective strategy and may reduce the number of OC cases and OC deaths, as well as unintended pregnancies. Health care administrators and obstetrician-gynecologists should continue to support salpingectomy as an alternative to TO for women desiring permanent contraception.

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Comparing 2 sonographic scoring systems for distinguishing benign from malignant ovarian tumors

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Objectives: To compare sonographic ovarian abnormalities using the Kentucky Morphology Index (MI) and the IOTA ADNEX models to distinguish malignant from benign ovarian tumors.

Methods: The group studied was drawn from 44,475 women who were enrolled in the Kentucky Ovarian Screening Program, which had received 270,302 ovarian screening by transvaginal ultrasonography representing 264,623 screening years. Persisting abnormalities resulted in the surgical removal of the ovarian tumor in 603 women. Surgical pathology was available for all tumors. Surgical staging was performed in accordance with FIGO standards. The MI score is determined by tumor structure and size (http://ovarianscreening.info/morphologyindex.html). The ADNEX model records age, oncology center referral status, the diameter of the lesion, the diameter of the largest solid part, the number of locules, the number of papillary projections, the presence of acoustic shadows, the presence of ascites and serum CA-125. The ADNEX model online calculator was used as created by its originators at http://www.iotagroup.org/adnexmodel/site%20iota.html. At least 8 of the 9 ADNEX parameters were needed for inclusion with CA-125 as the only exception since the calculator accounts for its presence or absence. Paired X^2analysis was conducted for significance at the 0.05 level.

Results: A rising score for both the MI and ADNEX sonographic scoring systems correlates with increasing risk of malignancy (ROM). Using a cutoff for malignancy of MI greater than 4 and ADNEX greater than 40, the MI had a significantly higher sensitivity for predicting ovarian cancer (OvCa) than ADNEX (82.1% vs 45.8%, $P < .05$, as indicated in the table). For the ADNEX model, the majority of malignancies (54%, 32/59) had a probability of malignancy less than 40%. The specificity for the ADNEX model was significantly higher than for MI (96.3% vs 65.2%, $P < .05$). Importantly, the MI model was better than the ADNEX at identifying stage I ovarian malignancies (78.7% vs 31.4%, $P < .05$).

Conclusions: Both the MI and ADNEXA methods are readily available and useful in predicting ovarian malignancy. The Kentucky MI has higher sensitivity whereas the ADNEX model has higher specificity at the cutoff used. Low risk of malignancy (0–40%) characterized more than half of the malignancies in the ADNEX model, compared with only 17.8% for tumors with MI less than 5.

Table 1

Comparative Performance For Distinguishing Ovarian Malignancy by the Kentucky Morphology Index and the IOTA ADNEX Methods

MI	Total	OvCa[1]	Stage I[2]	Benign[3]	ROM*	ADNEX	OvCa[1]	Stage I[2]	Benign[3]	ROM*
0	*16*	*0*	*0*	*16*		*0*	*25*	*12*		
1	*45*	*1*	*0*	*44*	*2.2*	*0-10*	*12*	*11*	*265*	*4.3*
2	*53*	*1*	*1*	*52*	*1.9*	*>10-20*	*7*	*4*	*83*	*7.8*
3	*118*	*3*	*2*	*115*	*2.5*	*>20-30*	*8*	*6*	*27*	*22.9*
4	*127*	*10*	*7*	*117*	*7.9*	*>30-40*	*5*	*3*	*12*	*29.4*
5	125	28	16	97	22.4	>40-50	8	6	9	47.1
6	46	11	8	35	23.9	>50-60	6	2	1	85.7
7	40	13	7	27	32.5	>60-70	3	2	4	42.9
8	17	8	4	9	47.1	>70-80	2	1	1	66.7
9	14	8	1	6	57.1	>80-90	2	0	0	100.0
10	2	1	1	1	50.0	>90-100	6	0	0	100.0
Total	603	84	47	519			84	47	402	

Superscripts identify significantly different paired comparisons P < .05

*Actual risk of malignancy

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Ovarian Cancer Early Detection and Prevention Program (OCEDPP): A specimen and data study
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Objectives: To describe the Ovarian Cancer Early Detection and Prevention Program (OCEDPP): the program population, background, goals, and results to date. The OCEDPP was established to identify new prevention approaches and therapies, and to improve the quality of life for women at increased risk for developing cancer and those already diagnosed.

Methods: Since 1998, the OCEDPP has enrolled 2,051 women ages 18 to 80 years with a personal or family history of ovarian cancer, *BRCA* mutation carriers, and women with Lynch, Li-Fraumeni, or Cowden syndrome syndromes. Screened women were followed up to 4 times a year and received CA-125 blood tests, transvaginal ultrasounds, a breast examination, and symptom assessment. Women recruited to the research protocol provided samples of whole blood, serum, plasma, as well as tissue from diagnostic or prophylactic surgeries. The OCEDPP biospecimen repository currently houses more than 50,000 patient specimens. In addition, participants completed a baseline health questionnaire covering personal and family history, and risk factors.

Results: The OCEDPP subject population is 78.1% Caucasian, 5.1% African-American, 1.9% Asian, 2.1% Hispanic, and 12.8% other. Approximately 10% of the population received *BRCA* testing; 196 were identified to be *BRCA* carriers (83% Caucasian, 4.6% African-American, and <1% Asian). We identified 658 families with ovarian cancer in a first-degree relative, 44 families with ovarian cancer in 2 or more relatives, and 85 families with ovarian cancer in a first- and second-degree relative. The diagnostic summary of subjects included 427 (21%) with breast cancer; 70 (3.4%) with ovarian cancer (25 diagnosed with ovarian cancer <50 years); 40 (2.0%) with endometrial cancer; 8 (<1%) fallopian tube cancers; and 20 (1%) with colorectal cancer. Of the 51 subjects who died, over 25% were diagnosed with ovarian cancer. Three subjects developed ovarian cancer during the course of the risk screening program.

Conclusions: The detection rate of ovarian cancer remains low (<1%). Paradigm changes including revised precision methods are needed for more efficient screening of high-risk patients. Further research should focus on exploring specific mutations and cellular and molecular pathways in this patient population to better tailor risk management and treatment.

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139 - Featured Poster Session
Determining the most effective strategy to screen women with ovarian cancer for *BRCA 1/2* germline mutations
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Objectives: To determine the most effective screening method for discovering *BRCA*1/2 germline mutations in women with ovarian cancer.

Methods: A total of 125 women with ovarian cancer had their tumor and blood tested for both germline and somatic *BRCA*1/2 mutations. A decision analytic model was used to determine the most effective screening method.

Results: In the cohort of 125 patients, 17 were found to have germline mutations (11 had somatic mutations). Five screening strategies were analyzed: (1) testing all women with ovarian cancer; (2) testing all women with high-grade ovarian cancer; (3) testing all women with high-grade serous ovarian cancer; (4) testing women with an ovarian cancer and a family history of breast/ovarian cancer; (5) or testing all women with a high-grade serous ovarian cancer or a family history of breast/ovarian cancer. Only screening of all high-grade cancers found all of the germline mutations. Despite this fact, the most effective strategy in identifying mutations was using a 3-generation family pedigree.

Conclusions: The most effective method for determining which women with ovarian cancer should be tested for *BRCA* 1/2 germline mutations is family history.

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Preparing for the unexpected: Panel-based testing of ovarian cancer patients reveals actionable variants in noncanonical genes
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Objectives: A new paradigm in genetic testing for ovarian cancer is emerging. With next-generation sequencing (NGS), clinicians can choose to test only high-penetrance genes or a more comprehensive panel of 30+ cancer genes, for roughly the same cost. The clinical utility of high-penetrance genes such as *BRCA1*, *BRCA2*, and the mismatch repair (*MMR*) genes associated with Lynch syndrome is established. New National Comprehensive Cancer Network (NCCN) guidelines make other genes without typical gynecologic malignancies actionable for prevention of other malignancies. We report data on the prevalence of cancer gene variants in ovarian cancer patients, including genes with recent changes to management guidelines.

Methods: Our study included 550 consecutive patients with ovarian cancer who were referred for testing at Invitae. Genomic DNA variants were identified using an NGS-based hereditary cancer panel with up to 34 genes; panel size was determined by the ordering clinician. Patients' medical histories were obtained from test forms and were deidentified for this analysis.

Results: A likely pathogenic (LP) or pathogenic (P) variant was identified in 63 (12%) of 550 patients. Of the 63 mutation carriers, 48 (78%) had a P/LP variant in a canonical ovarian cancer gene (*BRCA1*, *BRCA2*, *MLH1*, *MSH2*, *MSH6*, *EPCAM*, *PMS2*, or *TP53*), whereas 14 (22%) had a P/LP variant in a noncanonical gene (*FANCC*, *PALB2*, *MUTYH*, *RAD51C*, *ATM*, *STK11*, *NBN*, or *CHEK2*).

Conclusions: Multigene panel testing identified P/LP variants in 8 genes not associated with ovarian cancer risk, which would have been missed by a high-penetrance ovarian cancer panel. These 8 genes predispose to other malignancies for which there are prevention guidelines, such as breast surveillance with magnetic resonance imaging, as recommended by NCCN. These data highlight the benefit of expanded gene panels for the evaluation of hereditary ovarian cancer and the effect of these results on cancer surveillance protocols.

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141 - Featured Poster Session
Value of prophylactic mastectomy in *BRCA* mutation carriers with ovarian cancer
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Objectives: Society of Gynecologic Oncology (SGO) guidelines recommend genetic evaluation of all women with epithelial ovarian cancer (OC). Women with life-threatening OC who are at high genetic risk need an informed discussion of options to reduce the additional risk of breast cancer (BC). We wished to determine the survival benefit and costs of risk-reducing mastectomy (RRM) versus breast screening among women with a new diagnosis of OC who are identified as *BRCA* mutation carriers.

Methods: A decision model was constructed using a modified Markov structure to compare survival and costs associated with 2 mortality reduction strategies for women with a new diagnosis of stage II-IV OC and a *BRCA* germline mutation: (1) RRM, and (2) screening with annual MRI and mammography. Outcomes were mean cost, mean overall survival time, and cost-effectiveness of each strategy. We examined OC diagnosis at 4 ages: 40, 50, 60, and 70 years. OC and BC disease-specific survival were from Surveillance, Epidemiology and End Results Program (SEER) data. Published hazard ratios were used to account for the effects of each mutation type on survival. BC incidence in mutation carriers using each strategy was modeled using prospective, published data. Costs were from Centers for Medicare and Medicaid Services (CMS) reimbursements, hospital costs of mastectomy + reconstruction, and SEER/Medicare. Monte Carlo probabilistic sensitivity analysis was performed.

Results: For a *BRCA1* carrier diagnosed with OC at age 40 years, RRM achieves a survival advantage of 8 months compared with annual screening and is highly cost-effective, with an incremental cost-effectiveness ratio (ICER) of $12,298/year of life saved (YLS). At ages 50, 60, and 70 years, RRM provides 6, 3, and 1.5 additional months, with ICERs of $24,255, $56,881, and $143,207 per YLS, respectively. RRM affords a *BRCA2* carrier gains of 7, 5, 3, and 2 months, respectively, at ages 40, 50, 60, or 70 years, and is cost-effective at ages 40, 50, and 60 years but is not cost-effective at age 70 years (ICER of $119,557/YLS; Figure). At age 40 years, there is a 99% probability that RRM costs less than $100,000/YLS, which decreases to 24% (*BRCA1*) or 36% (*BRCA2*) by age 70 years.

Conclusions: For women with OC diagnosed before age 60 years and who are at high genetic risk, RRM achieves modest life expectancy gains, with an acceptable cost increase compared with annual breast screening. Past age 60 years at OC diagnosis, RRM is unlikely to be cost-effective, with diminishing gains in life expectancy.

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142 - Featured Poster Session
Gynecologic health surveillance and outcomes in *BRCA* mutation carriers following risk-reducing salpingo-oophorectomy
E.N. Prendergast, M. Green, M. Zakhour, J. Lester, A.J. Li, C. Walsh, B.J. Rimel, R.S. Leuchter, B.Y. Karlan and I. Cass.
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Objectives: To characterize patterns of gynecologic surveillance for *BRCA1* and *BRCA2* mutation carriers following risk-reducing salpingo-oophorectomy (RRSO).

Methods: An institutional review board–approved, retrospective review of health surveillance among *BRCA1/2* mutation carriers following RRSO was performed. Women with *BRCA1* or *BRCA2* mutations who underwent RRSO were identified from the years 2000 to 2013. Women with occult carcinoma at RRSO were excluded from analysis. The frequency of hormone replacement therapy (HRT or ERT), abnormal uterine bleeding, and cervical pathology were abstracted.

Results: One hundred ninety-two *BRCA* mutation carriers underwent RRSO: 112 *BRCA1*, 73 *BRCA2*, 5 *BRCA1&2* and 2 *BRCA*-NOS with median ages of 46, 46, 46, and 43, respectively (*P* = NS). Median follow-up was 6.5 years. Seventy-nine (41%) women had a prior diagnosis of breast cancer. Seventy-nine (41%) women had a concomitant hysterectomy including 53% (n = 36) with a prior diagnosis of breast cancer. Breast cancer was not associated a higher likelihood of hysterectomy (*P* = .12). Of eligible women, 68 (35%) received either HRT or ERT for an average of 4 ± 3.3 years. Women who had concomitant hysterectomy were more likely to use hormone therapy than women whose uterus remained in situ (46% vs 35%, respectively, P = .01). Concomitant hysterectomy did not affect the median length of HRT use (4 vs 5 years for women with an intact uterus). Of eligible women without breast cancer, premenopausal women were more likely to use ERT/HRT than postmenopausal women (52% vs 3%, *P* = .0001). Thirteen (11.5%) women with a uterus had abnormal bleeding during the follow-up period. Ten underwent endometrial biopsy with 1 diagnosis of cancer. Six women (5%) had abnormal cervical cytology which necessitated excisional biopsy in 1 patient for cervical intraepithelial neoplasia type III.

Conclusions: Use of HRT/ERT is common in *BRCA* mutation carriers following RRSO. *BRCA* mutation carriers who have a concomitant hysterectomy or are premenopausal at the time of RRSO are more likely to use HRT. Women who keep their uterus are at low risk of subsequent cervical or uterine pathology.

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143 - Featured Poster Session
Primary peritoneal carcinoma surveillance practices following risk-reducing salpingo-oophorectomy (RRSO) in *BRCA* mutation carriers
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Objectives: To describe primary peritoneal cancer surveillance among *BRCA1* and *BRCA2*mutation carriers following risk-reducing salpingo-oophorectomy (RRSO).

Methods: An institutional review board–approved, retrospective review of health surveillance among *BRCA1/2*mutation carriers following RRSO was performed from 2000 to 2013. Women with occult carcinoma at RRSO were excluded from analysis. Surveillance for primary serous peritoneal cancer (PSPC) after RRSO was recorded. Statistical analysis was done using the Wilcoxon matched-pairs signed rank test and analysis of variance.

Results: We identified 192 *BRCA* mutation carriers who underwent RRSO: 112 *BRCA1*, 73 *BRCA2*, 5 *BRCA1&2*, and 2 *BRCA*-NOS. Median duration of follow up was 6.5 years (0.1–15.6). Seventy-nine (41%) women had a concomitant hysterectomy.

Following RRSO, 43 women underwent at least 1surveillance ultrasound for PSPC; 6 underwent further negative evaluation. Ninety-nine women (52%) underwent CA125 surveillance. Of these women, 33 (17%) had annual and 46 (24%) semiannual CA-125 levels. Median change in pre- and postsurgical CA-125 values was greater in women who were premenopausal before RRSO compared with women who were postmenopausal (–3 vs –1.5 units/mL, *P* = .01).

Median CA-125 value after RRSO was unaffected by whether or not a patient had a concomitant hysterectomy (*P* = .12) or used HRT/ERT (*P* = .06). One asymptomatic patient had an abnormal CA-125 because of recurrent breast cancer. Three symptomatic patients (2%) were diagnosed with PSPC with elevated CA-125 and imaging demonstrating ascites and carcinomatosis.

Conclusions: Primary peritoneal carcinoma after RRSO is rare (2%). Pelvic ultrasound and CA-125 may have limited usefulness in surveillance for PSPC but alternatively should be used to evaluate symptoms. Premenopausal women had a greater change in CA-125 values after RRSO than premenopausal women.

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144 - Featured Poster Session

Examination of the time interval between diagnoses in women with metachronous primary endometrial and colorectal cancers supporting universal Lynch testing

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Objectives: The time interval between diagnoses of endometrial and colorectal cancers is not well established in women with metachronous primary tumors of both sites. We sought to examine the time interval between diagnoses, identify associations with clinicopathologic factors, and compare current genetic screening practices.

Methods: We identified 53 patients who developed both cancers between 1966 and 2014. These patients were divided into 2 groups based on having colorectal (group 1) or endometrial (group 2) cancer first. Risks of *MLH1*, *MSH2*, *MSH6*, or *BRCA1/2*mutations as well as the chance of developing a subsequent ovarian or breast cancer were estimated.

Results: There were 18 and 35 patients in groups 1 and 2, respectively. The mean time interval was longer in group 2, 70 vs 43 months (Table 1). Median progression-free survival (PFS) and overall survival (OS) for endometrial cancer tended to be longer in group 2 (PFS: 66 vs 58 mo and OS: 77 vs 58 mo). Median PFS and OS for colorectal cancer were significantly longer in group 1 (PFS: 22 vs 74 mo and OS: 22 vs 86 mo, Table 2). The estimated risk of any MMR mutations was at least 25% in most patients, with 21 patients having more than 50% and 13 patients more than 75% (Table 3).

Conclusions: The mean estimated prevalence of MMR mutation in patients with metachronous endometrial and colorectal cancers is 100-fold greater than in the general population. The time interval between the diagnosis of endometrial and colorectal carcinomas is 5.8 years if endometrial cancer develops first and 3.5 years if colorectal develops first. These results are useful in counseling women at risk.

Table 1a
Patient Characteristics.

		Group 1:CRC first	Group 2:EC first	Total (N)	P-value
Overall	N(%)	18 (34.0)	35 (66.0)	53 (100)	
Age at diagnosis of the first cancer in months	Mean Median	61.4(range 45-82) 59.5	58.9 (Range 24-86) 60	59.7	0.665
Time interval between diagnosis	Mean	1284 days or 43 months	2111 days or 70 months	1830 days or 61 months	0.182
EC Grade	1	7 (38.9%)	16 (45.7)	23 (43.4%)	0.610
	2	4 (22.2%)	10 (28.6)	14 (26.4%)	
	3	7 (38.9%)	9 (25.7)	16 (30.2%)	
CRC Grade	1	2 (11.1%)	2 (5.7)	4 (7.5%)	0.3512
	2	15 (83.3%)	26 (74.3%)	41 (77.4%)	
	3	1 (5.6%)	7 (20%)	8 (15.1%)	

EC Stage	I	12 (66.7%)	25 (71.4%)	37 (69.8%)	0.280
	II	2 (11.1%)	7 (20.0%)	9 (17.0%)	
	III	4 (22.2%)	2 (5.7%)	6 (11.3%)	
	IV	0 (0%)	1 (2.9%)	1 (1.9%)	
CRC Stage	I	8 (44.4%)	8 (22.9%)	16 (30.2%)	0.077
	II	8 (44.4%)	13 (37.1%)	21 (39.6%)	
	III	1 (5.6%)	12 (34.3%)	13 (24.5%)	
	IV	1 (5.6%)	2 (5.7%)	3 (5.7%)	
EC status at last follow up	Unknown	2 (11.1%)	4 (11.4%)	6 (11.3%)	0.659
	NED	8 (44.4%)	20 (57.1%)	28 (52.8%)	
	AD	8 (44.4%)	11 (31.4%)	19 (35.8%)	
CRC status at last follow up	Unknown	2 (11.1%)	3 (8.6%)	5 (9.4%)	0.633
	NED	7 (38.9%)	18 (51.4%)	25 (47.2%)	
	AD	9 (50.0%)	14 (40.0%)	23 (43.4%)	

EC=Endometrial cancer; CRC=Colorectal cancer; NED=no evidence of this disease; AD= with this disease

Table 1b
Survival Time in Months.

		Group 1:CRC first	Group 2:EC first	P-value
EC PFS	Median	58	66	0.219
EC OS		58	77	0.089
CRC PFS	Median	74	22	0.008
CRC OS		86	22	0.003
Combined PFS	Median	26	45	0.117
Combined OS		86	77	0.518
Cause of Death	From Cancer	10 (56%)	15(43%)	0.331
	Other Cause	1(11%)	8(23%)	
	Alive	6(33%)	12(34%)	

EC=Endometrial cancer; CRC=Colorectal cancer

145 - Featured Poster Session

Efficacy of levonorgestrel intrauterine device (LIUD) and transvaginal ultrasound (TVUS) as treatment and surveillance of women with early endometrial cancer (EC) and complex atypical hyperplasia (CAH) who are poor surgical candidates

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Objectives: The purpose was to investigate (1) the efficacy of levonorgestrel intrauterine device (LIUD) for treatment of early-stage endometrial cancer (EC) or complex atypical hyperplasia (CAH) in women with high body mass index

(BMI) or multiple significant comorbidities and (2) thickness of endometrial lining (EL) on transvaginal ultrasound (TVUS) as a surrogate marker for pathologic treatment response.

Methods: An institutional review board–approved, single-institution retrospective study identified patients who had high BMI or poor surgical candidates with biopsy-proven early-stage EC and CAH and subsequently treated with LIUD. Measurements of EL were obtained before treatment and serial TVUS (at the same institution) were performed to evaluate EL every 3 months. Endometrial biopsies (EMB) were performed concordantly with TVUS to evaluate for clinical response. Clinical benefit rates (CBR) (complete response [CR] + partial response [PR] + stable disease [SD]) and progression-free survival (PFS) were calculated using follow-up EMB results. Maximum likelihood ordinal logistic model was used to predict a clinical response based on EMB compared with changes in EL on serial TVUS.

Results: A total of 32 patients were included: 9 (28.1%) with CAH and 23 (71.9%) with early EC. The mean BMI was 49.3 kg/m^2 and the mean Revised Cardiac Risk Index was 2.5. CR was achieved in 13 (50.0%), PR in 4 (15.4%), SD in 5 (19.2%), and progressive disease in 4 (15.4%). CBR was 84.6%, with a mean PFS of 3.3 years. The ordinal logistic model showed a 20% reduction in EL from baseline predicted an 85.4% rate of no progression and 55.9% CR/PR. A 50% reduction of EL from baseline predicted a 94.8% nonprogression rate and 79.6% CR/PR. Importantly, of the 4 patients who progressed and failed, the EL was thickened or increasing and the model correctly predicted progression.

Conclusions: In select patients with high BMI or significant comorbidities, LIUD is a reasonable first alternative to treat EC or CAH. EL, as measured on serial TVUS, is a good surrogate marker to predict response in this unique approach to a difficult patient population.

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146 - Featured Poster Session
Ovarian cancer in elderly women ≥ 70 years of age: Our clinical experience
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Objectives: We sought to review and present our clinical experience in the management of elderly women 70 years of age or older with ovarian cancer.

Methods: Single institution retrospective chart review of all ovarian, fallopian tube and peritoneal cancer diagnosed in women ages 70 years or older between January 1993 and December 2012 was performed. Patient demographics, tumor characteristics, treatment history, and postoperative complications were abstracted. Survival was calculated using the log-rank test.

Results: A total of 88 patients of age 70 years or older at diagnosis were identified during the study period. The mean age at the time of diagnosis was 76 years (range 70–90 years). Stage was distributed as follows: 9 stage I, 6 stage II, 54 stage III (47 stage IIIC), and 17 stage IV. Two patients were not staged or incompletely staged. Seventy-four percent were found to have serous histology, 9% had at least 3 comorbidities, and 3.4% had 4 or more comorbidities. Of the patients, 4.5% had a synchronous malignancy (1 patient had a grade 3 comorbid malignancy according to the adult comorbidity evaluation-27). Twenty-two patients (25%) received neoadjuvant chemotherapy whereas 59 patients (67%) underwent primary debulking surgery. Among the patients that underwent primary debulking or interval debulking, optimal cytoreduction was achieved in 52 patients (61.18%), suboptimal cytoreduction in 29 (34.12%), and “peek and shriek” in 2 (2.35%). Among all patients who underwent surgery during their treatment, only 22 patients (26.5%) went on to receive adjuvant chemotherapy. The major reason to not proceed with chemotherapy was poor performance status. Eighty patients (91%) had an estimated blood loss of less than 1 L. Postoperative complications included fever (4.65%), anemia requiring blood transfusion (56.98%), postoperative ileus (11.63%), malnutrition requiring initiation of total parenteral nutrition (1.16%), and urinary tract complications (3.49%). The mean length of hospital stay was 6 days (range, 0–18 days). Four perioperative deaths were recorded. Mean overall survival in this cohort was 49 months (3–216 mo) and progression-free survival was 32 months (7–216 mo).

Conclusions: Surgery appears to be well tolerated in the elderly who have less than 3 comorbidities and may be comparative to the younger population; however, they are less likely to undergo adjuvant chemotherapy after surgical resection because of low performance status.

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147 - Featured Poster Session
Characteristics of 10-year survivors of high-grade serous ovarian carcinoma
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Objectives: High-grade serous carcinoma (HGSC) generally presents at an advanced stage with poor overall survival. However, the clinical features of long-term (LT; >10 years) survivors have not been well characterized.

Methods: A multicenter research consortium was established among 5 participating academic centers in the United States. Patient selection criteria included a diagnosis of stage III/IV high-grade serous ovarian, fallopian tube, or primary peritoneal carcinoma with at least 10 years of follow-up from the date of initial diagnosis. Nonserous, borderline tumors and low-grade serous subtypes were excluded.

Results: A total of 203 LT survivors with HGSC were identified. Median age at diagnosis was 57 years (range 37–84 years). Most patients had stage IIIC (72.4%) disease at presentation. Of those who underwent primary cytoreductive surgery, optimal cytoreduction (residual disease of no more than 1 cm in maximal diameter) was achieved in 143 (85.6%) patients, and 46.6% of all patients had a complete gross resection. After a median follow-up of 144 months, 88 (46.8%) patients did not develop recurrent disease. Twenty-one patients (11.2%) had 1 recurrence during the follow-up interval, 19 patients (10.1%) had 2 recurrences, and 60 patients (31.9%) had more than 2 recurrences. Of the 79 patients tested for *BRCA1* and *BRCA2* germline mutations, 43 (54.4%) carried a deleterious mutation. Of note, 24 (14%) patients had suboptimal cytoreductive surgery, 16 (11%) had a platinum-free interval of less than 12 months, and 100 (53%) with recurrent disease were surviving 10 or more years after diagnosis.

Conclusions: Long-term survivors of advanced HGSC generally have clinical features including optimal surgical cytoreduction and platinum-sensitive disease. The majority of these patients will develop recurrent disease with many being treated with multiple therapeutic regimens. Future work will compare the clinical features of this LT survivor cohort of "exceptional" responders with the characteristics of HGSC patients with less favorable outcomes.

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148 - Featured Poster Session
Antibiotics and the commensal microbiota: Impact on survival in women with epithelial ovarian cancer
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Objectives: Antibiotic use disrupts the commensal microbiota, which can influence local and systemic metabolism, inflammation, and immunity. In antibiotic-treated mice, tumor cells respond more poorly to chemotherapy. We hypothesized that antibiotic use during primary treatment for women with ovarian cancer negatively influences survival.

Methods: We performed a retrospective review of patients with epithelial ovarian cancer undergoing primary cytoreductive surgery between June 1996 and June 2006. All patients were subsequently treated with chemotherapy. We abstracted data regarding antibiotics, infection, and clinicopathologic factors. Patients receiving 1 dose of preoperative surgical prophylaxis were not considered antibiotic users. Statistical analyses included Fisher exact, Kaplan-Meier survival, and Cox regression analyses.

Results: We identified 238 patients meeting review criteria. Most patients in this cohort had advanced-stage disease (n = 214, 90%) and high-grade histology (n = 234, 98%). Two hundred and ten patients (88%) underwent optimal cytoreduction. Eighty-seven (37%) patients were treated with antibiotics in the interval between cytoreductive surgery and completion of chemotherapy. The most common antibiotics prescribed included piperacillin, cefotetan, metronidazole, and ciprofloxacin. The most common indications for antibiotic use were extension of prophylaxis after surgery (n = 26, 30%), superficial surgical site infection (n = 13, 15%), and urinary tract infection (n = 12, 14%). No patient died of infectious complications. Median progression-free survival for antibiotic users was 15 months compared with 21 months for nonusers ($P = .048$). Overall survival was statistically shorter for antibiotic users (44 months) compared with nonusers (54 months, $P = 0.012$). Multivariate analysis identified that antibiotic use retained significance as an independent poor prognostic factor ($P < .001$) after controlling for age, stage, grade, and cytoreduction status.

Conclusions: Antibiotic use was common in this cohort, and strongly correlated with poor survival. While treatment of infection is necessary, the effects on the microbiome may influence response to chemotherapy. Limitation of prolonged antibiotic prophylaxis should be considered.

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149 - Featured Poster Session
Disparity in survival between white and African American patients with uterine serous carcinoma: Changes in clinical characteristics, pattern of care and outcome over time from 1988 to 2011
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Objectives: Our study employs the Surveillance, Epidemiology, and End Result (SEER) database to determine if outcome disparities between white and African American patients with uterine serous carcinoma (USC) have changed over time.

Methods: Women with USC were identified using the SEER database from 1988 to 2011 (n = 8,230), and grouped into 2 cohorts: white (W) and African American patients (AA). Years of the study were divided into 3 periods (1988–1997, 1998–2004, and 2005–2011). Overall (OS) and disease-specific survivals (DSS) were estimated. KM survival curves and Cox regression models were used.

Results: Over the 3 time periods, African American patients continued to be younger, less likely to be married, and less likely to have cancer-directed surgery and extensive lymphadenectomy compared with white patients. On the other hand, when stratified by the 3 time periods, no difference in stage distribution, rate of lymph node metastasis, and adjuvant radiation was found between the 2 racial groups. In multivariable analysis, adjusting for age, race, marital status, stage, cancer-directed surgery, extent of lymphadenectomy, adjuvant radiation, and geographic location, AA race was significantly associated with worse DSS and OS in the 3 time periods compared with white race. AA patients were more likely to die of uterine cancer than their white counterparts by 29% in 1988–1997 (95% CI 1.03–1.62, $P = .027$), 40% in 1998–2004 (95% CI 1.21–1.63, $P < .0001$), and 34% in 2005–2011 (95% CI 1.13–1.59, $P = .0008$). A slight improvement in the difference in OS over time was noted between AA and white patients. AA patients were more likely to die from any cause compared with their white counterparts by 46% in 1988–1997 (95% CI 1.23–1.73, $P < .0001$), 39% in 1998–2004 (95% CI 1.23–1.56, $P < .0001$) and 26% in 2005–2011 (95% CI 1.10–1.45, $P < .0001$).

Conclusions: Significant improvement in outcome was noted in both racial groups over time. However, AA patients continued to have worse outcomes than white patients over time.

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150 - Featured Poster Session
Survival endpoints for young women with early-stage uterine endometrioid carcinoma: A matched analysis
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Objectives: Younger age is viewed as a favorable prognostic factor in women with early-stage endometrial carcinoma (EC) but the available data are controversial. Survival endpoints were compared between 2 groups of patients with early-stage EC solely of endometrioid histology: women 45 years or younger and similarly matched older women.

Methods: We identified 1,254 patients with 2009 FIGO stage I-II EC who underwent hysterectomy at our institution between January 1990 and December 2014. We created 2 matched groups based on FIGO stage, tumor grade, lymph node dissection status and the type of adjuvant management (observation, pelvic external beam, or vaginal brachytherapy). Recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) were calculated for the 2 groups.

Results: A total of 516 patients (86 younger patients and 430 older patients, matched 1:5) were included in this study. Median follow-up was 42.8 months for the entire study cohort (35.2 months for younger and 49.0 for older patients). The 2 groups were well balanced except for the obvious greater age in the older group ($P < .0001$) and a higher percentage of myometrial invasion in older patients ($P = .003$). There were no significant differences between younger and older groups with regard to 5-year RFS (94% younger vs 91% older, $P = .69$). Similarly, there was no significant difference with regard to DSS (96% younger vs 97% older, $P = .90$). There was no significant difference between younger and older patients in terms of 5-year OS (89% for both groups, $P = .99$), but 10-year OS was 83% for younger women compared with 68% for older patients, ($P = .1$). On multivariate analysis for DSS for the entire study

cohort, high tumor grade and the presence of lower uterine segment involvement were the only 2 predictors of shorter DSS ($P = .01$). On multivariate analysis for RFS, higher stage and the presence of lymphovascular space invasion were the only 2 predictors of shorter RFS ($P < .0001$ and $P = .01$, respectively). Older age and higher stage were the only 2 predictors of shorter OS ($P < .0001$ and $P = .01$, respectively).

Conclusions: When matched based on tumor stage, grade, and adjuvant management, our study suggests that there is no difference between younger and older patients with early-stage EC. High tumor grade, stage, and the presence of lymphovascular invasion remained as independent predictors of survival endpoints in women with early-stage EC.

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151 - Featured Poster Session
A pilot study of pNGVL4a-CRT/E7 (detox) in conjunction with imiquimod for patients with HPV 16+ cervical intraepithelial neoplasia 2/3
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Objectives: The purpose of this study was to evaluate the safety and efficacy of intralesional injection of the DNA plasmid vaccine, pNGVL4a-CRT-E7(detox), in combination with topical imiquimod in women with biopsy-confirmed HPV16-associated cervical intraepithelial neoplasia (CIN) 2/3.

Methods: An expansion cohort was added to a phase I trial evaluating the safety, efficacy, and immunogenicity of pNGVL4a-CRT/E7(detox) administered alone, intradermally (via gene gun), intramuscularly, or directly into the cervix (intralesional), in women with HPV16+ CIN2/3. In this expansion cohort, patients received intralesional injection of pNGVL4a-CRT/E7(detox) at a dose of 3 mg, with concurrent application of 5% imiquimod cream at the injection site, at study weeks 0, 4, and 8. At week 15, patients underwent standard of care loop electrosurgical excision procedure (LEEP). Patients were monitored for clinical and laboratory adverse effects and for clinical efficacy by comparison of pre- and post-treatment histopathologic findings.

Results: Twenty-one women with CIN 2/3 recruited from dysplasia clinics in participating institutions were screened for human papillomavirs (HPV) 16. Eight (42%) of 19 women were confirmed to be HPV 16+ and, of these, 7 consented to participate in this trial. pNGVL4a-CRT-E7(detox), in combination with topical imiquimod was well tolerated and no grade 3 or 4 events were seen. Five patients completed vaccination and underwent LEEP, and 2 are still in the vaccination phase. Of the 5 patients who underwent LEEP, 1 had no evidence of CIN2/3 and 4 had persistent CIN 2/3.

Conclusions: Preliminary analysis demonstrates that the combination of intralesional pNGVL4a-CRT/E7(detox) and topical imiqimod is well tolerated. Accrual is ongoing and planned immunogenicity studies in the peripheral blood and in the target tissues will be performed once accrual is completed.

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152 - Featured Poster Session
Impact of invitation and reminder letters on cervical cancer screening participation in Ontario
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Objectives: To explore the impact of mailing invitation and reminder letters on cervical cancer screening to patients who had not received a Pap smear test in the previous 3 years.

Methods: A cross-sectional study was used to describe factors associated with screening and screening patterns for eligible women. A cohort design was used to compare the impact of invitation and reminder letters on Pap smear uptake comparing women who received the intervention (n=99,278) with a historical nonintervention group (n=130,068). Factors that might influence screening participation were included as covariates in a multivariable logistic regression model.

Results: A total of 1,150,783 women were mailed an invitation letter. Overall, 26.7% of women who had a Pap smear test 3 to 5 years earlier and 9.8% of women with no Pap smear test in the previous 5 years were screened within 9 months after the intervention. On cohort analysis, 14.1% of women in the intervention group and 8.5% of women in the nonintervention group had a Pap smear test within 9 months. Being mailed an invitation letter (OR 1.8, 95% CI 1.7–1.8) was associated with a greater likelihood of screening. Controlling for covariates, the letter intervention

was associated with 9-month screening for both women with a Pap smear test 3 to 5 years earlier (OR 1.7, CI 1.6–1.8) and those with no Pap smear test in the previous 5 years (OR 1.8, CI 1.7–1.9). The effect of all covariates on screening participation was significant. The most significant covariates included being rostered to a Primary Enrollment Model physician practice (OR 1.6, 95% CI 1.6–1.7) and age. Increasing age was negatively associated with likelihood of screening participation. Women aged 65 to 69 years had the smallest odds of screening (OR 0.5, 95% CI 0.5–0.6) compared with women aged 30 to 34 years.

Conclusions: The invitation and reminder letter strategy increased cervical cancer screening participation. Additional strategies are needed that could encourage women who are reluctant to be screened to participate and to remove barriers to screening for eligible women. A significant unscreened rate among older women and among individuals who had no Pap smear test in the previous 5 years underscores the need for further targeted strategies.

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153 - Featured Poster Session

Comparing the health and economic impacts of cervical cancer screening strategies using the Cancer Risk Management Model (CRMM)

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Objectives: The Cancer Risk Management Model–Human Papillomavirus (CRMM-HPV) is a Canadian population multitype HPV transmission and cervical cancer microsimulation model that projects the effects of HPV vaccination and cervical cancer control strategies.

Methods: A comparison was undertaken of 3 screening strategies in an HPV (6/11/16/18) vaccinated population: (1) triennial Pap smear in 25 to 69 year olds (PAP3); (2) triennial Pap smear in 25 to 29 year olds with HPV DNA testing every 5 years from ages 30 to 69 years (PAP3/HPV5), and (3) triennial Pap smear in 25 to 29 year olds and Pap/HPV cotesting every 5 years from ages 30 to 69 years (cotest). The following assumptions were made: (1) 70% HPV vaccination rate among girls aged 12 years with the vaccination program starting in 2007, and (2) screening participation rate of 70% for eligible women with screening beginning in 2015. The model simulated historical screening patterns. Health and economic outcomes were compared among the 3 screening strategies to assess cost-effectiveness. Future costs and life-years were discounted at 3%.

Results: Cotesting demonstrates a 5.8% reduction in incidence and mortality per 100,000 compared with the Pap smear, on average, between 2015 and 2050. Over a lifetime, PAP3/HPV5 and cotesting resulted in 2.3% and 7.5% fewer cases than PAP3, respectively, and 2.9% and 7.9% fewer deaths compared with Pap3, respectively. Cotesting was projected to require the most annual colposcopies, 201,800, versus 148,900 and 102,600 for Pap3 and Pap3/HPV5 scenarios, respectively. When aggregating lifetime costs of vaccination, cervical screening and treatment, PAP3/HPV5 was the least costly, $20.48 billion compared with PAP3 ($22.28 billion) and cotest ($27.98 billion). For direct screening costs, the cotest was the costliest ($23.22 billion), compared with PAP3/HPV5 ($16.04 billion) and PAP3 ($17.58 billion). PAP3/HPV5 and cotesting produced projected gains in quality-adjusted life-years. PAP3/HPV5 had the dominant incremental cost-effectiveness ratio (ICER) over cotesting compared with PAP3 (Figure 1).

Conclusions: According to CRMM-HPV, in a partially vaccinated population, cotesting had the highest screening costs and resulted in the lowest cervical cancer incidence and mortality. The cost savings resulting from PAP3/HPV5, together with the projected gains in quality-adjusted life-years, results in a dominant ICER over cotesting compared with PAP3.

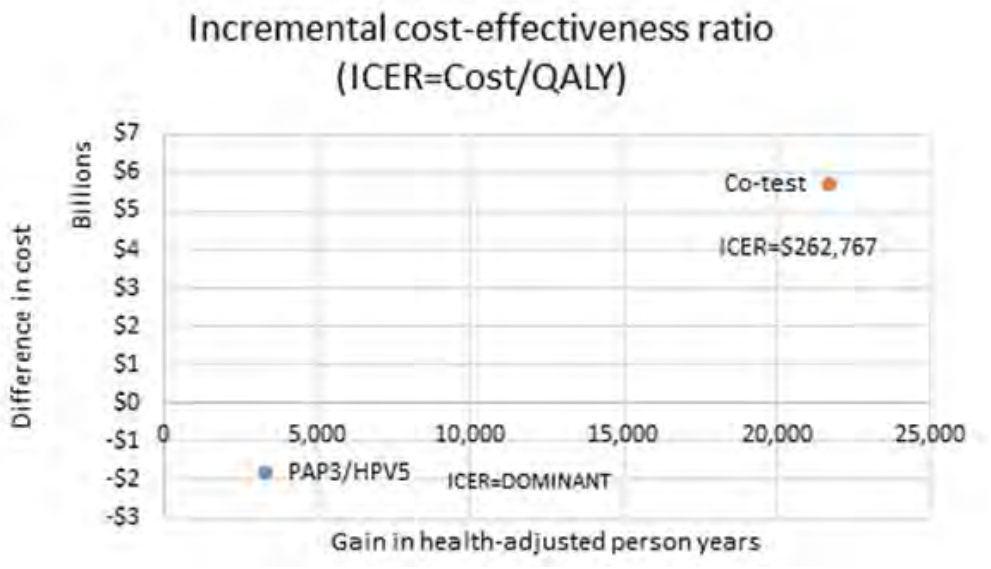

Fig. 1
Incremental Cost-effectiveness Ratio.

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154 - Featured Poster Session
Contribution of cervical cytologic testing to the diagnosis of endometrial and ovarian cancer
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Objectives: To determine the contribution of cervical cytologic testing to the diagnosis of endometrial and ovarian cancers.

Methods: Women who underwent cervical cytology screening within Kaiser Permanente Northern California over a 5-year study period were identified. An abnormal cervical cytology was defined as the following: atypical glandular cells (AGC), other (normal postmenopausal endometrial cells), or malignant. We confirmed all endometrial and ovarian cancer cases via our local cancer registry during the determined study period. Laboratory databases, including reasons for the visit and the history provided with the Pap requisition, were reviewed to determine symptoms of endometrial or ovarian cancer.

Results: From 2009 through 2014, a total of 1,545,126 women underwent cervical cytology testing. Of these, a total of 4,826 (0.3%) were found to have abnormal glandular cell cytology results. During this study period, we identified 3,898 primary invasive endometrial cancers and 1,434 primary invasive ovarian cancers. Among women diagnosed with endometrial and ovarian cancer, 194/3,898 (5.0%) and13/1,434 (0.9%) had abnormal cervical cytology in the 12 months prior to their cancer diagnosis, respectively. Based on review of the laboratory data and visit notes alone, 114/194 (58.7%) and 8/13 (61.5%) of those with abnormal cytology were symptomatic at the time of screening.

Conclusions: Most women who were diagnosed with endometrial or ovarian cancer within 1 year of receiving an abnormal cervical cytology result conceivably related to their cancer were symptomatic from their cancer at or before the time of screening. Failure to diagnose otherwise unsuspected endometrial or ovarian cancer has been described as one potential reason to avoid replacing cotesting with primary HPV screening. However, improved clinical outcomes with presymptomatic detection of endometrial cancer have not been demonstrated. Performance of cervical cytology on 1.5 million women for the purpose of detecting the number of occult endometrial or ovarian cancers described above does not seem warranted.

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155 - Featured Poster Session
Risk of venous thromboembolism in minimally invasive versus open hysterectomy for endometrial cancer
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Objectives: Venous thromboembolism (VTE) is common after pelvic surgery for malignancy. Patients with endometrial cancer are increasingly undergoing minimally invasive surgery (MIS) which may decrease VTE risk. We sought to determine if open surgery is an independent risk factor for VTE compared with MIS in patients with endometrial cancer.

Methods: Patients undergoing surgery for a gynecologic malignancy between 2008 and 2013 were identified from the National Surgical Quality Improvement Database using ICD-9 and CPT codes. This is a retrospective cohort study of 2 patient groups: those who underwent open surgery and those who underwent MIS with a primary outcome of VTE. VTE events were defined as a deep vein thrombosis requiring therapy or a pulmonary embolism, and were recorded for 30 days postoperatively. Demographic, procedure, and complication data were collected. Descriptive statistics and binary logistic regression were used for analysis.

Results: Of 9,948 patients who underwent hysterectomy for the treatment of endometrial cancer, 61.9% had MIS and 38.1% had open surgery. Patients undergoing open surgery had a VTE incidence of 2.2% whereas those who underwent MIS had an incidence of 0.7% ($P < .0001$). Mean time to VTE diagnosis was 10.5±8.8 days in the MIS group and 13.6 ± 9.3 days in the open group ($P = .072$). Those who underwent MIS and had VTE were more likely to have their VTEs diagnosed after hospital discharge compared with open surgery patients with VTE (72.7% vs 42.7%, $P = .001$). Older patients ($P < .007$), longer operating room time ($P < .0001$), higher work relative value unit ($P < .0001$), and higher Charlson comorbidity score ($P < .0001$) were all associated with VTE. Nonwhite race ($P = .14$), smoking ($P = .42$), diabetes ($P = .85$), body mass index ($P = .16$), lymph node dissection ($P = .13$), and hypertension requiring medication ($P = .61$) were not associated with VTE. In a multivariable model controlling for age, operative time, and Charlson comorbidity score, open surgery remained associated with VTE (OR 2.98, 95% CI 2.04–4.35).

Conclusions: For the treatment of endometrial cancer, MIS is independently associated with a decreased risk of VTE compared with open surgery. Nearly three-quarters of patients with MIS with VTE had their VTEs diagnosed after hospital discharge, raising the question of extended prophylaxis in this population.

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156 - Featured Poster Session
Effect of extended venous thromboembolism prophylaxis in women undergoing surgery for epithelial ovarian cancer
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Objectives: To determine the effect of extended 28-day venous thromboembolism (VTE) prophylaxis on VTE rates within 30 days and 6 months of debulking surgery for epithelial ovarian cancer (EOC).

Methods: This historical cohort study estimated incidence of VTE within 30 days and 6 months of debulking surgery in women who received extended VTE prophylaxis (28 days low-molecular-weight heparin [LMWH]) versus those who did not. Women undergoing primary, secondary, and interval debulking for EOC from January 1, 2009, to June 30, 2014 were included. Chronic anticoagulation and VTE before surgery or hospital discharge were exclusion criteria. Secondary analysis was performed on a subset of women who underwent primary debulking surgery (PDS).

Results: Of 590 women undergoing debulking surgery, 90 (15.3%) received prophylactic LMWH. Within 30 days, 16 women were diagnosed with VTE, for a cumulative incidence of 2.9% (95% CI 1.5–4.2), which was not significantly different between those who did and did not receive LMWH ($P = .32$; 30-day rate, 1.2% vs 3.1%). By 6 months, 53 women were diagnosed with VTE, for a cumulative incidence of 9.9% (95% CI 7.3–12.4) with no significant difference between those who did and did not receive LMWH ($P = .98$; 6-month rate, 10.2% vs 9.9%).

The PDS subset included 484 women; 63 (13.0%) received extended LMWH. Within 30 days of surgery, 15 women were diagnosed with VTE, for a cumulative incidence of 3.3% (95% CI 1.6–4.9), with no significant difference between those who did and did not receive LMWH ($P = .47$; 30-day rate, 1.6% vs 3.4%). One patient died of a PE within 30 days of surgery; she had PDS and did not receive LMWH. By 6 months, 41 women were diagnosed with VTE, for a cumulative incidence of 9.3% (95% CI=6.6–12.0) and no significant difference with or without LMWH ($P = .54$; 6-month rate, 6.8% vs 9.6%).

Although postoperative LMWH was not associated with VTE rates, history of VTE and measurable residual disease were associated with increased risk of VTE at 30 days and 6 months. High surgical complexity was associated with increased 6-month VTE risk (Table 1).

Conclusions: Among women undergoing any EOC debulking surgery, VTE rates tripled by 30 days when LMWH was not used; among PDS, VTE rates doubled by 30 days. Because 1 in 10 women with operable EOC develop VTE within 6 months, extending VTE prophylaxis through adjuvant chemotherapy should be studied.

Table 1
Univariable analysis of factors affecting venous thromboembolism rates within 30 days and 6 months of all debulking surgeries and primary debulking surgeries.

	30 days			6 months	
	Unadjusted HR (95% CI)	P		Unadjusted HR (95% CI)	P
All debulking surgery					
LMWH on dismissal	0.38 (0.05, 2.84)	0.34		1.01 (0.48, 2.15)	0.98
Residual disease		0.02			<0.001
No	Reference			Reference	
Yes, measurable (≤1 cm)	.92 (1.45, 10.61)			3.63 (2.09, 6.30)	
History of DVT/PE	6.07 (1.38, 26.71)	0.02		3.85 (1.39, 10.69)	0.01
Surgical complexity		0.25			0.04
Low (0-3)	Reference			Reference	
Intermediate (4-7)	0.81 (0.25, 2.65)			0.59 (0.31, 1.12)	
High (8+)	2.17 (0.66, 7.12)			1.53 (0.79, 2.95)	
Primary debulking surgery					
LMWH on dismissal	0.48 (0.06, 3.64)	0.48		0.73 (0.26, 2.04)	0.55
Residual disease		0.06			<0.001
No	Reference			Reference	
Yes, measurable (≤1 cm)	3.39 (1.21, 9.50)			4.05 (2.18, 7.50)	
History of DVT/PE	7.82 (1.76, 34.67)	0.01		4.47 (1.38, 14.48)	0.01

Abbreviations: LMWH, low molecular weight heparin; DVT, deep venous thrombosis; PE, pulmonary embolism; CI, confidence interval; HR, hazard ratio

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157 - Featured Poster Session
A risk assessment score for postoperative VTE among patients undergoing minimally invasive surgery for gynecologic cancer
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Objectives: Women undergoing minimally invasive surgery (MIS) for gynecologic malignancies have rates of venous thromboembolism (VTE) that range from 0.2% to 2.3%. Many have advocated against pharmacologic prophylaxis, given the low risk. However, there may be a subgroup who are at sufficient risk to warrant prophylaxis. We developed a risk assessment score to predict VTE in the gynecologic oncology patient undergoing MIS.

Methods: Patients undergoing MIS hysterectomy for the treatment of endometrial or cervical cancer from 2008 to 2013 were selected from the National Surgical Quality Improvement Database using ICD-9 and CPT codes. VTE was defined as a deep vein thrombosis requiring therapy or a pulmonary embolism and were recorded for 30 days postoperatively. Caprini and Rogers scores were calculated for all patients. Multivariable logistic regression was used to identify predictors of venous thromboembolism and an MIS VTE risk score was made by assigning points to each odds ratio. Area under receiver operating characteristic curve (AUROC) was used to assess discrimination of all VTE risk assessment scores.

Results: We identified 6,707 patients with endometrial (91.1%) or cervical cancer (8.9%) who underwent MIS hysterectomy. Lymphadenectomy was performed in 58.1%. The incidence of clinical VTE was 0.7% (48/6707). The multivariable logistic regression model contained variables associated with VTE: body mass index BMI >40 (OR 1.9, 95% CI 1.1–3.5), operative time >180 minutes (OR 1.8, 95% CI 1.0–3.3), age >60 years (OR 3.7, 95% CI 1.8–7.7), and hospital stay >1 day (OR 3.1, 95% CI 1.8–5.6). In bivariable analysis lymphadenectomy, radical hysterectomy, and

Charlson comorbidity score were not associated with VTE. Our model had good discrimination with an AUROC of 0.75. In contrast, the AUROC in this population for the Caprini score was 0.65 and for the Rogers score was 0.54. VTE rates for the MIS VTE risk score were 0.17% (4/2,291, score 0–3), 0.48% (15/3,108, score 4–6), and 2.2% (29/1,308, score >7).

Conclusions: This MIS VTE risk score estimates the risk of postoperative VTE among gynecologic oncology patients undergoing MIS. This model has improved discrimination over the Caprini and Rogers score currently used in the American College of Chest Physician guidelines, and identifies a subpopulation of MIS gynecologic surgery patients who may benefit from pharmacologic prophylaxis.

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158 - Featured Poster Session
Modeling bad behavior: Overcoming anti-VEGF resistance in vivo
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Objectives: The anticipated addition of anti–vascular endothelial growth factor (VEGF) drugs to chemotherapy has led to only incremental benefits, as survival gains have been modest, because of the emergence of resistance and rebound tumor growth after the termination of anti-VEGF therapies. Collapse of survival curves and clinical benefit after the cessation of bevacizumab has also been seen. We set out to create a murine model of clinical resistance to antiangiogenic therapy to allow further investigation into the mechanisms of resistance and methods by which it may be overcome.

Methods: We established a syngeneic mouse model of anti-VEGF resistance using immune-competent C57BL/6 mice. Tumor establishment with luciferase-labeled IG10 ovarian cancer cells was confirmed with bioluminescence imaging. Mice were randomized to (1) control or (2) B20 mAb, a murine monoclonal VEGF-A antibody. We also investigated the effect of adding other drugs at the emergence of resistance.

Results: Mice were imaged with bioluminescence weekly to monitor tumor growth. Those receiving B20 mAb were divided into B20-sensitive or B20-resistant groups. B20-resistant mice were defined as those with increased tumor growth, by increased bioluminescence intensity. This marked clinical resistance to anti-VEGF therapy. Immune cells were isolated from tumors of B20-sensitive and B20-resistant mice and subjected to FACS profiling. A 5-fold increase in macrophages was seen in tumors of B20-resistant mice compared with B-20–sensitive mice (5.31% vs 0.08%, $P < .0001$). We added zoledronic acid, a bisphosphonate known to deplete macrophages, at the emergence of resistance. The combined treatment was then continued until mice became moribund. The addition of zoledronic acid at the emergence of resistance halted tumor growth and significantly prolonged survival, compared with either control or anti-VEGF therapy only ($P < .001$).

Conclusions: To our knowledge, this is the first murine model of acquired resistance to anti-VEGF therapy. This model allows for more detailed study of the mechanisms by which resistance occurs. Further, it offers the opportunity to add other chemotherapeutic or drug agents at the emergence of resistance, in hopes of discovering more successful strategies to overcome resistance. Our data suggest that stromal cells, such as macrophages, may play a role in resistance to anti-VEGF therapy and this should be further investigated.

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159 - Featured Poster Session
Obesity is an independent predictor of risk for venous thromboembolism in patients undergoing minimally invasive surgery for gynecologic malignancies
P.C. Mayor, J.B. Szender, E. Zsiros, P.J. Frederick, S.B. Lele and K.O. Odunsi. *Roswell Park Cancer Institute, Buffalo, NY, USA*

Objectives: The purpose of this study is to determine the effects of obesity on the rate of venous thromboembolism (VTE) in patients undergoing minimally invasive surgery for gynecologic malignancy.

Methods: We inspected the National Surgical Quality Improvement Program (NSQIP) Participant Use Files from 2005 to 2013 for subjects undergoing minimally invasive surgery (CPT Codes 58500 to 58599) for gynecologic malignancies (ICD-9 codes 179-184). VTE that occurs within 30 days of surgery is a reported variable in the data set. Body mass index (BMI) was used to place subjects into categories: underweight, with BMI less than 18.5 kg/m^2; normal weight, with BMI of 18.5 to 25.0 kg/m^2; overweight, with a BMI of 25.1 to 30.0 kg/m^2; and obese, with a BMI of 30.1 kg/m^2 or greater. An a priori model of expected interaction was performed to identify factors that contribute

to VTE that are readily available in the dataset and included 3 preoperative risk factors (age, smoking status, and functional status) and 2 intra/postoperative risk factors (length of hospitalization and length of operation). The BMI categories were compared using a χ^2 test with a nominal value of $P < .05$ as a test for significance. Logistic regression was performed with model 1 controlling for preoperative risk factors, model 2 controlling for intra/postoperative risk factors, and model 3 controlling for all 5 factors.

Results: We identified 7,266 subjects who underwent minimally invasive surgery for gynecologic malignancies. Fifty-three (0.73%) developed VTE within 30 days of surgery. VTE was twice as common in subjects who were overweight (RR 2.6, 95% CI 1.3–3.9) and 4 times as common in subjects who were obese (RR 4.4, 95% CI 3.23–5.57) compared with patients of normal weight. Overall, for each 5 kg/m^2 increase in BMI, the risk of VTE increased 21.5% (RR 1.215, 95% CI 1.09–1.36). For models 1, 2, and 3, for each 5 kg/m^{2}increase in BMI, the risk of VTE increased 25.3% (RR 1.253, 95% CI 1.12–1.4), 21.0% (RR 1.253, 95% CI 1.12–1.4), and 25.5% (RR 1.255, 95% CI 1.12–1.41), respectively.

Conclusions: Increasing BMI has a significant impact on the rate of VTE in this patient population even after controlling for multiple other contributing factors. Consideration for thromboprophylaxis in obese patients in this population may be warranted.

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160 - Featured Poster Session
Incidence and the timing of thromboembolic events in ovarian cancer patients undergoing neoadjuvant chemotherapy
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Objectives: Venous thromboembolism (VTE) is a frequent event in ovarian cancers that has a negative impact on overall survival. The purpose of this study is to identify the incidence and timing of VTE in ovarian, fallopian tube, and primary peritoneal cancer patients undergoing neoadjuvant chemotherapy (NAC) to determine patient groups that may benefit from thromboembolic prophylaxis.

Methods: A retrospective cohort study was performed in patients diagnosed with ovarian, fallopian tube, and primary peritoneal cancer at the University of Michigan from January 2009 to May 2014. Primary mode of therapy was noted as NAC vs PDS. VTE events were recorded for the entire cohort. The timing of each VTE event in those who received NAC was categorized into 1 of 3 time periods: VTE as a presenting symptom, during NAC treatment before surgery, and during or after postsurgery adjuvant chemotherapy treatment. The primary outcome was the rate and timing of VTE in patients undergoing NAC treatment. The secondary outcome was the comparison of VTE events between the NAC and PDS treatment groups.

Results: A total of 620 patient cases were identified for analysis. A total of 26% of patients (n = 161) received NAC. Overall incidence of VTE in patients receiving NAC was 30.4% (n = 49). Of these, VTE was a presenting symptom in 26.5% (n = 13), during NAC cycles before debulking surgery in 26.5% (n = 13) and postsurgery in 47% (n = 23). The overall incidence of VTE was higher in patients undergoing NAC (30.4%), compared with PDS (19.2%) ($c^2(1) = 8.783$, $P < .05$). However, after excluding patients presenting with VTE at diagnosis, the difference did not reach statistical significance (24.3% NAC vs 19.2%, $P = .18$).

Conclusions: Nearly one-third of patients with no VTE at presentation undergoing NAC for ovarian cancer experienced a VTE event before surgery. This is a time of high tumor burden in patients who are more likely to be older, with higher comorbidities, and lower functional status. Thromboembolic prophylaxis in these patients during NAC may decrease the incidence of VTE events. Therefore, a prospective study investigating the use of thromboembolic prophylaxis during the NAC is warranted.

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161 - Featured Poster Session
Hypoxia-facilitated exosomal release from ovarian cancer cells is regulated by STAT3 and is associated with increased metastatic tumor burden
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Objectives: To investigate how hypoxia facilitates the secretion of exosomes in the tumor microenvironment and how these exosomes contribute to tumor metastasis and drug resistance in ovarian cancer.

Methods: Exosomes were obtained through ovarian cancer cell lines and human specimens. The cell lines cultures were performed in normoxic and hypoxic (1%) conditions. After institutional review board approval, ascites samples were obtained from patients undergoing laparotomy or paracentesis for ovarian cancer. Released exosomes were then isolated using Exo-quick. A nanoparticle tracking analyzer was used to quantify their size and concentration. Size was confirmed with transmission electron microscopy. Western-blotting was done to identify the exosomes with specific markers CD9, CD63, and EpCam and to confirm the presence of oncoproteins. We further analyzed the migratory potential of these exosomes in normal and cancer cell lines as well as with an in vivo orthotopic ovarian tumor model. Transfection was done to knock down STAT3 in ovarian cancer cell lines to elucidate its effect on exosome release.

Results: Exosome concentration was increased 2- to 4-fold in hypoxic (vs normoxic) conditions. The knockdown of STAT3 in ovarian cancer cell lines reduced the release of exosomes in the setting of hypoxia. The hypoxic exosomes increased the migration potential of normal and cancer cell lines. In addition, these exosomes were found to carry the activated form of oncoproteins such as pSTAT3 and FAS. Ovarian cancer cell cultures performed in the presence of hypoxic exosomes and injected into mice showed more aggressive tumor growth and metastatic spread including prominent mesenteric nodules. In comparison, mice injected with ovarian cancer cells that underwent cultures with normoxic exosomes experienced tumor development at the primary site (ovary) of tumor injection, but had no evidence of metastasis.

Conclusions: Hypoxia-mediated release of exosomes from ovarian cancer is influenced by STAT3. Hypoxic exosomes carry oncogenes and are associated with increased tumor burden and metastatic spread. These findings suggest that hypoxia-mediated exosome release facilitated by STAT3 may play an important role in the development of advanced ovarian cancer and serve as a target for therapeutic intervention.

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162 - Featured Poster Session

Expression of alcohol dehydrogenase 5 in ovarian carcinoma: Effect on prognosis and therapeutic potential

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Objectives: S-nitrosoglutathione (GSNO), a physiologic nitrosylating agent, significantly inhibits ovarian cancer (OC) growth by promoting nitrosylation of various genes and inhibiting inflammation. GSNO is catabolized by alcohol dehydrogenase 5 (ALDH5) leading to reduction in the process of nitrosylation. Our aim was to evaluate ALDH5 expression in type I and type II OC tumor tissue microarray (TMA) and its relation with the expression of inflammatory markers and survival and to explore the role of ALDH5 inhibition in treating OC.

Methods: Immunohistochemical (IHC) staining for ALDH5 protein expression was performed on TMA for 360 cases with OC (292 serous, 12 endometrioid, 43 mucinous, and 13 clear cell carcinoma). IHC for COX-2, iNOS, eNOS, and NFkB was performed on a subset of cases (n = 120). Each marker was scored by combining staining intensity and percentage of stained cells to establish H-score. Data were analyzed with the Fisher exact test and Kaplan-Meier survival analysis. Expression of ALDH5 in various OC cell lines was determined using quantitative polymerase chain reaction. OC cell lines were treated with ALDH5 inhibitor (N6022) in the presence or absence of GSNO and cell survival was assayed by MTT. We also investigated the effect of GSNO in an immunocompetent isogenic mouse model of OC which expressed lower level of ALDH5.

Results: High ALDH5 expression was significantly associated with type II OC (high-grade serous and endometrioid carcinoma) versus type I (borderline serous, low-grade serous, low-grade endometrioid, mucinous, and clear cell carcinoma) ($P = .003$). High ALDH5 expression was significantly associated with increased COX-2 ($P = .001$) and NFkB expression ($P = .001$). The overall survival (OS) was shorter in patients with high ALDH5 expression (median OS: 32 vs 49 mo) without a significant statistical difference. Expression of ALDH5 in OC cell lines showed inverse correlation with cytotoxic effect of GSNO. Moreover, inhibition of ALDH5 potentiated cytotoxicity of suboptimal doses of GSNO in OC cell lines ($P < .05$). In a preclinical mouse model, oral administration of GSNO at 1 mg/kg significantly attenuated tumor growth and ascites accumulation ($P < .01$).

Conclusions: High ALDH5 expression was significantly associated with type II OC and inflammatory mediators. Inhibition of ALDH5 could be a potential therapeutic target in OC.

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163 - Featured Poster Session

The prevalence of viral DNA in epithelial ovarian cancer and correlation with clinical outcomes

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Objectives: The National Cancer Institute estimates that infectious agents are responsible for 15% to 20% of cancers worldwide. Although no infectious agent has been shown to directly induce the transformation of ovarian epithelial cells, molecular studies support an association between infectious agents and ovarian cancer (OVCA). Human papillomavirus (HPV), cytomegalovirus, and Epstein-Barr virus have all been associated with OVCA. In this study, we describe the prevalence of virus in 101 samples of primary ovarian cancer as well as a correlation with clinical outcome.

Methods: Viral DNA from 101 tumor samples from patients with epithelial OVCA was extracted and submitted for multiplex polymerase chain reaction (PCR). Luminex technology was then applied to identify PCR-amplified viral DNA for 115 specific viruses from 5 viral families (polyomavirus, herpesvirus, cutaneous gamma HPV, cutaneous beta HPV, and mucosal alpha HPV). Descriptive statistics were performed. Univariate analyses were performed with Pearson correlation test and chi-squared test. The log-rank test and Cox proportional hazard model were used to associate clinical variables and viral presence with survival.

Results: Forty-six tumor specimens (45%) contained at least 1 virus. One specimen contained 4 distinct viruses. Univariate analyses demonstrated a significant association between increasing age and increased number of viruses in a specimen (P = .048). Stage, optimal surgical debulking, and initial response to platinum therapy were not associated with the presence of virus. The risk of death was increased with increasing number of viruses present in the specimen (HR 1.44; P = .012). However, in a multivariate analysis, only stage and response to platinum therapy were significantly associated with survival.

Conclusions: Forty-five percent of tumor samples from our study were positive for the presence of virus. The presence of virus was significantly associated with decreased overall survival. Further work is required to determine if the presence of virus nucleic acid signifies an oncogenic event or if it merely represents passenger contamination.

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164 - Featured Poster Session

Rad6 inhibition sensitizes ovarian cancer cells to platinum drugs by attenuating activation of multiple DNA repair networks

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Objectives: Ovarian cancer (OC) platinum resistance is often attributable to an increase in DNA repair. Rad6 is an E2 ubiquitin–conjugating enzyme that plays a central role in the activation of several DNA repair pathways. Rad6, in conjunction with its E3 partner Rad18, is vital for the activation of trans-lesion synthesis (TLS) DNA damage tolerance by monoubiquitinating PCNA; and the activation of the Fanconi anemia (FA) DNA repair pathway critical for DNA crosslink repair. We aimed to determine if inhibition of Rad6 could attenuate the DNA damage repair signaling induced by platinum drugs, and thereby overcome OC platinum resistance.

Methods: OC cell lines were used to evaluate Rad6-mediated ubiquitin signaling. Both genetic and pharmacologic inhibitors of Rad6 were used and compared with controls in cancer growth and clonogenic assays. Responsiveness to platinum chemotherapy was tested in combination with Rad6 inhibitor. Standard Western blotting techniques were used to measure protein levels with or without Rad6 inhibition. Immunostaining was used to visualize DNA damage foci formation.

Results: Rad6B was overexpressed in OC with increasing intensity by immunohistochemistry with increasing stage. Inhibition of Rad6 was effective in blocking DNA repair pathway mediators such as FANCD2, PCNA, γH2AX. Treatment with siRNAs or a small molecule inhibitor led to growth inhibition and attenuated clonogenic potential of OC cells. In addition, OC cells were sensitized to carboplatin by both genetic and pharmacological inhibition of Rad6. Genetic knockdown of Rad6 resulted in a threefold reduction in the IC_{50} value of carboplatin, and the IC_{50} value for carboplatin was reduced fivefold after treatment with a small molecule inhibitor. Moreover, Rad6 inhibition potentiated DNA damage induced by platinum drugs and sensitized platinum-resistant OC cells to carboplatin. Immunostaining confirmed that Rad6 inhibition attenuated FANCD2 foci formation, indicating reduced DNA repair.

Conclusions: Rad6 inhibition reduced OC cell growth, but also consistently blocked carboplatin-induced PCNA monoubiquitination and FA pathway activation. This resulted in a sustained increase in DNA damage and an increase in cancer cell death. Together, our data indicate that inhibition of Rad6 holds therapeutic potential for the treatment of OC alone or in combination therapy.

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165 - Featured Poster Session
Omental macrophages: Drivers of ovarian cancer metastatic colonization
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Objectives: Metastatic ovarian cancer remains an urgent clinical problem. The homing and invasion of cancer cells into the omental adipose tissue, the preferred site of ovarian cancer metastasis, is a critical step in disease progression. Improving patient outcomes requires a mechanistic understanding of how cancer cells colonize the omentum and ultimately give rise to widespread peritoneal metastases. Unlike other peritoneal adipose tissues, omental adipose contains immune aggregates known as milky spots, which contain macrophages, B, T, natural killer (NK), and stromal cells within capillary nests. Our data show that milky spots play an active role in ovarian cancer metastatic colonization to omentum. We hypothesize that macrophages in the milky spots play a crucial role in promoting ovarian cancer progression.

Methods: Immunocompetent mice were injected with syngeneic murine ID8 and immunocompromised mice were injected with human (SKOV3ip.1, CaOV3, HeyA8), ovarian cancer cells. After 7 days postinjection, mice were killed and analyzed for the distribution of cancer cells.

Results: We found metastases in omental milky spots and not in the adipose-lacking milky spots. Use of genetic models (C57BL/6, Athymic Nude, Beige Nude, Rag1$^{-/-}$, Igh6$^{-/-}$ mice) ruled out a requirement of B, T, and NK cells in ovarian cancer cell homing to milky spots, suggesting a critical role for macrophages in this process. We further show that depletion of omental adipose tissue macrophages abrogates cancer cell colonization of milky spots. In vitro assays demonstrated that omental adipose-conditioned medium significantly increased the migration of cancer cells compared with media conditioned by adipose-lacking milky spots. Cytokine array of omental adipose-conditioned medium revealed higher concentration of macrophage-secreted cytokines (e.g., MCSF-1, IL10) than control medium conditioned by adipose-lacking milky spots.

Conclusions: We showed that omental milky spots are the preferential site for cancer colonization of peritoneal adipose. Further, we identified omental macrophages as the key mediators of colonization. Future studies are focused on understanding the cancer cell–macrophage interactions that can be targeted therapeutically to disrupt metastatic growth and extend disease-free survival.

Posters

166 - Poster
Molecular profiling of triple-negative endometrial cancers and triple-negative breast cancers reveals unique expression profiles
N.L. Jones[a], J. Xiu[b], S.K. Reddy[b], S. Chatterjee[a], A. Buckley de Meritens[a], A.I. Tergas[c], W.M. Burke[c], J.D. Wright[c] and J.Y. Hou[c]. [a]*NYPH, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA,* [b]*Caris Life Sciences, Irving, TX, USA,* [c]*Columbia University College of Physicians and Surgeons, New York, NY, USA*

Objectives: We aim to compare genetic and molecular features between triple-negative endometrial cancer (TNEC) and triple-negative breast cancer (TNBC).

Methods: A total of 3,133 endometrial cancer specimens submitted for molecular profiling testing from March 2011 to July 2014 were evalauted using multiplatform profiling, which included a combination of sequencing (Sanger or next-generation sequencing), protein expression (immunohistochemistry), and/or gene amplification (chromogenic or fluorescence in situ hybridization). The molecular profiles of 545 TNECs and 2,049 TNBCs were identified based on reported pathology, and compared using the Fisher exact test.

Results: Compared with an incidence of 15% to 20% TNBC in breast cancer literature, we found 17% (545/3,133) TNEC in our cohort. Of 545 TNEC cases, 13% were endometrioid, 22% serous, 26% carcinosarcoma, 7% clear cell, and 22% other. Compared with TNBC, TNEC showed 1.9 mutations per case whereas TNBC showed 1.2 mutations per

case ($P < .01$). Table 1 shows a list of molecular and genomic alterations found in TNBC and TNEC. TNBC and TNEC had similar frequencies of the *BRCA1* and *BRCA2* mutations. Although common to both, *TP53* mutations were more frequent in TNBC, as was androgen receptor expression. *MGMT* and *ERCC1* were more commonly mutated in TNBC suggesting aberrant DNA repair. DNA synthesis pathway involvement was more common in TNEC with greater *TS*, *RRM1*, and *TOPO2A* expression, though TNBC had greater *TOPO1* expression. PD-1 expression was more common in TNEC, suggesting immune pathway involvement. The PI3K/AKT/mTor pathway was more commonly involved in TNEC with greater *PTEN*, *PIK3CA*, *KRAS*, *NRAS*, and *FBXW7* mutations as well as greater *PTEN* expression. Finally, TNEC has greater cMET expression and CTNNB1 mutation, suggesting poor prognosis and Wnt pathway involvement, respectively.

Conclusions: Based on the genes studied, the differences between TNEC and TNBC in their molecular pathways are significant. Further studies are warranted to validate these findings in clinical trials.

Table 1
Molecular Profile Differences between Triple-negative Endometrial Cancers and Triple-negative Breast Cancers**.**

	Marker	TNEC	TNBC	*P*-value
IHC	AR	4%	18%	< 0.01
	cMET	16%	9%	
	ERCC1	10%	48%	
	MGMT	41%	57%	
	PD-1	74%	59%	
	PTEN	50%	35%	
	RRM1	46%	34%	
	TOP2A	91%	80%	
	TOPO1	44%	67%	
	TS	68%	35%	
SEQ	TP53	56%	66%	
	PIK3CA	25%	14%	
	KRAS	20%	1%	
	NRAS	0%	2%	
	PTEN	18%	5%	
	FBXW7	13%	1%	
	CTNNB1	8%	0%	
	AKT	3%	1%	
	BRCA2	14%	19%	> 0.05
	BRCA1	10%	17%	

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167 - Poster
Molecular profiling reveals distinct molecular landscape in 545 cases of triple-negative endometrial cancer
N.L. Jones[a], J. Xiu[b], S.K. Reddy[b], A. Buckley de Meritens[a], S. Chatterjee[a], A.I. Tergas[c], W.M. Burke[c], J.D. Wright[c] and J.Y. Hou[c]. *[a]NYPH, Columbia University Medical Center and Weill Cornell Medical College, New York, NY, USA, [b]Caris Life Sciences, Irving, TX, USA, [c]Columbia University College of Physicians and Surgeons, New York, NY, USA*

Objectives: We aim to compare genetic and molecular features of triple-negative endometrial cancers (TNEC) with non-TNEC to identify possible therapeutic targets.

Methods: A total of 3,133 endometrial cancer specimens submitted for molecular profiling testing from March 2011 to July 2014 were evalauted using multiplatform profiling, which included a combination of sequencing (Sanger or next-generation sequencing), protein expression (immunohistochemistry), and /or gene amplification (chromogenic or fluorescence in situ hybridization). The molecular profiles of 545 TNEC and 2,162 non-TNEC were identified based on reported pathology, and compared using the Fisher exact test.

Results: The frequency of TNEC in our cohort was 17%. Of 545 TNEC cases, 13% were endometrioid, 22% serous, 26% carcinosarcoma (MMMT), 7% clear cell, and 22% other. Table 1 shows molecular and genomic alterations between TNECs and non-TNECs. Compared with non-TNEC, TNECs had more frequent *TP53* and *BRCA1* mutations.

Greater involvement in the DNA synthesis pathway was noted with higher *TOPO1*, *TOPO2*, *TS*, and *RRM1* expression. Immune modulatory, FGFR and Wnt pathways were less often altered with lower PDL1 expression and FGFR2, CTNNB1 mutations, respectively. PI3K/Akt/mTOR pathway aberrations were less common in TNEC with fewer *PIK3CA*, *PTEN*, and *AKT* mutations. Finally, AR and TLE3 expression were less common in TNEC than in non-TNEC.

Conclusions: TNEC appears to have a distinct molecular background from non-TNEC. Differences were seen in pathways involved in DNA repair, DNA synthesis, immune modulatory function, and the PI3K/Akt/mTOR pathway. Further studies are warranted to validate these findings in clinical trials.

Table 1
Molecular profiles unique to triple-negative endometrial cancers.

	Marker	TNEC	non-TNEC	P-value
IHC	AR	4%	28%	P < 0.05
	PD-L1	14%	28%	
	PTEN	50%	37%	
	RRM1	46%	37%	
	TLE3	18%	14%	
	TOP2A	91%	79%	
	TOPO1	44%	38%	
	TS	68%	48%	
SEQ	TP53	56%	37%	
	PIK3CA	25%	35%	
	PTEN	18%	33%	
	BRCA1	17%	5%	
	FBXW7	13%	7%	
	CTNNB1	8%	15%	
	FGFR2	4%	8%	

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The effect of obesity on adjuvant treatment after a diagnosis of endometrial cancer
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Objectives: To examine the rates of complications from chemotherapy and radiation therapy (RT) based on obesity status in patients with endometrial cancer (EC). Concerns about toxicity and overdosing in obese patients exist, despite recommendations against treatment modifications for obesity.

Methods: We performed a retrospective cohort study on 542 surgically managed EC patients treated at a single institution between 2006 and 2011. Obesity was defined as a body mass index of 30 kg/m^2 or more. Demographic and pathologic data, details of adjuvant chemotherapy and RT, and adverse outcomes were abstracted. Adverse outcomes included dose reduction, treatment delay, or treatment cancellation. Adverse events were graded by the National Cancer Institute Common Toxicity Criteria. Descriptive statistics were performed, with data compared using the X^2 and Wilcoxon-Mann-Whitney tests.

Results: A total of 158 (30.9%) women underwent adjuvant chemotherapy and 44.9% of these women were obese. Overall, 30.6% of patients required a dose-reduction, 33.8% had a dose delay, and 19.7% had a treatment cancellation, but this was not statistically significant for obese versus nonobese women (P = .692, P = .181, and P = .492, respectively). There was no statistically significant difference in reported adverse events (P = .826). Two hundred and one patients (38.1%) received RT and 33.3% were obese. There was no difference in treatment delay or cancellation according to obesity (P = .867, P = .22). Obese women were significantly more likely to complain of fatigue (P = .04) and late gastrointestinal (GI) side effects (P = .023).

Conclusions: Obese EC patients do not have a significantly increased risk of requiring adjuvant treatment adjustments or adverse clinical outcomes related to chemotherapy or RT, except for an increase in fatigue and late-onset GI side effects with RT. Women should be able to tolerate appropriate weight-based treatment doses without concern for provoking excess toxicity related to obesity.

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169 - Poster

Molecular pathogenesis of endometrial intraepithelial neoplasia: Precursor to endometrial carcinoma

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Objectives: To characterize the relationship between DNA mismatch repair (*MMR*), *ARID1A*, and *PTEN* in endometrial intraepithelial neoplasia (EIN).

Methods: Type 1 endometrial carcinoma typically develops from a precursor lesion, endometrial hyperplasia, or EIN. The DNA *MMR* system prevents tumor progression by correcting errors that occur during DNA replication and is present in a proportion of endometrial cancers. Tumor suppressor genes *ARID1A* and *PTEN* are also implicated in the molecular pathogenesis of endometrial carcinoma. Previous studies have shown that in endometrial carcinoma, *MMR* deficiency may be associated with *ARID1A* mutations. However, in EIN, the relationship between loss of expression (LOE) of *MMR*, *ARID1A*, and *PTEN* has yet to be established.

In a retrospective review, we identified 113 patients with EIN on endometrial biopsy from 2009 to 2014. Tissue microarray blocks were evaluated with immunohistochemical stains using antibodies against *MLH1*, *PMS2*, *MSH2*, *MSH6*, *ARID1A*, and *PTEN*. Statistical analyses were performed, with a $P < .05$ considered statistically significant.

Results: In EIN, rates of LOE of *MMR*, *ARID1A*, and *PTEN* were 4.4% (n = 5), 6.2% (n = 7), and 50.4% (n = 57), respectively. Loss of MMR expression was not significantly associated with expression of ARID1A ($P = 1.000$) or PTEN ($P = .2062$). Development of a subsequent invasive malignancy was not significantly associated with LOE of *ARID1A* ($P = .1135$), DNA *MMR* ($P = .2424$), or *PTEN* ($P = .1670$). When combined, LOE of *ARID1A* and *MMR* was significantly associated with subsequent cancer ($P = .0109$).

Conclusions: In this series of EIN, the frequency of *PTEN* LOE (50.4%) agreed with that seen in previous studies. Unlike rates demonstrated in endometrial carcinoma, the proportion of LOE in *MMR* (4.4%) and *ARID1A* (6.2%) seen in the precursor lesion were relatively low and thus seem to be nonessential in the development of EIN. There were no cases of concordant LOE of *MMR* and *ARID1A*, suggesting independent pathways or differences in temporal patterns in gene expression during the premalignant phase. When combined, LOE of *ARID1A* and *MMR* was significantly associated with the development of a subsequent malignancy, suggesting potential prognostic markers, which will require further evaluation.

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Endometrial cancer arising in adenomyosis versus endometrial cancer coexisting with adenomyosis: Different entity?

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Objectives: Although adenomyosis is one of the most common benign histologic findings seen in hysterectomy specimens of women with endometrial cancer, the characteristics and outcomes of endometrial cancer arising in adenomyosis (EC-AIA) have not been well elucidated. The aim of this study was to evaluate histopathologic findings and disease-free survival (DFS) of EC-AIA compared with endometrial cancer coexisting with adenomyosis (EC-A).

Methods: EC-AIA cases were identified through a systematic literature search (n = 46). EC-A cases were identified from a historical cohort that underwent hysterectomy-based surgical staging in 2 institutions (n = 350). Statistical comparisons of the 2 groups were performed in univariate and multivariate analyses.

Results: The EC-AIA group was significantly older than the EC-A group (mean, 58.9 vs 53.8, $P = .002$). For tumor characteristics, 63.6% of EC-AIA cases reported tumor in the myometrium without endometrium extension, and the EC-AIA group was significantly more likely to have tumors with more than 50% myometrial invasion (51.6% vs 19.4%, $P < .001$) and to have high risk of nonendometrioid subtypes (22.2% vs 6.6%, $P = .001$). Tumor grade, stage, and rate of nodal metastasis were similar (all, $P > .05$). On univariate analysis, the EC-AIA group had a significantly decreased 5-year DFS compared with the EC-A group (72.2% vs 85.5%, $P = .001$). On multivariate analysis, controlling for age, histology, tumor grade, and stage, EC-AIA remained an independent prognostic factor associated with decreased DFS compared with EC-A (adjusted HR 3.32, 95% CI 1.12–9.92, $P = .003$).

Conclusions: EC-AIA has distinct tumor characteristics and a poorer survival outcome than EC-A, suggesting a benefit to recognizing this unique entity as an aggressive variant of endometrial cancer.

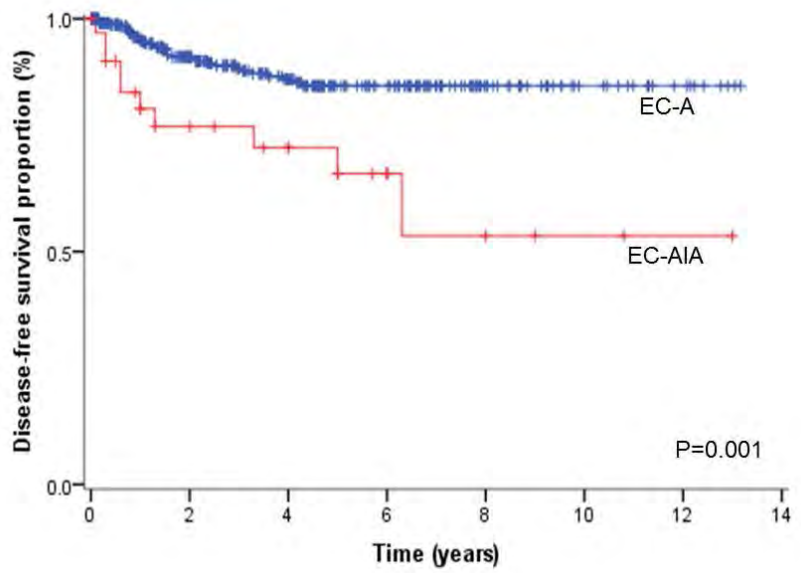

Fig. 1

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Predictors of survival after recurrence in women with early-stage endometrial carcinoma

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Objectives: Factors predictive of survival after recurrent early-stage endometrial cancer have not been thoroughly investigated. The purpose of this study was to explore the impact of different prognostic factors including type of salvage management on disease-specific survival (DSS) and overall survival (OS) after recurrence.

Methods: Following institutional review board approval, we identified 104 women with 2009 FIGO stage I-II uterine endometrioid carcinoma who developed disease recurrence between January 1990 and December 2014. Patients who received adjuvant chemotherapy after primary surgery were excluded from this analysis. The Kaplan-Meier approach and Cox regression analysis were used to assess DSS and OS after recurrence and to determine factors influencing survival endpoints.

Results: Median age of the study cohort was 65 years with a median follow-up time of 42.8 months after hysterectomy. Sixty patients (57.7%) had stage IA, 30 (28.9%) had stage IB, and 14 (13.5) had stage II disease. Median time to recurrence was 15.8 months. Fifty-six patients (54%) had pelvic-only recurrence (vaginal and/or pelvic), whereas 48 (46%) had extrapelvic recurrences. Patients with low-grade tumors and pelvic-only recurrences were associated with longer DSS and OS compared with patients with grade 3 tumor and/or extrapelvic recurrences (P = .05). Five-year DSS calculated from the date of recurrence for the entire cohort was 44%. The 5-year DSS was longer for patients with pelvic-only recurrence compared with patients with extrapelvic recurrences (66% vs 18%, P < .0001). The 5-year DSS was longer for radiation-naïve patients than for patients who received prior adjuvant radiation therapy (51% vs 34%, P = .023). Neither time to recurrence nor type of salvage treatment was a significant predictor for DSS or OS. On multivariate analysis of DSS and OS, pelvic-only recurrence (P < .001) was the only significant predictor of longer DSS and OS.

Conclusions: In women with recurrent early-stage endometrial carcinoma, our study suggests that the site of recurrence (pelvic vs extrapelvic) is the only predictor of survival. In addition, we found that radiation naiveté correlated with longer DSS, while low-grade tumors and pelvic-only recurrence were associated with a significantly improved DSS and OS. Longer time to recurrence and type of salvage treatment were not significant predictors of DSS and OS.

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Older age is no longer an adverse prognostic factor in women with early-stage endometrial carcinoma: A matched analysis

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Objectives: Older age is viewed as an adverse prognostic factor in women with endometrial carcinoma (EC). It is unclear whether this is because of its interaction with other well-known adverse prognostic factors or its independent prognostic impact. To study this issue, survival endpoints were compared between 2 groups of patients with early-stage EC solely of endometrioid histology: women 70 years or older (group 1) and similarly matched younger women (group 2).

Methods: We identified 1,254 patients with 2009 FIGO stage I-II EC who underwent hysterectomy at our institution between January 1990 and December 2014. We created 2 matched groups based on FIGO stage, tumor grade, lymph node dissection status, and the type of adjuvant management (observation, pelvic external beam, or vaginal brachytherapy). Recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) were calculated for the 2 groups.

Results: A total of 594 women were included in this study in 2 groups (each with 297 patients, matched 1:1). Median follow-up was 50 months. The two groups were well balanced except for age ($P < .001$) and higher body mass in younger patients ($P < .001$). There was no significant difference in the site of initial recurrence between the 2 groups. There were no significant differences between older and younger patients with regard to 5-year RFS (85% vs 87%, $P = .52$). Similarly, there was no significant difference with regard to DSS (93% for both groups, $P = .77$). As expected, 5-year OS was shorter in older patients (76% vs 88%, $P < .001$). On multivariate analysis for RFS and DSS, high tumor grade and the presence of lymphovascular space invasion (LVSI) were the only 2 predictors of shorter RFS and DSS ($P = .01$, $P = .02$) and ($P = .01$, $P = .01$), respectively. In addition to older age ($P < .001$), high tumor grade and the presence of LVSI were the only predictors of shorter OS ($P = .03$ and $P = .02$, respectively).

Conclusions: Although older age is viewed as an adverse prognostic factor in women with early-stage EC, our study suggests that when older patients are matched with younger patients based on tumor stage, grade, and adjuvant management, the prognostic effect of old age disappear. High tumor grade and the presence of lymphovascular invasion remained as independent predictors of survival endpoints in women with early-stage EC.

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Predictive capacity of 3 comorbidity indices in estimating survival endpoints in women with early-stage endometrial carcinoma

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Objectives: The negative impact of medical comorbidity on survival endpoints in women with endometrial carcinoma (EC) is well known. Few validated comorbidity indices are available for clinical use, eg, Charlson Comorbidity Index (CCI), Age-Adjusted Charlson Comorbidity Index (AACCI), and Adult Comorbidity Evaluation-27 (ACE-27). The study goal is to evaluate which index correlates the best with survival endpoint in women with early-stage EC.

Methods: For this institutional review board–approved study, we identified 1,132 women with endometrioid carcinoma FIGO stages I-II who underwent hysterectomy from 1987 to 2011. The 3 comorbidity indices at the time of hysterectomy were retrospectively calculated by physician chart review. Univariate and multivariate modeling with Cox regression analysis was used to determine the significant predictors of survival endpoints. Kaplan-Meier and log-rank test methods were used to evaluate survival outcomes.

Results: After a median follow-up of 60 months, 262 deaths were recorded (42 from EC [16%] and 220 [84%] from other causes). For each of the studied comorbidity indices, the highest scores were significantly correlated with poorer overall survival (OS). The hazard ratio of death from any cause was 3.92 (95% CI 2.95–5.20) for AACCI, 2.25 (95% CI 1.73–2.94) for CCI, and 1.57 (95% CI 1.23–2.01) for ACE-27. Lymphovascular space involvement, tumor grade, lower uterine segment involvement, and AACCI were independently predictive of OS. None of the 3 comorbidity indices were significantly predictive of disease-specific or recurrence-free survival.

Conclusions: While all 3 comorbidity indices were significantly correlated with OS in women with early-stage EC, age-adjusted Charlson comorbidity index was the only independent predictor of OS and should be considered for evaluating comorbidity in future EC patients.

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Epidemiologic characteristics of ovarian cancer in Korean women

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Objectives: This study was designed to evaluate the epidemiologic characteristics of ovarian cancer in Korean women, and to provide references for further understanding the actual status and planning with regard to screening and treatment modalities.

Methods: We collected data including the age-standardized incidence rates (ASR), prevalence rates, disease spreading, and survival rates from the websites of the Statistics Korea and Korea Central Cancer Registry from 1999 to 2012.

Results: A total of 23,594 women were diagnosed with ovarian cancer from 1999 to 2012. Despite a minor decline in the total cases of ovarian cancer in 2000 and 2009, it has been steadily increasing and has peaked up to 2,167 cases in 2012. The ASR of ovarian cancer has also shown steadily increasing tendency from 5.5 per 100,000 women in 1999 to 6.5 per 100,000 women in 2012. A similar increasing trend was noted in the case of age-standardized prevalence rates, with a peak of 23 per 100,000 in 2012. The mean age-specific incidence rate peaked in the 75 to 79 year olds and 80 to 84 year olds in 1999 to 2002. After that, however, it has peaked at younger ages over the years, such as the age group of 60 to 64 years in 2010 to 2012. In the analysis of disease spreading, distant disease was the most common (41.1%), followed by localized (27.7%), regional (15.8%), and unknown (15.5%) disease among 12,903 women diagnosed with ovarian cancer. The 5-year survival rates of the women with ovarian cancer showed a steadily increasing trend from 58.7% in 1993 to 1995 to 61.9% in 2008 to 2012.

Conclusions: An increasing trend of the incidence and ASR of ovarian cancer is evident, especially in postmenopausal women. With the excellent medical insurance system and accessibility to health care, however, early disease was more common compared with previous reports. The 5-year survival rate of women with ovarian cancer was relatively poor compared with other gynecologic malignancies like cervical and uterine cancer.

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Fertility preservation and pregnancy outcomes in women with cervical cancer following robotic radical trachelectomy

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Objectives: Given the increasing use of robotic radical trachelectomy (RRT) in early-stage cervical cancer with limited obstetric outcomes data, we sought to describe rates of fertility preservation and pregnancy outcomes after RRT.

Methods: A retrospective cohort study was conducted of all women undergoing attempted fertility-preserving RRT at a single institution from May 2007 to June 2015. Demographic, pathologic, and surgical variables were collected. Patient phone interviews were conducted to ensure completeness of data. Descriptive statistics were used.

Results: Of 28 women who underwent RRT, median age was 29 years (range, 17–39 years), median body mass index (BMI) was 25 kg/m2 (range, 18–35), and median distance traveled was 129.5 miles (range, 20–1,057 miles). Stage distribution was IA1 with lymphovascular space invasion (LVSI) - IA2 (25%), IB1 (68%), and IB2-IIA (7%). Final histology was squamous (54%), adenocarcinoma (36%), or other (11%). LVSI was present in 39%. No patients had parametrial or nodal involvement. Median OR time was 217 minutes (range, 129–377 min). There were no intraoperative complications. Nine women (32%) had 30-day complications (urinary tract infection 7%, abscess 11%, lymphocyst 7%). The 30-day readmission rate was 14% (n = 4). Six women (21%) had a chronic complication (cervical stenosis 7%, lymphedema 4%, dyspareunia 4%, postcoital bleeding 7%). There were 2 recurrences (7%) and 1 death (4%) at a median follow-up of 12 months (range, 1–83 mo). Fertility was preserved in 82%. Loss of fertility was associated with higher stage (P = .005), tumor size greater than 2 cm (57% vs 5%, P = .009), and residual cancer in trachelectomy specimen (33% vs 9%, P = .026). Age, race, BMI, histology, OR time, LVSI, and complications were not associated with loss of fertility. Of 23 women retaining fertility, 12 have attempted or are attempting pregnancy. There have been 10 pregnancies, all conceived spontaneously, among 8 women, at a median follow-up time of 12 months (range, 1–83 mo). Median time to conception was 23 months (range, 9–70 mo). Seventy percent of

pregnancies ended in live birth with 4 at more than 37 weeks, 3 at 35 to 37 weeks, and no births at less than 35 weeks. Of pregnancies not ending in live birth, 2 were elective abortions and 1 was a molar pregnancy.

Conclusions: Fertility was preserved in most women undergoing RRT. RRT offers women a choice after a diagnosis of cervical cancer with acceptable obstetric outcomes.

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Validity of currently available venous thromboembolism risk scores among gynecologic oncology patients

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Objectives: Gynecologic oncology patients undergoing surgery are at a high risk of venous thromboembolism (VTE). Risk assessment models, such as the Caprini and Rogers score, have been validated and applied in some surgical disciplines. However, their performance in a large gynecologic oncology population is unknown.

Methods: Patients undergoing surgery for cervical, ovarian, uterine, vaginal, and vulvar cancers between 2008 and 2013 were identified from the National Surgical Quality Improvement Database using ICD-9 codes. Demographic, procedure, and complication data were collected. Caprini and Rogers scores were calculated for each patient. VTE events were defined as a deep vein thrombosis (DVT) requiring therapy or a pulmonary embolism (PE) and were recorded for 30 days postoperatively.

Results: Of 17,713 patients, 1.8% developed VTE (DVT 1.0%, PE 0.9%, and 0.2% both DVT and PE). There were 13 deaths among VTE patients and 30-day mortality was 0.7% for the entire population and 4.2% for patients with VTE ($P < .0001$). No patients were classified by the Caprini score as low risk, 0.1% were medium risk, 3.0% were high-risk (score 4), and the remaining 96.9% were highest risk (score >5). The Caprini score did not correlate with VTE. The high-risk group had a paradoxically higher incidence of VTE of 2.5% compared with the highest-risk group, 1.7% ($P = .40$). However, when the highest risk Caprini score group was substratified, it was accurate in predicting VTE. The incidence of VTE was 1.2% (score 5), 1.3% (score 6), 2.1% (score 7), and 2.5% (score >8). The relationship was linear ($R^2 = 0.93$, $P = .02$). The Rogers score performed well. Only 0.2% of patients were low risk (score <7), 36.9% were medium risk (score 7–10), and 63.0% were high-risk (score >10). VTE incidence and the Rogers score had a linear relationship ($R^2 = 0.998$, $P = .026$). The low-risk group had a VTE incidence of 0%, the medium-risk group was 1.03%, and the high-risk group was 2.21%.

Conclusions: Gynecologic oncology patients score very high on current VTE risk assessment models. The Caprini score does not accurately discriminate relative VTE risk among gynecologic oncology patients, because 97% are in the highest-risk category. However, a modified version of the Caprini score and the Rogers score accurately identify VTE risk among gynecologic oncology patients.

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Epithelial-mesenchymal transcription factor Snail contributes to progression of ovarian cancer via let-7 miRNA repression

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Objectives: Metastasis of epithelial ovarian carcinomas (EOC) involves epithelial-mesenchymal transition (EMT) mediated by transcription factors, such as Snail. Snail binds to the promoter region of tumor suppressor let-7 microRNAs (miRNAs). Low let-7 levels correlate with decreased survival in EOC. We aimed to characterize the mechanism of Snail and let-7 interactions and their impact on metastasis progression, using: (1) EOC cell lines, and (2) orthotopic patient-derived mouse xenograft (PDX) model with Snail knockdown (KD).

Methods: *Cell lines:* OVSAHO (EOC cell line) was treated with epidermal growth factor to induce EMT. Gene expression of Snail and let-7 family miRNAs was analyzed with quantitative polymerase chain reaction (qPCR). Let-7i promoter luciferase with and without Snail were cotransfected into OVSAHO and 293T (human embryonic kidney) cell lines and followed by measurements of luciferase activity. *Orthotopic xenografts:* Six-week-old nude (J:NU) mice, 5 per experiment, underwent ovarian bursa injections of luciferized: (1) A2780 (1×10^6 cells), (2) OVCAR8 control versus Snail KD (5×10^5 cells), and (3) patient-derived EOC cells (control) versus Snail KD (5×10^5 cells). Bioluminescence was quantified (IVIS Lumina) over 21 days; mice were then sacrificed because of high tumor burden.

Results: *EOC cell lines:* Increased expression of Snail correlated with decreased let-7 expression in OVSAHO cell line on qPCR. Cotransfection of Snail significantly repressed let-7i promoter luciferase activity in both OVSAHO and 293T cell lines ($P < .03$; 2-tailed t test). *Orthotopic xenografts:* EOC cell line xenograft and PDX reproducibly phenocopy EOC in terms of primary tumor growth and metastasis progression over 21 days after injection, as quantified by bioluminescence and direct measurements. Preliminary data demonstrate decreased tumor burden via bioluminescence quantification in Snail KD versus control in PDX (Figure 1) and OVCAR8 Snail KD versus control xenografts (data not shown).

Conclusions: We propose that the inverse relationship between Snail and let-7 miRNA plays an important role in EOC metastasis. Our collaborators have demonstrated that delivery of mesoporous silica nanoparticles (MSNs) loaded with modified Twist (another EMT TF) siRNA result in smaller breast cancer tumors in xenografts. Further studies are underway to develop a similar experimental set up in our EOC PDX model.

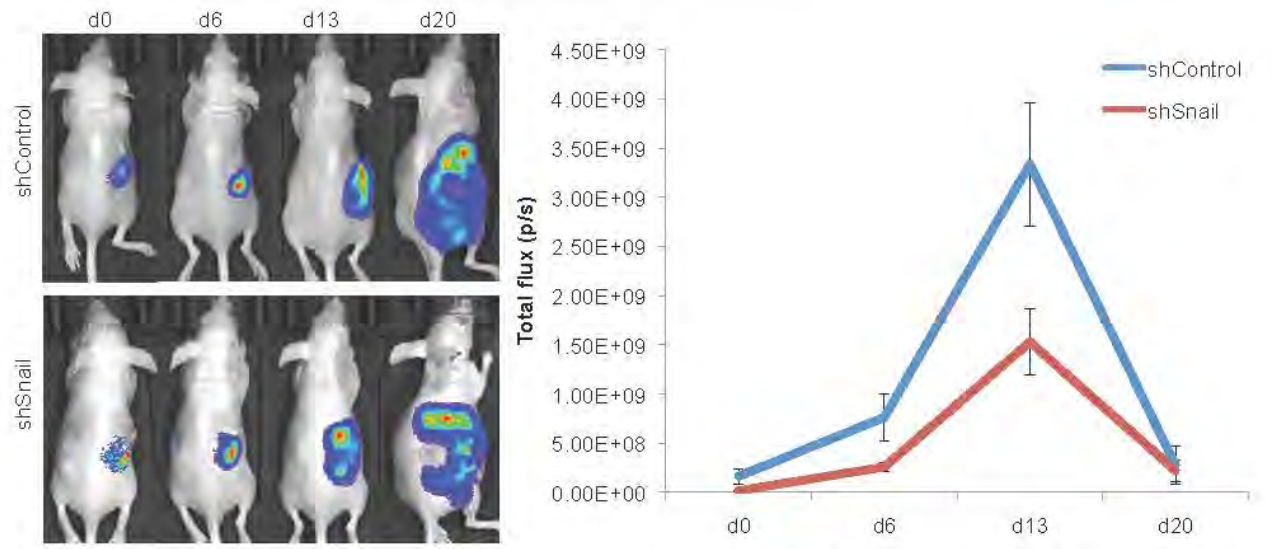

Figure 1. Bioluminescent assessment of tumor progression post ovarian bursa injection of luciferized patient-derived epithelial ovarian cancer cells collected upon initial presentation from ascitic fluid. Lentivirally-delivered shRNA was used to knock down Snail (shSnail) or control (shControl) in cells from the same patient sample. Cells were injected into nude mice orthotopically (ovarian bursa) on day 0. Left panel: Photos represent bioluminescence (IVIS Lumina) on days 0,6,13, and 20 post injection. Right panel: Quantitation of bioluminescence (total flux, photons per second). N=3. Error bars: standard error.

Fig.1
Tumor Progression Post Ovarian Bursa Injections of Patient-derived Ovarian Cancer Cells, Control vs. Snail Knockdown.

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The DISINFECT initiative: Decreasing the incidence of surgical INFECTions in gynecologic oncology
J.S. Taylor, C.A. Marten, D.C. Bodurka, J.K. Burzawa, M.F. Munsell, K. Potts, A.M. Nick, L.A. Meyer, C.F. Levenback and K.M. Schmeler. *The University of Texas MD Anderson Cancer Center, Houston, TX, USA*

Objectives: To evaluate the impact of a bundled intervention on surgical site infection (SSI) rates after surgery for gynecologic cancer.

Methods: We performed a quality improvement (QI) project to decrease SSI rates after open and minimally invasive surgery (MIS) using the following interventions: patient education; preoperative antibacterial soap; appropriate antibiotic prophylaxis with redosing; change of gloves and use of clean instruments at surgical closure; surgical dressing for 48 hours; and a postdischarge phone call to assess for infection. SSI was defined as an infection of the surgical incision or organ space requiring antibiotics. Baseline SSI rate within 30 days of surgery was obtained from chart review (May 1, 2014, to June 30, 2014) and compared with postintervention (April 16, 2015, to July 15, 2015) data. Patient demographics, clinical characteristics, compliance, and SSI rates were compared between groups using the Fisher exact and Mann-Whitney tests.

Results: A total of 166 baseline cases were compared with 241 postintervention cases. Median body mass index for the baseline and postintervention groups was 27.6 and 28.2 kg/m^2, respectively (P = .66). Seventy-five baseline MIS surgeries (45%) were performed versus 138 (58%) in the postintervention cases (P = .02). Disease sites in the baseline and postintervention groups included the ovary (51% vs 33%), uterus (22% vs 25%), cervix (4% vs 9%), and benign disease (23% vs 34%). Chemotherapy and/or radiotherapy was given preoperatively in 37 (22%) baseline cases compared with 36 (15%) postintervention cases (P = .07). Bowel resection was performed in 44 (27%) and 58 (24%) baseline and postintervention cases, respectively (P = .64). Overall SSI rate decreased from baseline to postintervention (12% vs 6.6%, P = .04). Skin infections (superficial and deep) decreased by half from baseline (9%) to postintervention (4.6%; P = .05) (odds ratio [OR] 0.48, 90% CI 0.24–0.94). However, organ space infections did not differ (3.6% baseline vs 2.9% postintervention, P = .44). SSI after open surgery also decreased by half (20% vs 11%, P = .05) (OR 0.48, 90% CI 0.24–0.95) but not after MIS (2.7% vs 3.6%, P = .52). Postintervention compliance was 61% for preoperative antibacterial soap; 91% for glove change; and 88% for closing instruments. Correct prophylactic antibiotic use was not different (69% baseline vs 75% postintervention, P = .13), but antibiotic redosing improved postintervention (87% baseline vs 94% postintervention, P = .02).

Conclusions: This interim analysis of an ongoing QI project found a significant decrease in overall SSI rates using a bundled intervention. The largest decreases were seen in skin infections and SSI after open surgery.

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Molecular pathogenesis of endometrial intraepithelial neoplasia: Precursor to endometrial cancers
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Objectives: To characterize the relationship between DNA mismatch repair (*MMR*), *ARID1A*, and *PTEN* in endometrial intraepithelial neoplasia (EIN).

Background: Type 1 endometrial carcinoma typically develops from a precursor lesion, endometrial hyperplasia, or EIN. The DNA *MMR* system prevents tumor progression by correcting errors that occur during DNA replication and is present in a proportion of endometrial cancers. Tumor suppressor genes *ARID1A* and *PTEN* are also implicated in the molecular pathogenesis of endometrial carcinoma. Previous studies have shown that in endometrial carcinoma, *MMR* deficiency may be associated with *ARID1A* mutations. However, in EIN, the relationship between loss of expression (LOE) of *MMR*, *ARID1A*, and *PTEN* has yet to be established.

Methods: A retrospective review identified 113 patients with EIN on endometrial biopsy from 2009 to 2014. Tissue microarray blocks were evaluated with immunohistochemical stains using antibodies against *MLH1*, *PMS2*, *MSH2*, *MSH6*, *ARID1A*, and *PTEN*. Statistical analyses were performed using a value of $P < .05$ as statistically significant.

Results: In EIN, LOE rates of *MMR*, *ARID1A*, and *PTEN* were 4.4% (n = 5), 6.2% (n = 7), and 50.4% (n = 57), respectively. LOE of *MMR* was not significantly associated with expression of *ARID1A* (P = 1.000) or PTEN (P = .2062). Development of a subsequent invasive malignancy was not significantly associated with LOE of *ARID1A* (P = .1135), DNA *MMR* (P = .2424), or *PTEN* (P = .1670). When combined, LOE of *ARID1A* and *MMR* was significantly associated with subsequent cancer (P = .0109).

Conclusions: In this series of EIN, the LOE frequency of PTEN (50.4%) agreed with that seen in previous studies. Unlike rates demonstrated in endometrial carcinoma, the proportion of LOE of *MMR* (4.4%) and *ARID1A* (6.2%) seen in the precursor lesion were relatively low and thus seems to be nonessential in the development of EIN. There were no cases of concordant LOE of *MMR* and *ARID1A*, suggesting independent pathways or differences in temporal patterns in gene expression during the premalignant phase. When combined, LOE of *ARID1A* and *MMR* was significantly associated with the development of a subsequent malignancy, suggesting potential prognostic markers, which will require further evaluation.

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180 - Poster
Comparing sexual health history collection preferences among gynecologic oncology patients and OB/GYN patients
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Objectives: Following radiation therapy (RT), gynecologic oncology patients report high rates of sexual dysfunction. However, little is known regarding preferences of communication of sexual health among these patients and their healthcare providers. The aim of this study was to compare the attitudes of female oncology and benign obstetrics/gynecology (ob/gyn) patients about overall sexual health and preferences regarding sexual history collection.

Methods: Survey results were obtained from 75 women who presented for follow-up care for gynecologic cancers in the radiation oncology department and 383 women seeking care in the outpatient ob/gyn setting. The survey included the female sexual function index (FSFI), questions about perception of sexual function changes related to aging, and patients' preferred method of sexual history collection among the following options: filling out a form, with nursing staff in person, with primary care physician in person, with ob/gyn in person, or by online survey. X^2 tests were used to analyze the survey results.

Results: Of women who underwent RT for gynecological cancer 53.3% agreed that sexual problems are an unavoidable part of aging, while 36.2% of benign patients agreed with this statement (P = .023). Forty-four percent of women who underwent RT reported giving their sexual history to a physician as their preferred sexual health history collection method compared with 55.4% of benign patients (P = .028). While 29.3% of female oncology patients and 23.0% of ob/gyn patients listed filling out a form as their primary preference, only 4.0% and 2.7% of patients, respectively, chose an online survey as their most preferred method. Few patients selected nursing staff in person as their primary preference.

Conclusions: Gynecologic oncology patients who received RT were more likely to accept declines in sexual function as normal aging and less likely to prefer communicating sexual history directly to their physicians compared with women without cancer. Both groups listed online survey as their least preferred method of sexual history collection. To improve the quality of cancer survivorship among gynecologic oncology patients, further study is needed to determine best methods of ascertaining sensitive sexual health information.

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181 - Poster

Who presents satisfied? Factors associated with patient satisfaction among gynecologic oncology patients

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Objectives: Patient satisfaction (PS) is used as a quality metric in cancer care. However, non-modifiable factors may be associated with PS. We examined associations between patient factors and PS among women presenting to a gynecologic oncology clinic.

Methods: Patients seeking surgical management at a tertiary care center were enrolled in a prospective cohort study over 12 months. The Patient Satisfaction Questionnaire (PSQ-18) was administered. It measures PS in 7 domains of health care: general satisfaction, technical quality, interpersonal manner, communication, financial aspects, time with doctors and accessibility on a 5-point Likert scale. Scores were converted to "satisfied" versus "unsatisfied/equivocal" based on a cutoff of 3.5. Demographics and medical factors were obtained from the medical record. X^2, t test, and multivariable logistic regression were used.

Results: A total of 208 patients were enrolled. Median age was 58 years (22–93 years) and median PSQ-18 score was 70.5 (42–90). The study included 78.4% white (n = 165), 16.8% black (n = 38), and 4.8% other minorities (n = 5). Education level was as follows: 25.5% had a high school education or less (n = 53), 31.7% had some college/trade school education (n = 66), and 42.8% were college graduates or higher (n = 89). Insurance status was as follows: 7.2% uninsured (n = 15), 8.7% Medicaid/Medicare alone (n = 18), and 84.1% some private insurance (n = 175). Several non-modifiable factors were associated with PS. White patients had higher interpersonal PS than minorities (86.1% vs 65.1%, P < .01). The uninsured had lower interpersonal (60.0% vs 83.4%, P = .02), financial (26.7% vs 60.6%, P = .01), and accessibility (33.3% vs 67.4%, P = .01) PS. Increasing education was associated with higher interpersonal (P = .03) and accessibility (P = .01) PS. Less time traveled was associated with accessibility PS (P = .01). There was no association between clinical factors (age, body mass index, comorbidities, or cancer) and PS. On multivariable logistic regression, white race (adjusted odds ratio [aOR] 2.7, 95% CI 1.2–6.0) and each 20 minutes less traveled (aOR 1.2, 95% CI 1.03–1.3) were the strongest drivers of PS.

Conclusions: Patient satisfaction scores among patients presenting to a gynecologic oncology clinic are associated with non-modifiable demographic, financial, and geographic factors. Pay for performance measures that use summed PS scores may penalize hospitals for patient-mix driven inequities.

182 - Poster

Accuracy of the EasyChip HPV blot genotyping assay in detecting high-risk HPV genotypes in SurePath Pap specimens

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Objectives: The EasyChip human papillomavirus (HPV) blot is a commercially available HPV genotyping assay that can be used for HPV assay validation or clinical HPV research. To evaluate its genotyping accuracy, we compared the EasyChip HPV blot with real-time/HPV type-specific polymerase chain reaction (PCR) assays in detecting the 8 high-risk HPV types in SurePath Papanicolaou (Pap) cytology specimens.

Methods: One hundred fifty-four SurePath Pap specimens with abnormal Pap test results and HPV genotyping results using the EasyChip HPV blot obtained at our institution were selected. A real-time PCR assay was used to detect the 8 HPV genotypes (HPV16, 18, 31, 33, 35, 45, 52, and 58). An HPV type-specific PCR assay was used to resolve the discrepancies in the results between the 2 HPV assays. HPV genotyping concordances between EasyChip HPV blot and PCR assay results were evaluated.

Results: A total of 95 Pap specimens were qualified for data analysis (Table 1). We observed high concordances between EasyChip HPV blot and real-time/type-specific PCR assay results, with very good agreement collectively for the 8 high-risk HPV genotypes (94%; κ value, 0.874, 95% CI 0.776–0.971) (Table 2) and for HPV16 and HPV18 (96%; κ value, 0.899 95% CI 0.802–0.996) (Table 3). HPV16 was the most frequent HPV genotype (24%) according to the EasyChip HPV blot. HPV16/18 positivity increased in parallel with the abnormal Pap classification grade (21% in atypical squamous cells of undetermined significance specimens to 69% in high-grade squamous intraepithelial lesion specimens) and the dysplastic severity on follow-up biopsy analysis (13% in cervical squamous intraepithelial neoplasia [CIN] type 1 specimens to 72% in CIN 3 specimens).

Conclusions: The EasyChip HPV blot is a reliable HPV genotyping assay that can be used for HPV assay validation and clinical HPV studies.

Table 1

Distribution of Pap Cytology and Follow-up Biopsy Results (n=95).

Pap Results	**Follow-up Biopsy (%)**					
	Benign	**CIN1/VAIN1**	**CIN2/VAIN2**	**CIN3/VAIN3**	**Carcinoma**	**Total**
ASC-US	9 (20)	24 (55)	4 (9)	5 (11)	2 (5)	44
ASC-H	1 (25)	0	0	2 (50)	1 (25)	4
LSIL	0	21(62)	10 (29)	2 (6)	1 (3)	34
HSIL	0	0	0	9 (69)	4 (31)	13
Total	10	45	14	18	8	95

CIN: cervical intraepithelial neoplasia; VAIN: vaginal intraepithelial neoplasia
ASC-US: atypical cells of undetermined significance
ASC-H: Atypical squamous cells of undetermined significance-cannot exclude HSIL
LSIL: low grade squamous intraepithelial lesion
HSIL: High-grade squamous intraepithelial lesion

183 - Poster

Comparison of serum CA-125 and human epididymis protein 4 (HE4) in response assessment after neoadjuvant chemotherapy in advanced-stage ovarian carcinoma

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Objectives: Primary cytoreduction is challenging in patients who present with extensive intra-abdominal disease. This makes a rationale for a neoadjuvant chemotherapy approach in these patients. CA-125 levels and radiological imaging are currently used to assess response after neoadjuvant chemotherapy. This study was conducted to determine the role of serum HE4 levels in response assessment after neoadjuvant chemotherapy in these patients.

Methods: This prospective study includes 44 patients including 28 stage IIIC (63.6%) and 16 stage IV (36.4%) patients. Standard neoadjuvant chemotherapy (3 to 4 cycles of paclitexal and carboplatin) was given after confirming the diagnosis with fine-needle aspiration cytology or biopsy. Serum CA-125 and HE4 levels along with imaging were done before starting neoadjuvant chemotherapy and before interval cytoreduction. Response to chemotherapy was assessed and correlated with changes in CA-125 and HE4 levels.

Results: Mean change in values of CA-125 and HE4 before and after neoadjuvant chemotherapy were 1,173.28 ± 367.30 and 1,125.02 ± 384.72, respectively (*P* = .0001 each). The sensitivity, specificity, and positive and negative predictive value of CA-125 in predicting response were 92.3%, 22.22%, 63.1%, and 66.6%, respectively. Both the sensitivity and negative predictive value of HE4 was 100%. The specificity and positive predictive value of HE4 were 94.11% and 96.42%, respectively. Overall accuracy of CA-125 and HE4 to predict response was 63.63% versus 97.72%. Among patients in whom HE4 levels normalized after neoadjuvant chemotherapy, no non-responders were identified in this subgroup. This is in comparison to the finding that one-third of patients who were actually non-responders showed normalization of CA-125 levels.

Conclusions: Our results show that HE4 is a useful and better marker than the traditionally used CA-125 to assess response of neoadjuvant chemotherapy in advanced-stage ovarian cancer patients who are not ideal candidates for upfront surgery. It should be studied further and should be considered in incorporating in guidelines for response assessment in ovarian carcinoma patients undergoing neoadjuvant chemotherapy.

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184 - Poster

Upregulation of long noncoding RNA HOXA11 antisense promotes tumor progression and stemness maintenance of cervical cancer cells

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Objectives: Despite progress in diagnostics and treatment, the prognosis for cervical cancer remains poor. Long noncoding RNA (LncRNAs) may be useful biomarkers of poor prognosis and tumor metastasis in several cancers. However, the functions of ncRNAs are only partially understood. HOXA11 antisense RNA (nonprotein coding), also known as HOXA11 AS, is an LncRNA that is transcribed from the antisense strand of the gene encoding the homeobox gene *HOXA11*. HOXA11 AS negatively regulates the expression of the *HOXA11* gene. In this study, we examined the expression and the functional role of HOXA11 AS in cervical cancer.

Methods: The effects of a specific differentially expressed HOXA11 AS on tumor progression were investigated in vitro and in vivo. HOXA11 AS expression was determined in cervical cancer tissues (n = 95) and corresponding normal tissues (n = 30) with real-time reverse transcriptase polymerase chain reaction. To determine the role of HOXA11 AS in cell proliferation, migration, and invasion, RNA interference was used to knock down HOXA11 AS expression in HeLa and Caski cervical cancer cells.

Results: The expression of HOXA11 AS in cervical cancer tissues was significantly higher than that in normal tissues. Knock down of HOXA11 AS decreased cell proliferation, migration, and invasion in HeLa and Caski cells. In addition, HOXA11 AS knock down decreased the expression of vascular endothelial growth factor, matrix metalloproteinase-9, and epithelial-mesenchymal transition (EMT), which are important for cell motility and metastasis. Functionally, knock down of HOXA11 AS inhibited tumor growth. Furthermore, we observed that the cervical cancer stem cell (CSC) subpopulation (CD133+/CD44+) presents much higher levels of HOXA11 AS compared with the non–stem cell subpopulation. These results indicate that HOXA11 AS acts as a key regulator that controls the multiple signaling mechanisms involved in EMT. Altogether, our data suggest that the role of HOXA11 AS in tumorigenesis occurs through EMT triggering and stemness acquisition.

Conclusions: HOXA11 AS is highly expressed in cervical cancer tissues and is associated with cervical cancer progression. Our data have shown that HOXA11 AS expression drives EMT and CSC formation in different cancer cell lineages. These findings suggest that HOXA11 AS promotes tumorigenesis by activating the EMT genetic program. HOXA11 AS may represent a novel biomarker for prognosis and serves as a promising therapeutic target in cervical cancer.

185 - Poster

Risk factors to predict vaginal, pelvic/abdominal recurrence or distant metastasis in patients with low-grade endometrial endometrioid adenocarcinoma: Multi-institutiona

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Objectives: Low-grade endometrial endometrioid adenocarcinomas (LGEECa) can recur in the vagina (VRec), pelvic and abdominal region (PARec), or distant sites (DMet). Tumor size, histopathologic features, and lymph node involvement at presentation have been linked to the development of these recurrences. However, the amount of information on risk factors to predict site of recurrence is limited.

Methods: In this multi-institutional study, we analyzed data from 589 patients with FIGO grades 1 and 2 LGEECa and found 116 patients with VRec, PARec, or DMet. They were compared with 187 age-matched controls with negative lymph nodes, no adjuvant treatment, and no recurrences; mean follow-up times were 44 and 59 months, respectively. Cox proportional hazards analysis was used to identify univariable and multivariable risk factors for each type of recurrence ($P < .05$).

Results: Forty-one patients had VRec, 33 had PARec (pelvic soft tissue, 14; abdominal tissue, 9; liver capsule, 5; retroperitoneum, 3; colorectal wall, 2), and 42 had DMet (lung, 19; lymph nodes, 17; bone and soft tissue, 5; brain, 1) as the initial site of recurrence. Univariate and multivariate analysis of histopathologic features are summarized in Table 1. In addition, features associated with vagina-only recurrence included superficial myometrial invasion ($P = .002$); low nuclear grade ($P = .03$); lymphovascular invasion (LVI) adjacent to tumor, but not deeper than invasive tumor front ($P < .001$); less than 5% microcystic elongated and fragmented pattern (MELF) at invasive tumor front ($P = .014$); and no pelvic lymph node metastasis at presentation ($P = .019$). These features were not significantly different from controls.

Conclusions: (1) Features of LGEECa that predicted VRec included superficialy invasive, low nuclear grade tumors with minimal MELF, minimal or no LVI, and no lymph node metastasis. These features were more closely related with tumors that did not recur than with recurrent tumors. (2) LGEECa with PARec differed from those with VRec, because the tumors were larger and deeply invasive and MELF at invasive tumor front, suggesting a different dissemination route than tumors with VRec. (3) Significant predictor features of LGEECa with DMet included intraglandular tumor necrosis, cell clusters at the invasive front and adjacent to areas of LVI, and cervical stromal involvement. The latter feature might be indicative of venous rather of lymphatic invasion.

Table 1

Most significant predictors of site of recurrence in low grade endometrial carcinoma.

Predictors of specific site recurrence	DMet (42)	PARec (33)	VRec (41)
Size > 3 cm	$P < 0.03$	$P < 0.04$	No
Necrosis	$P < 0.03$	No	No
Solid component > 10%	No	$P < 0.009$ *	No
Depth of MI > 10 mm	$P < 0.002$	$P < 0.02$	No
Myoinvasion > 70%	$P < 0.02$	$P < 0.05$	No
MELF at invasive tumor front	$P < 0.001$	$P < 0.005$	No
Cell clusters at invasive tumor front	$P < 0.03$	No	No
Cell clusters adjacent to LVI foci	$P < 0.001$ *	No	No
LVI	Any foci ($P < 0.003$); Any location ($P < 0.001$)	>5 foci ($P < 0.03$); deeper than tumor front ($P < 0.04$)	One or less foci ($P < 0.03$)
Cervical stromal involvement	$P < 0.004$	No	$P < 0.05$

LUS	No	$P < 0.03$	No
LN metastasis	Any pelvic ($P < 0.01$); Any paraaortic ($P < 0.03$)	> 5 pelvic LNs; ($P < 0.03$) *	No
Treatment	Increased recurrence rate in pts with any treatment modality ($P < 0.001$)	Increased recurrence rate in pts with chemotherapy only ($P < 0.001$)	No

LVI= lymphovascular invasion; LN= lymph node; LUS, lower uterine segment; MELF, microcystic elongated and fragmented pattern; MI, myometrial invasion; pts= patients
* persisted in multivariate analysis

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Changes in the ovarian microenvironment due to physiologic and iatrogenic aging
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Objectives: During the female reproductive lifespan, the fixed number of primordial follicles declines with a complete cessation of reproductive function at menopause. Radiation therapy, a major treatment modality for various cancers, can accelerate this process through germline DNA damage resulting in compromised fertility outcomes. Much less is known about how aging affects the ovarian microenvironment, which consists of fibroblasts, immune cells, and endothelial cells. We hypothesize that aging—both physiologic and iatrogenic (due to ionizing radiation)—alters the ovarian stroma through extracellular matrix (ECM) remodeling, tissue fibrosis, and chronic sterile inflammation.

Methods: Using a physiologic aging mouse model (6–12 weeks and 14–17 months; CB6F1 and CD1 strains), we analyzed the relationship between reproductive age and stromal changes in the mammalian ovary. We used standard histologic methods to quantify the ovarian reserve. Masson trichrome and Sirius red stains along with immunocytochemistry (with antibodies for collagen I/IV, fibronectin, laminin) showed a reorganization of ECM and basement membrane. Fluorescence microscopy with a macrophage-specific antibody (F4/80) and electron microscopy was used to show increased presence of macrophages in aged ovaries.

Results: Aging was associated with altered levels and organization of ECM and basement membrane proteins. Evidence of increased fibrosis was noted in aged ovaries with significant macrophage infiltration.

Conclusions: Striking age-related changes in the ovarian stroma occur and likely represent a suboptimal milieu for follicular development that ultimately contributes to poor gamete quality. Experiments are ongoing to determine whether cellular senescence underlies these changes and whether similar mechanisms occur in response to irradiation treatment. These experiments will provide further insight into the pathophysiology of radiation therapy.

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187 - Poster
Cerclage during trachelectomy for early-stage cervical cancer
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Objectives: Cervical cancer is one of the most commonly diagnosed cancers for women of reproductive age in the United States. Fertility-preserving options such as trachelectomy for early-stage cervical cancer may allow these patients to conceive; however, after trachelectomy, these patients are at risk for obstetric complications. This survey's objective is to better understand practices to standardize and optimize outcomes for patients undergoing this procedure.

Methods: An electronic survey was taken of all Society of Gynecologic Oncology (SGO) members. Eligible participants were identified using the 2015 SGO membership directory. We collected demographic information as well as participants' current practices and opinions on cerclage placement at the time of trachelectomy. Whether a surgeon performs cerclage at the time of trachelectomy was evaluated for association with surgeon characteristics, including years of practice, gender, age, practice setting, and geography.

Results: A total of 1,598 members were sent an electronic survey, with 121 completed for analysis. Of the 121 surveyed, 66% report placing cerclages at the time of trachelectomy. Participants were identified as strictly academic

(51%), community-affiliated academic (41%), or strictly private practice (5%). Eighty-eight percent of participants were from the United States, with the east and west coast representing 19% and 17%, respectively. With regard to conserving the uterine artery, 58% of respondents report doing so and 41% of respondents reported not doing so. Most (95%) use a cephalosporin for preoperative surgical site infection prophylaxis. Forty-seven percent of respondents use prolene suture, 10.5% use goretex, 33% use mersilene, and 9% use ethibond or nylon. About 13.7% of respondents recommend waiting at least 3 months before attempting conception, 39% of respondents recommended waiting 6 months before attempting conception, 39% of respondents recommended waiting 12 months, 2% of respondents recommended waiting 24 months, and 4% recommended waiting other periods (typically longer). The most common complication from these procedures was cervical stenosis in 50% of respondents.

Conclusions: Sixty-six percent of physicians perform cerclage at the time of trachelectomy for early-stage cervical cancer. There is significant variation in the methods surrounding placement of the cerclage at the time of trachelectomy for cervical cancer.

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Surgical trainee participation and perioperative outcomes in complex gynecologic surgery: An educational dilemma

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Objectives: To assess the association of resident and fellow trainee participation on surgical outcomes of ovarian, fallopian tube, and primary peritoneal cancer (OvFTPP) debulking surgeries.

Methods: All surgical debulking cases for OvFTPP cancer that had concurrent documentation of trainee participation were reviewed from the National Surgical Quality Improvement Program (NSQIP) database of prospectively collected surgeries from 2006 to 2012. Trainee participation included "resident" (identified as PGY1-4) and "fellow" (PGY5+). The highest level of trainee present at each case was recorded and cases were distributed into 3 cohorts: (1) no trainee, (2) resident only, and (3) fellow present. Rate of transfusion, operative time, and 30-day outcomes were compared using multivariable logistic regression models controlling for patient risk factors and complexity of surgery. Surgical complexity was characterized by performance of other gynecologic oncology procedures and concurrent nongynecologic (urologic, gastrointestinal) surgery.

Results: A total of 1,173 patients were identified. Trainee participation was not associated with increased 30-day complication rate or hospital length of stay. After controlling for age, body mass index, comorbidities, function status, and surgical complexity, mean operative time was significantly longer with residents (+49 min, 95% CI 35–62, $P <$ .001) and even longer with fellows (+71 min, 95% CI 56–86, $P <$ .001). Patients were 2.8 times (95% CI 1.68–4.66, $P <$ .001) more likely to receive a blood transfusion with resident participation and 5.1 times (95% CI 3.0–8.61, $P <$ .001) with fellow participation controlling for surgical complexity.

Conclusions: The presence of surgical trainees during debulking surgery for OvFTPP cancer was associated with significantly longer operative time and more blood transfusions. Methods of improving efficiency while maintaining safety when incorporating trainees into surgeries need to be identified. Development of a standardized surgical curriculum with objective assessments including training both inside and outside the operative suite should be considered.

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189 - Poster

Need for additional training in genetic counseling among gynecologic oncology providers

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Objectives: National Comprehensive Cancer Network guidelines recommend genetic counseling and testing for all ovarian cancer and certain endometrial cancer patients. The objective of this study was to evaluate practice patterns and identify potential needs in genetic counseling among gynecologic oncology providers.

Methods: An anonymous 48-item online survey was sent to members of the Society of Gynecologic Oncology assessing attitudes and behaviors related to genetic counseling. Descriptive statistics were performed.

Results: A total of 233 (18.2%) of 1,280 members responded to the survey. Of these, 199 (85.4%) respondents were gynecologic oncologists. Only 37.5% of all providers felt adequately trained to provide genetic counseling to their patients. Barriers included lack of time (20.1%), lack of training (10.3%), and both (26.8%). Among respondents, 5.4% of providers did not feel genetic counseling was within their scope of practice. Half (53.6%) of the providers expressed a desire for additional training and 22.5% reported either no prior training or independent reading as their only source of education. Nearly all (87.5%) providers confirmed access to a certified genetics counselor and the majority (61.8%) stated they defer all genetic testing to these specialists. Most providers would consider sending multigene panels (86.7%) and testing for genes that do not currently have guideline-supported actions (77.6%). With limited data on cancer risk for low or intermediate penetrant genes, wide variability was seen regarding screening and/or prevention strategies recommended to patients who test positive for deleterious mutations that do not have clear management guidelines (Figure 1). Similarly, there was no consensus on screening and/or prevention strategies recommended to patients who test positive for variants of unknown significance for any gene tested.

Conclusions: Based on our survey results, there is a need for additional training and further development of guidelines for genetic counseling in gynecologic malignancies. With the rapid expansion of multigene panel testing, there is a lack of consensus on what genes to test for as well as what screening and prevention strategies to recommend.

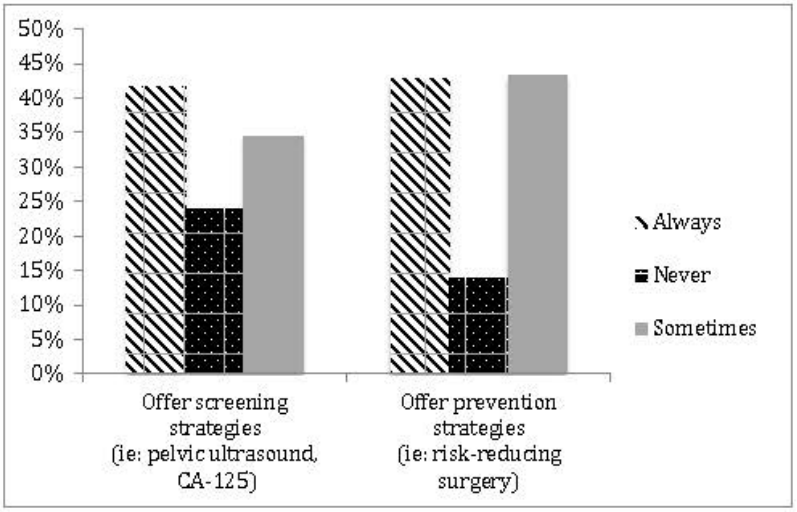

Fig. 1
Provider recommendations to patients who test positive for deleterious mutations that do not have clear management guidelines.

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190 - Poster
Obesity exposure across the lifespan leads to increased tumor growth in a genetically engineered mouse model of serous ovarian cancer
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Objectives: The effect of obesity across the lifespan on tumor growth was explored using a genetically engineered mouse model of serous ovarian cancer (OC).

Methods: A crossover diet study design was employed using the K18-g$T_{121}^{+/-}$; $p53^{fl/fl}$;$Brca1^{fl/fl}$ (KpB) OC mouse model exposed to a high-fat diet (HFD; 60% kcal from fat) and/or a low-fat diet (LFD; 10% kcal from fat) at different time points across the lifespan. Eight dietary exposures were examined (Table 1) (n = 8–12 mice per diet group). Obesity exposures were initiated as follows: (1) To examine in utero effects, mice once pregnant were placed on a LFD or HFD. Pups were weaned onto the same diets as mothers or switched to the opposite diet. (2) Adolescent exposure occurred from weaning at 3 weeks of age until 6 weeks. (3) Adult obesity was initiated at 6 weeks of age. All mice were killed at 32 weeks of age. Immunohistochemistry was performed to assess Ki-67, caspase-3, AMPK, and targets of the mTOR pathway. Global, untargeted metabolomics was used to identify obesity-dependent markers of OC.

Results: Only mice exposed to a HFD in adulthood became significantly obese (C, E, and H) except for in utero HFD exposure (G) compared with lean control mice (A) or mice exposed to first HFD in adolescence then LFD in adulthood (D and F). Importantly, there were significant increases in tumor size in all mice with any exposure to HFD, except the mice only exposed in utero (G). The largest tumors were in group E with obesity exposure in utero and during adolescence and adulthood. Adulthood exposure induced larger tumors (B, C, H) than during adolescence (D and F). When tumors from group B (obese) versus group A (lean) were studied, increased expression of phosphorylated-AMPK and targets of the mTOR pathway was found, along with higher levels of apoptosis. The OCs from obese mice had evidence of increased fatty acid oxidation, decreased glycolysis, and impaired mitochondrial function compared with lean controls.

Conclusions: Obesity during adulthood had a greater influence on OC aggressiveness than adolescent exposure to a HFD. A switch in diet from a HFD in adolescence to a LFD in adulthood resulted in a favorable decrease in mouse weight. Despite this, ovarian tumor size was still increased in these groups, suggesting that obesity-driven changes may become fixed and no longer modifiable by altering the metabolic environment.

Table 1
Mouse and Tumor Weight at Sacrifice by Dietary Exposure.

GROUP	*IN UTERO*	ADOLESCENT	ADULT-HOOD	MOUSE WEIGHT G (SD)	TUMOR WEIGHT G (SD)
A (CONTROL)	LFD	LFD	LFD	29.8 (2.0)	1.3 (0.6)
B	LFD	LFD	**HFD**	37.0 (7.6)*	2.8 (1.5)**
C	LFD	**HFD**	**HFD**	44.4 (9.4)*	2.5 (1.3)*
D	LFD	**HFD**	LFD	32.8 (5.5)	1.8 (0.4)*
E	**HFD**	**HFD**	**HFD**	43.1 (9.6)*	3.1 (1.9)*
F	**HFD**	**HFD**	LFD	32.3 (3.8)	2.1 (0.6)*
G	**HFD**	LFD	LFD	36.0 (7.7)*	1.8 (1.2)
H	**HFD**	LFD	**HFD**	48.9 (8.6)*	2.6 (1.5) *

*$P < 0.05$, **$P < 0.01$, all groups were compared to Group A (control)

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191 - Poster
Preoperative predictive factors for complete cytoreduction and survival outcome in epithelial ovarian and peritoneal cancer after neoadjuvant chemotherapy
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Objectives: To identify preoperative predictive factors for complete cytoreduction and survival outcome in epithelial ovarian cancer and peritoneal cancer after neoadjuvant chemotherapy (NACT).

Methods: We performed a retrospective analysis of 90 patients with epithelial ovarian cancer and peritoneal cancer. Patients were divided into 2 groups according to residual tumor at interval debulking surgery. Clinicopathologic, surgical, and follow-up data were compared.

Results: CA-125 levels before the interval debulking surgery after completion of NACT were higher in the residual tumor group (153.5 vs. 45.3 U/mL, $P = .012$). The change in CA-125 after NACT was higher in the no residual tumor group (96.4% vs 91.6%, $P = .009$). Patients with residual tumor showed lower disease-free and overall survival outcomes than patients with no residual tumor. In univariate analysis, CA-125 less than or equal to 100 U/mL and a change after NACT of more than 80% were preoperative predictive factors for complete cytoreduction. In multivariate analysis, a CA-125 change of more than 80% after NACT was an independent preoperative predictive factor for complete cytoreduction ($P = .047$). In univariate and multivariate analysis, a CA-125 change of 80% or less after NACT and progressive disease on follow-up image during NACT was an independent preoperative predictive factors for 1-year disease-free and overall survival ($P = .035$ and $P < .001$, respectively).

Conclusions: A large change in CA-125 after NACT is an independent preoperative predictive factor for complete cytoreduction. Also, it is an independent preoperative predictive factor for early recurrence and death with progressive disease on follow-up image after NACT.

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192 - Poster

Nestin: A biomarker of aggressive uterine cancers

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Objectives: To investigate the potential prognostic and predictive value of nestin expression in well-annotated uterine cancers.

Methods: Nestin expression and previously published type I versus type II biomarkers (ER, PR, and TFF3 vs p53 and IMP3, respectively) were evaluated with immunohistochemistry in uterine cancer tissue microarrays. Biomarkers were evaluated as low versus high nestin, with high categorized as more than 10% positive staining. The relationships between nestin and clinicopathologic factors, biomarkers, and outcome were evaluated using the Fisher exact test, logistic/Cox modeling, or Kaplan-Meier method with log-rank testing.

Results: There were 323 eligible cases, of which 34% had advanced-stage disease and 42% had non-endometrioid cancer. High nestin, observed in 19% of cases, was significantly more common in advanced-stage disease, non-endometrioid cancers, grade 3 disease, positive lymphovascular space invasion (LVSI), larger tumors (>6 cm), and those with low-ER, low-PR, low-TFF3, high-p53, or high-IMP3 staining. Progression-free survival was worse overall in women with high versus low nestin (Fig 1A) as well as the subsets with lower risk disease (Fig 1B), of those who received no adjuvant therapy (Fig 1C), or those who received radiation therapy (Fig 1D). High nestin was also associated with worse cancer-specific and overall survival. High nestin was also associated with high p53 and IMP3 and inversely associated with ER, PR, and TFF3. The relationship between nestin and PFS was independent of stage, LVSI, and risk categorization but not type of uterine cancer.

Conclusions: High nestin was associated with aggressive features and poor outcome and may represent a predictive biomarker for improved treatment selection.

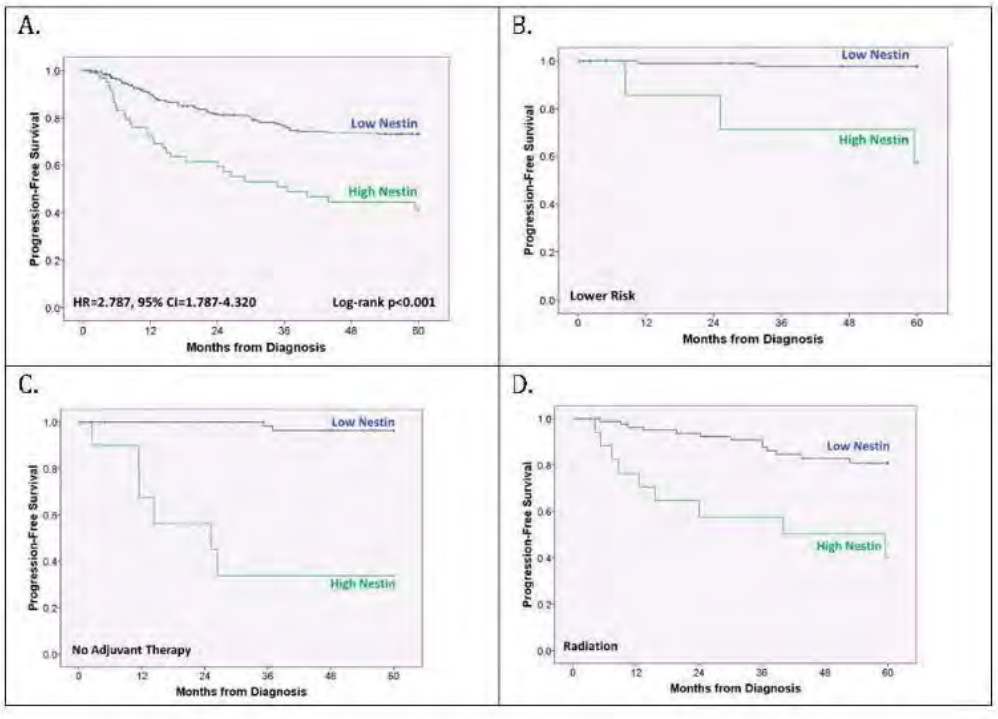

Fig. 1

Progression-free Survival Overall (A) and in the Subset with Lower Risk Disease (B) or Who Received No Adjuvant Therapy (C) or Radiation Rherapy (D).

193 - Poster

Early-stage clear cell ovarian carcinoma and the effect of adjuvant radiation on survival

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Objectives: Clear cell ovarian cancer (CCOC) is a less common subtype of epithelial ovarian cancer. Recent retrospective evidence demonstrated a potential benefit of radiation in a subset of patients with CCOC. The goal of our study was to assess the impact of adjuvant radiation on survival in patients with stage I and II CCOC and in a high-risk subset of patients.

Methods: A retrospective data collection and analysis were performed of all stage I and II CCOC patients treated at 2 tertiary centers between 1995 and 2014. Descriptive statistics and Kaplan-Meier survival probability estimates were completed. The log-rank test was used to compare survival curves.

Results: A total of 163 patients with stage I and II CCOC were identified. Median age was 54.6 years. Of these, 120 (73.6%) patients were treated with adjuvant chemotherapy, 44 (27%) with adjuvant radiation, and 37 (22.7%) received a combination of both modalities. Thirty-six patients received no adjuvant treatment. There was a total of 41 (25%) recurrences in the cohort. Five-year progression-free survival (PFS) for all patients was 70% and overall survival (OS) was 82%. Recurrences were seen in 12 (27.2%) of the 44 patients who received adjuvant radiation and 29 (24.3%) of those who were not treated with radiation. The 5-year PFS for patients treated with radiation was 82% and for those not treated with radiation was 81% (P = .75). On multivariable analysis, stage (IA/IB vs IC/II, P = .009) and adjuvant chemotherapy (P = .001) were found to be significantly associated with improved PFS. However, the only independent prognostic factor found to significantly correlate with OS was stage (P = .03). In all patients, on multivariable analysis, radiation was not significantly associated with a longer PFS (P = .63) or OS (P = .66). Adjuvant radiation was also not found to significantly improve PFS or OS in a subset of high-risk patients: stage IC with positive cytology and/or surface involvement and stage II (PFS: HR 1.18, 95% CI 0.55–2.54; OS: HR 1.04, 95% CI 0.40–2.69).

Conclusions: Adjuvant radiation was not found to be associated with a survival benefit in patients with stage I and II CCOC or in a high-risk subset of patients including those with stage IC cytology positive/ surface involvement and stage II patients. Adjuvant chemotherapy was significantly associated with a longer PFS, but this did not translate to an improved OS rate.

Table 1

Clinical Characteristics: Early Stage Ovarian Clear Cell Carcinoma.

Variable	All patients N=163	No adjuvant RT[1] N=119	Adjuvant RT N=44	P-value
Age, in years				0.27
Mean +/- SD	55.4+/-10.5	55.9+/-11.2	53.9+/- 8.2	
Median	54.6	54.7	54.5	
Range	32.7-81.6	32.7-81.6	35.6-74.4	
Stage				0.18
IA/IB	61 (37.4%)	47 (39.5%)	14 (31.8%)	
IC	87 (53.4%)	61 (51.3%)	26 (59.1%)	
II	15 (9.2%)	11 (9.2%)	4 (9.1%)	
Chemotherapy				0.07
No	43 (26.4%)	36 (30.3%)	7 (15.9%)	
Yes	120 (73.6%)	83 (69.7%)	37 (84.1%)	
"High Risk" group	59 (36.8%)			0.47
Stage IC positive cytology and/or surface involvement	44 (27%)	28 (23.5%)	16 (24.2)	
Stage II	15 (9.2%)	11 (9.2%)	4 (9.1%)	
Recurrence				0.71
No	122(74.8%)	90(75.7%)	32 (72.7%)	
Yes	41 (25.2%)	29 (24.3%)	12 (27.3%)	

1RT: radiotherapy

194 - Poster

The Advance Care Planning Readiness Scale: A novel measure of gynecologic oncology patients' willingness to discuss and accept end-of-life care

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Objectives: To develop and validate a scale that assesses the readiness of gynecologic oncology patients to engage in advance care planning.

Methods: The Advance Care Planning Readiness Scale (ACPRS) was validated across 3 independent samples of gynecologic oncology patients via a 3-step process. In step I, patients (n = 25) underwent cognitive interviewing to determine if the scale items were comprehensible and applied to them. We modified the scale (addition, removal, rewording, and merger of items) based on step I results. The revised scale was then administered to a new sample of patients (n = 110) to assess scale reliability and validity in step II. An exploratory factor analysis determined if the scale loaded onto unique factors. In step III, we administered the revised scale to a new sample of patients (n = 110) and a confirmatory factor analysis was conducted to test the factor structure proposed in step II. ACPRS scores were compared with end-of-life care (EOLC) outcome measures (completion of do-not-resuscitate [DNR] order and other advance directives (medical power of attorney or living will).

Results: See Table 1 for demographics and clinical characteristics. Based on patients' responses, the original 13-item ACPRS used in step I was modified to the 8-item ACPRS used in step II. The final 8-item ACPRS was valid, reliable (Cronbach α = 0.81), and had 2 primary factors (Willingness to Discuss EOLC and Acceptance of EOLC). Women with a medical power of attorney/living will had higher ACPRS total scores than those who did not have these documents (*P* = .003). Women with completed DNRs had higher ACPRS total scores than women without DNRs (*P* = .018).

Conclusions: The ACPRS is a valid and reliable 8-item scale to assess the readiness of gynecologic oncology patients to discuss advance care planning issues and is associated with completion of advance directives. This scale has the potential to greatly improve patient/provider communication regarding EOLC goals and can be easily used in the clinical setting.

Table 1

Demographic and Clinical Summary of Steps I, II and III.

		Step 1 N (%)	Step 2 N (%)	Step 3 N (%)	P-Value
Age	N	25	110	110	0.8008
	Mean (SD)	60.01 (10.47)	58.82 (12.06)	58.18 (14.19)	
	Median	63	61	58	
	Min - Max	41 – 81	24 – 82	28 – 85	
Race	White	21 (84.00%)	84 (76.36%)	82 (74.55%)	0.2474
	African American	1 (4.00%)	4 (3.64%)	9 (8.18%)	
	Hispanic	1 (4.00%)	18 (16.36%)	16 (14.55%)	
	Asian	0 (0.00%)	3 (2.73%)	2 (1.82%)	
	Other	2 (8.00%)	1 (0.91%)	1 (0.91%)	
Partnered Status	No Partner	6 (24.00%)	37 (33.94%)	37 (33.64%)	0.6396
	Partner	19 (76.00%)	72 (66.06%)	73 (66.36%)	
	Unknown/Missing	0	1	0	
Associate Degree or Higher	Elementary, HS, GED	7 (28.00%)	31 (28.18%)	48 (43.64%)	**0.0441**
	Associate, Undergraduate, Graduate	18 (72.00%)	79 (71.82%)	62 (56.36%)	
Identify with a Religion	No	2 (8.00%)	6 (5.45%)	14 (12.73%)	0.1597
	Yes	23 (92.00%)	104 (94.55%)	96 (87.27%)	
Cancer Site	Ovarian	10 (40.00%)	51 (46.36%)	59 (53.64%)	0.2981
	Uterine	11 (44.00%)	38 (34.55%)	26 (23.64%)	
	Cervical	4 (16.00%)	17 (15.45%)	17 (15.45%)	

	Vulvar/Vaginal	0 (0.00%)	4 (3.64%)	8 (7.27%)	
Stage	Not Staged	0 (0.00%)	12 (11.01%)	13 (11.82%)	0.7273
	Stage I	7 (29.17%)	31 (28.44%)	27 (24.55%)	
	Stage II	2 (8.33%)	9 (8.26%)	13 (11.82%)	
	Stage III	11 (45.83%)	43 (39.45%)	39 (35.45%)	
	Stage IV	4 (16.67%)	14 (12.84%)	18 (16.36%)	
	Unknown/Missing	1	1	0	
Cancer Management	Surveillance	13 (52.00%)	55 (50.00%)	46 (41.82%)	0.4125
	Primary/Recurrence	12 (48.00%)	55 (50.00%)	64 (58.18%)	
Current Treatment	Current Treatment	13 (52.00%)	55 (50.00%)	55 (50.00%)	> 0.9999
	No Treatment or Maintenance	12 (48.00%)	55 (50.00%)	55 (50.00%)	
Heard about DNR	No	1 (4.00%)	6 (5.45%)	8 (7.27%)	0.9255
	Yes	24 (96.00%)	104 (94.55%)	102 (92.73%)	
Heard about Advance Directive	No	5 (20.00%)	27 (24.77%)	28 (25.45%)	0.9301
	Yes	20 (80.00%)	82 (75.23%)	82 (74.55%)	
	Unknown/Missing	0	1	0	
Heard about Hospice	No	1 (4.00%)	0 (0.00%)	1 (0.91%)	0.1940
	Yes	24 (96.00%)	110 (100.00%)	109 (99.09%)	
Have DNR	No	20 (83.33%)	74 (67.27%)	79 (72.48%)	0.2793
	Yes	4 (16.67%)	36 (32.73%)	30 (27.52%)	
	Unknown/Missing	1	0	1	
Have Advance Directive	No	17 (68.00%)	56 (50.91%)	54 (49.09%)	0.2412
	Yes	8 (32.00%)	54 (49.09%)	56 (50.91%)	
DNR in Medical Record	No	25 (100.00%)	109 (99.09%)	108 (99.08%)	> 0.9999
	Yes	0 (0.00%)	1 (0.91%)	1 (0.92%)	
	Unknown/Missing	0	0	1	
Advance Directive in Medical Record	No	22 (88.00%)	90 (81.82%)	84 (76.36%)	0.3730
	Yes	3 (12.00%)	20 (18.18%)	26 (23.64%)	

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195 - Poster

Achieving universal BRCA1 and BRCA2 genetic testing with a novel care delivery model

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Objectives: *BRCA* testing is currently recommended by the Society of Gynecologic Oncology (SGO) and National Comprehensive Cancer Network (NCCN) for all high-grade ovarian cancer (HGOC) patients. Unfortunately, recent studies have published ovarian cancer genetic testing (GT) rates of 14.5% to 48.0%. We report the results of a novel care delivery model (NCDM) initiative that included integrated genetic counselor (GC) services, increased GC availability, assisted referral placement, physician-ordered GT at off-site clinics, and availability of a family outreach registry.

Methods: From September 2012 to June 2015, we collected retrospective and prospective data from a cohort of unselected patients who were seen for primary care and treatment (see Table). Data included demographics, tumor histology, GC uptake, GT uptake, GT outcome, and downstream effects (at-risk family members and participation in a family outreach registry). Tumor registry, medical records, and research databases were used to collect patient data.

Results: We identified 402 HGOC patients who received primary treatment (including but not limited to surgery, chemotherapy, and/or follow-up). To date, 342 (85%) patients were recommended to have GT, 305 (76%) had GT, and 46 (15%) had a deleterious mutation. Most common documented reasons for patients not having GT included: patient died, patient declined GC or GT, or elected to pursue elsewhere.

To date, 16 of 42 eligible patients with serous HGOC and a mutation have been enrolled in a family outreach registry study. These 16 patients have 32 living 1st-degree female relatives, 33 living 2nd-degree female relatives, and 28 living 3rd degree female relatives who are at risk to have the *BRCA* mutation and would benefit from GT.

Conclusions: Over a 33-month period, universal GT of HGOC yielded 85% recommended for GT, 76% tested, and 15% BRCA+. We report the highest published referral rate to date for a large gynecologic oncology practice. Utilization of our NCDM successfully increased referral and GT rates. Increased GT affects patients by allowing targeted therapeutic options, family cascade testing, cancer risk reduction, and prevention.

Table 1
Patient Demographics.

Demographics	**402 HGOC Pts**		**46 BRCA+***
White	306	76%	28
Hispanic	36	9%	7
Black	33	8%	4
Asian	23	6%	7
Other/Unknown	4	1%	0
Average age at presentation	62.4		62.4
Age range at presentation	25-92		31-75
Patients with second primary: breast cancer	42	10%	13**
Language Spoken			
English	387	96%	45
Spanish	8	2%	1
Arabic	4	1%	0
Other	3	1%	0
Marital Status			
Married	273	68%	34
Widowed	57	14%	4
Single	37	9%	5
Divorced	28	7%	1
Separated	4	1%	2
Other	3	1%	0

*Of the 46 BRCA+ patients, all but 2 had at least a component of high grade serous carcinoma.
** Only one breast cancer was diagnosed *after* the ovarian cancer diagnosis among patients with a BRCA mutation.

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196 - Poster
Pelvic and para-aortic lymph node mapping to diagnose micrometastasis by injection of indocyanine green in endometrial cancer
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Objectives: The therapeutic benefit of lymphadenectomy for endometrial cancer is debated. However, the presence of lymph node metastasis obviously compromises overall survival. At this point, the clinical significance of micrometastasis in lymph nodes remains unclear. The aim of this study was to assess the feasibility of detecting micrometastasis using fluorescence near-infrared imaging of indocyanine green (ICG) with laparotomy.

Methods: Since July 2014, 32 patients were enrolled for lymph node mapping. ICG, 1.25 mg, was injected into the cervical stroma at the 3 o'clock and 9 o'clock positions in patients who had pelvic lymphadenectomy (PLA) (n = 32) or both pelvic and para-aortic lymphadenectomy (PLA + PAN) (n = 13) and into the uterine fundal subserosa close to the beginnings of the bilateral tubes for patients who had PAN. PAN was performed in patients who were preoperatively diagnosed as histologically G3, serous, or clear cell adenocarcinoma and/or outer half of muscle invasion. ICG-stained lymph nodes detected with ICG fluorescence imaging camera during open abdominal surgery were sectioned 3-μm thick at 2-mm intervals for standard (H&E) staining. The section suspected to be micrometastasis was analyzed with immunohistochemistry using anticytokeratin antibody. Data were obtained for the number and location of ICG-stained lymph nodes, and the pathologic characteristics were also analyzed.

Results: ICG-stained lymph nodes were detected in all patients enrolled in this study. Twenty-one (65.6%) and 8 patients (61.5%) had bilateral pelvic or aortic ICG-stained lymph nodes, respectively. A median of 2.8 and 6.1 lymph nodes per patient was identified for PLA and PLA + PAN, respectively. Seven patients (22.6%) had lymph node metastasis, and 6 of these had metastasis in ICG-stained lymph node (85.7% sensitivity). Furthermore, 3 patients among them were diagnosed as having micrometastasis. No adverse events were identified.

Conclusions: Despite the small sample size, fluorescence imaging with ICG through intraoperative injection into the cervix and uterine fundus is a feasible method to detect micrometastasis. The results drawn in this study provide useful information for future study to consider patient management with micrometastasis by the expanding sample size and evaluating patient outcomes.

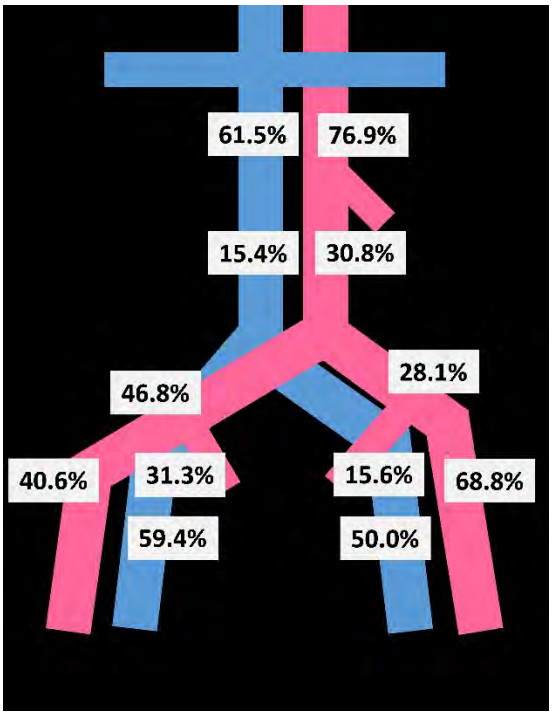

Fig. 1
Anatomic Distribution of ICN-stained Lymph Node.

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197 - Poster
Ovarian carcinosarcoma: A multi-institutional review of cases, treatment, and survival
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Objectives: Given the rarity of ovarian carcinosarcoma, we sought to analyze a contemporary multi-institutional case series of ovarian carcinosarcoma to better understand patient characteristics and outcomes of this rare epithelial ovarian cancer.

Methods: After institutional review board approval was obtained, a retrospective review was performed to identify all women diagnosed with ovarian carcinosarcoma between 2000 and 2015 at the University of Virginia and the University of North Carolina. Patient characteristics and clinical history were abstracted from longitudinal medical records. Statistical analysis was performed with SPSS. The association between independent prognostic variables and

overall survival was examined using Fisher exact test and independent samples *t* tests. Progression-free survival and overall survival were analyzed using Kaplan-Meier estimates.

Results: Forty-two patients were identified with a mean age at diagnosis of 65.4 years (standard deviation [SD], 12.5). Most patients were Caucasian (90.5%) with a mean body mass index of 27.0 kg/m^2 (SD 7.6) and baseline CA-125 level of 615.4 kU/L (SD 980.4). The majority (62%) of cases were FIGO stage IIIC or IV at diagnosis. All patients underwent surgical debulking and the majority (83%) received adjuvant chemotherapy. Of those treated with chemotherapy, 74% received carboplatin and paclitaxel. The median follow-up was 22.5 months (range, 1–165 mo). Fifty-two percent of patients had documented recurrence at a median time of 12 months (range, 0.2–45 mo) (Figure 1a). The most common site of recurrence was the abdominal cavity (59.0%), followed by the pelvis (27.3%), then extra-abdominal recurrences (13.6%). The median overall survival time was 26 months (range, 0.5–147 mo) (Figure 1b). The median overall survival was higher for stage I (36.6 mo) than stage II-IV (16.8 mo).

Conclusions: As with all epithelial ovarian cancers, most patients were diagnosed after menopause with late-stage tumors. Despite consistent treatment modalities, most patients in this cohort only survived slightly more than 2 years. Unlike uterine carcinosarcoma, patients with ovarian carcinosarcoma from this cohort do not appear to have more aggressive disease than the more common histologies of epithelial ovarian cancer, which historically have a relapse rate of 80% to 85% for stage III disease. Further data pooling from multiple institutions will be needed to better describe the survival characteristics of this rare disease.

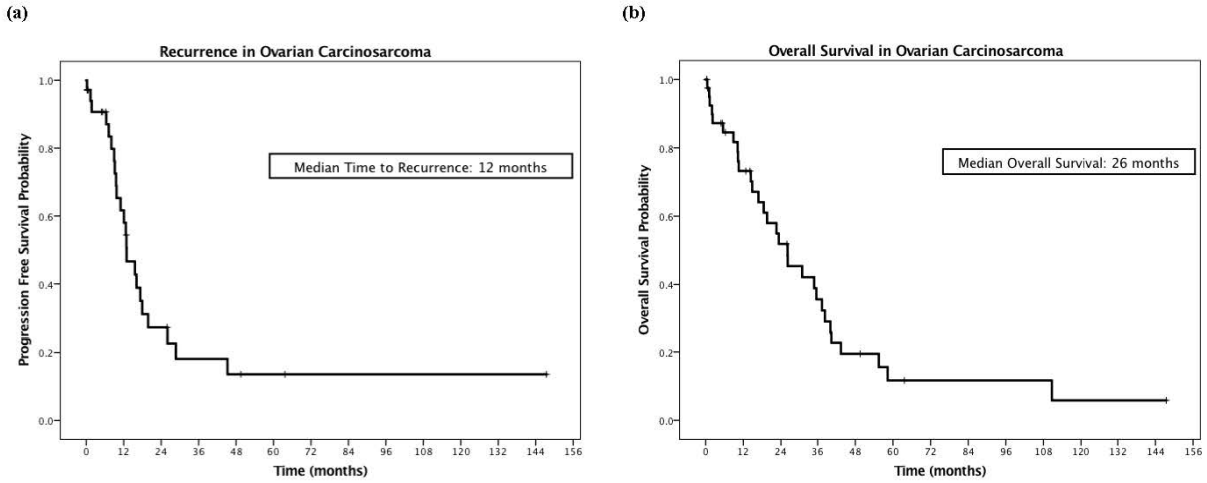

Fig. 1
Kaplan-Meier Analyses of (a) Time to Recurrence and (b) Overall Survival among Cases of Ovarian Carcinosarcoma Diagnosed at the University of Virginia and the University of North Carolina-Chapel-Hill from 2000-2015.

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198 - Poster
Institutional experience using interstitial brachytherapy for the treatment of primary and recurrent pelvic malignancies
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Objectives: The study aimed to assess the outcomes of patients at a single institution with locally advanced primary and recurrent pelvic malignancies treated with interstitial high or low dose rate brachytherapy (BT) using a modified Syed-Neblett template.

Methods: Between 1996 and 2010, 60 patients with locally advanced primary or recurrent pelvic malignancies were treated at a single institution with interstitial BT using a modified Syed-Neblett template. Thirty-three patients had primary malignancies, with 6.1% being stage I, 33.3% stage II, 45.5% stage III, and 15.2% stage IV; the remaining 27 patients had recurrent malignancies. Fifty-six received external beam radiation therapy (EBRT) as part of their treatment course. The median EBRT, BT, and EBRT + BT doses were 45 Gy, 20 Gy, and 65 Gy, respectively. Thirty-eight patients received concurrent chemotherapy with EBRT. Complete response (CR) was defined as the absence of residual disease on first follow-up. Toxicity was graded as per Radiation Therapy Oncology Group criteria.

Results: CR was achieved in 91%. For primary cancers at diagnosis, 5-year local control (LC), 5-year progression-free survival (PFS), and 5-year overall survival (OS) were 65%, 64%, and 42%, respectively. For recurrent cancers at

diagnosis, 5-year LC, 5-year PFS, and 5-year OS were 80%, 51%, and 37%, respectively. There was a significant difference in both OS and PFS among different tumor sites ($P < .05$), with vaginal cancers having the best 5-year OS (55%) and PFS (84%). There was a total of 1 acute toxicity more than grade 3, and 7 late toxicities greater than grade 3 with no grade 5 toxicities.

Conclusions: Our series suggests that interstitial BT using a modified Syed-Neblett template is a safe and effective treatment for primary or recurrent pelvic malignancies. This technique allowed effective LC of tumor with preservation of bladder and rectal functions in all except 2 of our patients. One developed a rectovaginal fistula, and the other required long-term urethral catheterization. Further studies regarding dosimetric predictors of toxicity, and continual follow-up are ongoing to determine the long-term efficacy of this approach.

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199 - Poster

Histone deacetylase as a promising therapeutic target in endometrial stromal sarcoma

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Objectives: The purpose of this study was to investigate the expression of histone deacetylase (HDAC) in endometrial stromal sarcoma (ESS).

Methods: Forty-one patients with ESS were eligible for the study. The immunohistochemical expression of HDAC was analyzed using tissue microarrays. Prognostic impact of clinicopathologic characteristics of patients and treatment methods were also investigated.

Results: Strong positive immune reaction was observed in 32 (78.0%), 23 (56.1%), 8 (19.5%), 36 (87.8%), 7 (17.1%), 30 (73.2%), 31 (75.6%), and 33 (80.5%) of HDAC 1, 2, 3, 4, 5, 6, 7, and 8 in ESS. Adjuvant therapy and radicality of surgery had no statistical relevance with disease-free and overall survival outcomes. Although not statistically significant, HDAC 1, 4, 6, 7, and 8 showed high frequency of strong immune reaction and a lower disease-free survival rates (100.0% vs 81.3%, $P = .202$; 100.0% vs 83.3%, $P = .393$; 90.9% vs 83.3%, $P = .579$; 90.0% vs 83.9%; and 100.0% vs 81.8%, $P = .207$).

Conclusions: All of the HDAC series were frequently expressed in ESS. Target therapy for HDAC1, 4, 6, 7, and 8, which especially showed high frequency of strong immunoreactivity, can be considered to be a promising therapeutic target to improve prognosis.

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200 - Poster

Financial toxicity among privately insured gynecologic oncology patients: Silent barriers to care

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Objectives: Patient-reported financial barriers to care are associated with poor cancer outcomes. Private insurance may protect against some financial barriers; however, out-of-pocket costs can be significant and prohibitive. We estimated the prevalence of financial barriers to care among women with private insurance presenting for gynecologic oncologic surgery.

Methods: Patients seeking surgical management at a tertiary care gynecologic oncology clinic were enrolled in a prospective cohort study from September 30, 2013 to October 6, 2014. They were administered a survey addressing financial and access-driven barriers to care. Demographics and medical factors were obtained from the medical record and comorbidities quantified using the Charlson comorbidity (CC) index. X^2 tests, *t*tests, and multivariable logistic regression were used.

Results: Of the 208 subjects, 84.1% (n = 175) had private insurance, 7.2% (n = 15) were uninsured, and 8.7% had Medicare/Medicaid alone (n = 18). Median age was 58 years (range, 22–93 years). Among privately insured patients, 59 (33.7%) experienced a financial barrier to care: 54 (30.9%) delayed health care in the last year because of financial barriers and 24 (13.7%) did not get needed health care services, such as medications, because of inability to afford them. Younger age was associated with both financially driven delays (53.5 vs 58.3 years, $P = .03$) and inability to afford services (48.1 vs 58.2 years, $P < .001$). Black patients were more likely to experience financial barriers (delays,

48.3% vs 27.4%, *P* = .03; services, 34.5% vs 9.6% *P* < .001), as were obese patients (body mass index >30) (services, 20.2% vs 7.0%, *P* = .01). Patients reporting financial barriers had lower mean CC scores (delays, 1.9 vs 2.5, *P* = .04; services, 1.1 vs 2.5, *P* = .002). On multivariable analysis, nonwhite race (odds ratio [OR] 4.4, 95% CI 1.6–12.2), each 5-year decrease in age (OR 1.2, 95% CI 1.01–1.5), and each 1-point decrease in CC score (OR 1.5, 95% CI 1.03–2.1) remained associated with inability to afford services.

Conclusions: A third of privately insured patients reported significant financial barriers to care before surgery. The disproportionate prevalence among younger, healthier patients may reflect increasingly high-deductible health plans. Insurance status is an inadequate screen to detect patients who have difficulty affording cancer care.

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201 - Poster
Single-incision manual palpation laparoendoscopic (SIMPLE) surgery for the evaluation of gynecologic malignancies prone to peritoneal spread
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Objectives: To report outcomes associated with single incision manual palpation laparoendoscopic (SIMPLE) surgery performed for gynecologic malignancies prone to peritoneal spread.

Methods: Women who underwent SIMPLE surgery for ovarian, fallopian tube, or high-grade endometrial cancer were identified. Demographic, surgical, and outcomes data were collected. Descriptive statistics were used.

Results: Twenty-nine women underwent SIMPLE surgery via a 9-cm umbilical incision. Preoperatively, 19 women (65.5%) had a high-grade endometrial cancer: 4 carcinosarcomas, 4 clear cell, 4 endometrioid, and 7 serous carcinomas. Stages were: IA (n = 12), IIIA (n = 1), IIICI (n = 3) and IIIC2 (n = 3). Positive pelvic and para-aortic lymph nodes (LN) were identified in 5 (26.3%) and 3 (15.8%) patients, respectively. None had omental involvement. Ten women (34.5%) had an ovarian or tubal malignancy: 4 serous, 2 mucinous, 2 endometrioid, 1 clear cell, and 1 granulosa cell carcinoma. Stages were: IA (n = 4), IC1 (n = 1), IC2 (n = 1), IIA (n = 1), IIIA2 (n = 1), IIIC (n = 2). None had positive LNs, but 2 (20.0%) had omental involvement. Procedures included hysterectomy (n = 24, 82.8%), removal of 1 or both adnexa (n = 26, 89.7%), pelvic (n = 25, 86.2%) or para-aortic (n = 19, 65.5%) LNs, omentectomy (n = 29, 100.0%), biopsies (n = 9, 31.0%), and appendectomy (n = 3, 10.3%). Median uterine weight was 92.8 g (95 CI 32–561.2). A median of 9 pelvic (95 CI 1–25) and 6 para-aortic (95 CI 1–22) LNs were removed. Operative time was 208 minutes (95 CI 91–290 minutes) with a postoperative stay of 1 day (95 CI 0–6 day). There were no conversions or reoperations. Thirty-day morbidity findings included: no transfusions, visceral injury, venous thromboembolic events, wound infections, or cuff dehiscence. There were 2 postoperative fevers, 3 cases of urinary retention and 2 readmissions for a small-bowel obstruction and fever. With a median follow up of 8 months (95 CI 0–23 months), there were no incisional hernias. One woman experienced a recurrence of her endometrial cancer and died. The remaining 28 women (96.5%) are alive without evidence of disease.

Conclusions: SIMPLE surgery for women with gynecologic malignancies is a minimally invasive technique that provides the opportunity to manually evaluate the peritoneal cavity and retroperitoneum without compromising surgical staging procedures or oncologic outcomes and is associated with low morbidity and quick recovery.

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202 - Poster
Vaginal cuff closure in robotic hysterectomy: A randomized controlled trial comparing barbed versus standard suture
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Objectives: We desired to determine if there was a measurable time savings through the use of V-Loc™ suture for vaginal cuff closure and what effect its use would have on the overall cost.

Methods: Women undergoing robotic hysterectomy were randomized into 2 groups, 1 group receiving VICRYL™ suture closure of the vaginal cuff (n = 34) and the other receiving the V-Loc (n = 33). Patients were blinded to their closure type. The primary outcome was vaginal cuff closure time while secondary outcomes included rates of granulation tissue formation, vaginal cuff dehiscence, and dyspareunia for either partner postoperatively.

Results: Vaginal cuff closure with the V-Loc was found to have a closure time of 3.2 ± 1.1 minutes while vaginal cuff closure with traditional VICRYL™ suture was found to have a closure time of 7.6 + 2.7 minutes. This indicates vaginal cuff closure with VICRYL™ takes 4.4 minutes longer than closure with the V-Loc ($P < .001$).

Conclusions: Vaginal cuff closure during robotic hysterectomy is significantly expedited by the use of V-Loc; however, under current billing practices, this likely does not result in a net cost savings as a result of decreased operative time. However, it is cost-neutral because suture costs are the same.

Table 1
Demographic and Baseline Characteristics.

Characteristic	VICRYL™ Closure (n=34)	V-Loc™ Closure (n=33)
Age (y)	55.2 ± 15.0	51.0 ± 14.8
Race		
White	24 (70.6)	23 (69.7)
Black	8 (23.5)	10 (30.3)
Other	2 (5.9)	0 (0.0)
BMI (kg/m^2)	32.3 ± 8.1	31.4 ± 8.4
Malignant Disease (%)	13 (39.4)	12 (35.3)

BMI, body mass index
Data are mean ± standard deviation or n (%)
No demographic characteristics were significantly different between the two groups

Table 2
Summary of Vaginal Cuff Closure Data.

	VICRYL™ Closure (n=34)	V-Loc™ Closure (n=33)	Difference*
Vaginal Cuff Closure Time (minutes)	7.6 ± 2.7	3.2 ± 1.1	4.4
Stitches Used (n=)	4.2 ± 0.5	5.9 ± 0.8	1.7
Sutures Used (n=)	1.9 ± 0.8	1.0 ± 0	0.9

Data are mean ± standard deviation
*p-values all < 0.001

Table 3
Secondary Outcome Data.

	VICRYL™ Closure (n=34)	V-Loc™ Closure (n=33)
Granulation Tissue Formation		
On Post Op Exam	1 (1.9%)	0
On 3 month telephone survey	1 (1.9%)	0
Total	2 (5.9%)	0
Vaginal Cuff Dehiscence		
On Post Op Exam	0	0
On 3 month telephone survey	1 (1.9%)	0
Total	1 (1.9%)	0
Vaginal Evisceration	0	0
Having Intercourse at 3 months	9 (26.5%)	9 (27.3%)
Dyspareunia^	4 (44%)	1 (11%)
Male Partner Dyspareunia^	0	0

Data are n (%); ^Reported as n (% of those having intercourse)

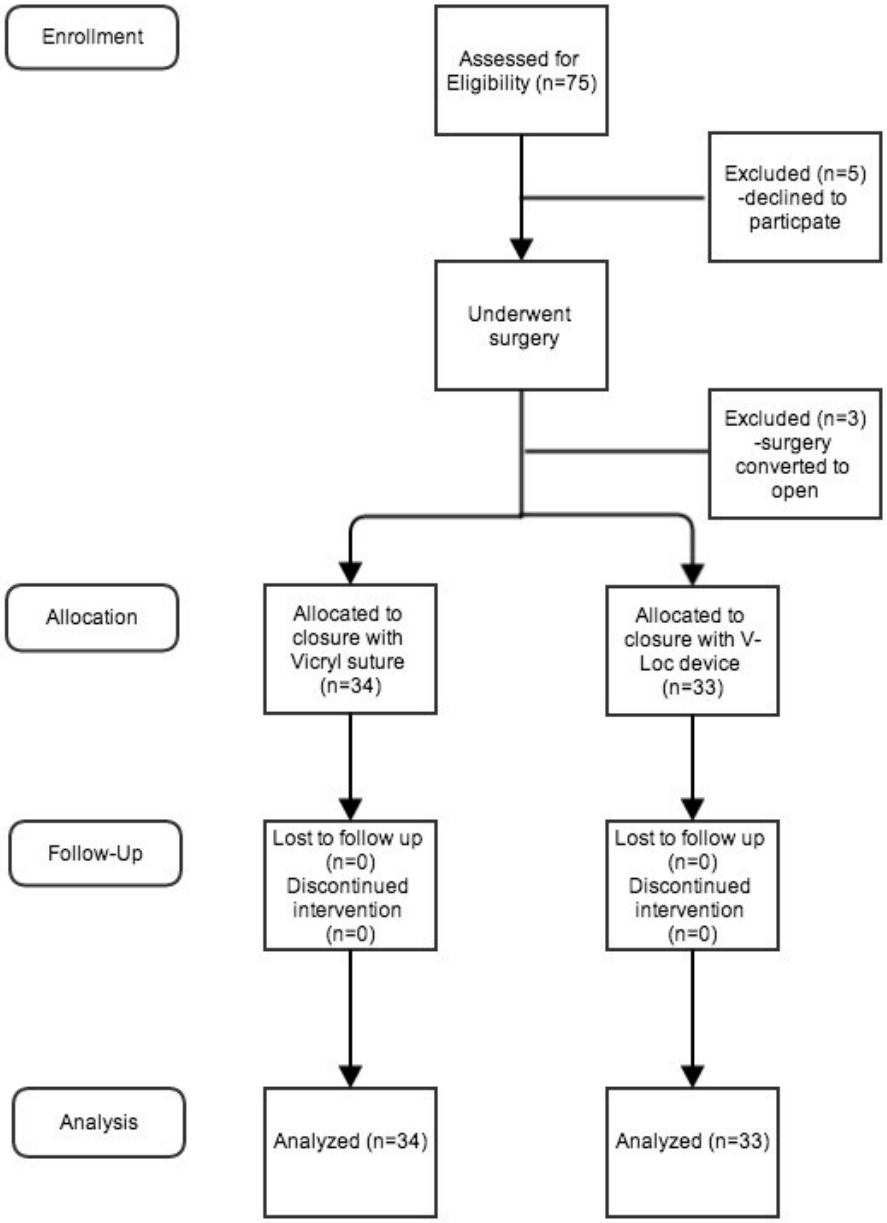

Fig. 1
Patient Selection.

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203 - Poster

Neuroendocrine carcinoma of the cervix: Poor survival despite aggressive treatment at all stages

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Objectives: Neuroendocrine carcinoma of the cervix (NECC) is a rare cervical tumor with a poor prognosis compared with squamous cell carcinoma of the cervix (SCCC). Previous studies have been limited by the rare incidence of this tumor. We identified a large cohort of patients with NECC and compared patterns of care and survival with those in patients with SCCC.

Methods: Women with NECC and SCCC diagnosed and recorded in the National Cancer Data Base between 1998 and 2011 were analyzed. Demographic, treatment, and survival data were compared. Survival was examined using Kaplan-Meier analyses and Cox proportional hazards models.

Results: A total of 101,240 with SCCC and 1,896 women with NECC were identified. Patients with NECC were more likely to be diagnosed before age 30 years (11.2% vs 5.3%, $P < .001$) and present with advanced stage IVB disease

(23.6% vs 5.9%, $P < .001$) compared with patients with SCCC. More patients with early stage (IA-IIA) NECC received adjuvant chemotherapy compared with those with SCCC (72.9% vs 18.1%, $P < .001$). For all stages, the risk of death was higher for NECC than for SCCC (stage IB-IIA: HR 2.92, 95% CI 2.45–3.47; stage IIB-IVA: HR 1.70, 95% CI 1.45–2.00; stage IVB: HR 1.14, 95% CI 0.91–1.43). Five-year survival for stage IB tumors was 80.4% (95% CI 79.7–81.0%) for SCCC compared with 55.4 (95% CI 49.3–61.2%) for NECC, whereas survival for those with IIIB tumors was 43.3% (95% CI 42.3–44.2%) vs 24.4% (95% CI 18.8–30.4%), respectively.

Conclusions: We characterize NECC as a clinically distinct tumor from SCCC with the following characteristics: younger age at diagnosis, poor response rates to chemotherapy, and decreased stage for stage survival compared with SCCC. This tumor follows an aggressive clinical course despite patterns of early multimodal treatment.

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204 - Poster

A novel insight of pathological parameters involved in recurrence and survival of patients with vulvar cancer: The importance of perineural infiltration and patterns of invasion

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Objectives: Because our knowledge related to prognostic factors for vulvar cancer is limited and inconsistent, our objective is to determine the clinicopathologic parameters and to identify their prognostic impact on recurrence and survival.

Methods: Patients with squamous vulvar cancer treated at our institution between 2000 and 2012 (n = 175) were retrospectively analyzed and further evaluated regarding the prognostic significance of different clinicopathologic variables, including age, diameter and location of the lesion, clinical tumor characteristics, depth of invasion, grade, lymphovascular space involvement (LVSI), and presence of vulvar intraepithelial neoplasia. Furthermore, the significance of perineural invasion and the types of invasive pattern were also evaluated. Time to recurrence was recorded, and disease-free survival and overall survival calculated. Cox regression analysis was used to identify factors independently associated with recurrence and survival.

Results: Multiple analysis of all tumor-related variables showed that the number of positive lymph nodes (LNs) was the only independently associated risk factor for recurrence. In addition, increased depth of invasion and tumor thickness were associated with greater risk for recurrence ([HR 1.20, 95% CI 1.16–1.25] and [HR 1.10, 95% CI 1.08–1.12], respectively). Cases with invasive or spray invasive pattern had greater risk for recurrence in a comparison of cases with confluent invasive pattern. The presence of LVSI and perineural invasion were also associated with 74% and 67% greater risk for recurrence, respectively (HR 1.74, 95% CI 1.02–2.96 and HR 1.67, 95% CI 1.00–2.79]. Also, multiple Cox regression analysis in a stepwise method showed that age at diagnosis, free surgical margins, and the total number of positive LNs were independently associated with survival.

Conclusions: LN metastasis and status of surgical margins were confirmed to be independent predictors for poor prognosis. Furthermore, number of positive LNs, spray invasive pattern, and perineural invasion correlated with increased risk for recurrence. These findings should be considered when identifying high-risk patients for further adjuvant therapy to prevent recurrence.

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205 - Poster

Endoscopic laser speckle contrast analysis: A novel method to assess blood flow in gynecologic surgery

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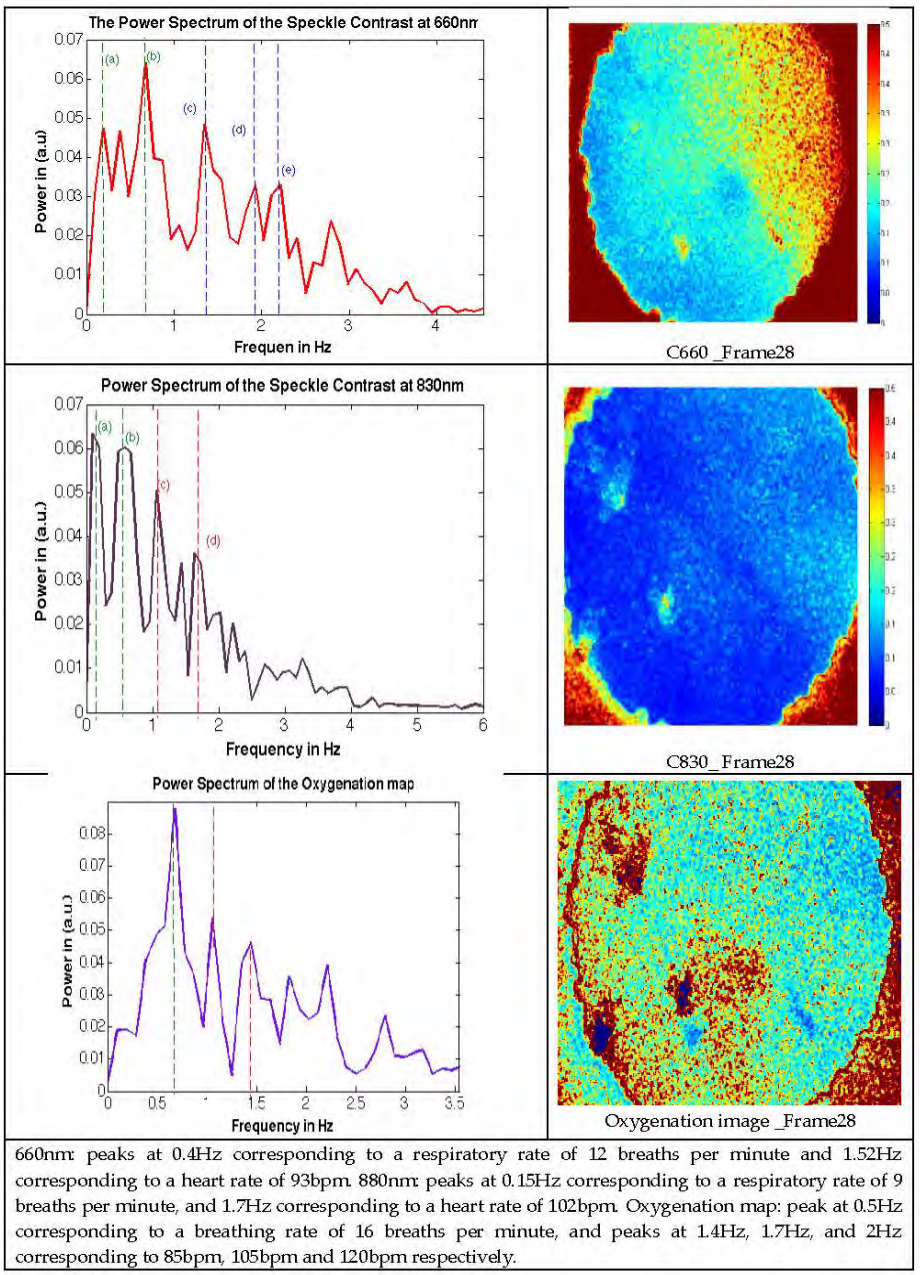
Objectives: To evaluate whether endoscopic laser speckle contrast analysis (eLASCA) could primarily assess uterine blood flow and circulatory function in uterine transplantation (UTx). Secondary aim was to use those data to provide information on crucial physiologic variables: respiratory and heart rates and oxygen saturation (SaO_2).

Methods: eLASCA was performed in 2 animal models. In rabbit UTx, eLASCA was carried out before recipient hysterectomy to pilot the technique and apparatus. In sheep UTx, eLASCA was performed before graft retrieval and 30 minutes after establishment of perfusion. Custom-written image analysis software was used to generate maps of spatial variations in blood flow, and Fourier signal analysis was performed to extract cardiac and respiratory rates.

Results: In rabbit UTx, eLASCA showed that blood flow can be picked up in the pelvis of a small animal. The sheep studies were performed before graft retrieval and after UTx in 2 operations, and before retrieval only in 1. The preliminary results show that eLASCA has the potential to determine blood flow, as well as heart and respiratory rates and relative oxygen saturation. Figure 1 demonstrates power spectrum graphs and oxygen maps that illustrate how this is done.

Conclusions: There are no standard intraoperative methods for simultaneous quantification of blood flow velocity, vascular anatomy, heart rate, and tissue oxygenation at the time of gynaecologic surgery. eLASCA is a novel imaging innovation that does not exist in medical practice and could offer a solution. It is a noncontact system that does not cause any tissue damage, and also provides real-time data. This gives information related to the presence of adequate blood flow to a particular tissue. From that information, heart and respiratory rates and oxygen saturation are calculated by measuring intensity fluctuations in reflected laser light because of backscattering by red blood cells.

This is the first time that eLASCA has been attempted in gynecology. Early results demonstrate its potential to quantify the health of the vasculature during extensive pelvic surgery. Currently its application is more qualitative than quantitative and some engineering challenges need to be resolved before it can be introduced in gynecologic oncology practice.



660nm: peaks at 0.4Hz corresponding to a respiratory rate of 12 breaths per minute and 1.52Hz corresponding to a heart rate of 93bpm. 880nm: peaks at 0.15Hz corresponding to a respiratory rate of 9 breaths per minute, and 1.7Hz corresponding to a heart rate of 102bpm. Oxygenation map: peak at 0.5Hz corresponding to a breathing rate of 16 breaths per minute, and peaks at 1.4Hz, 1.7Hz, and 2Hz corresponding to 85bpm, 105bpm and 120bpm respectively.

Fig. 1

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We banned the use of intracorporeal morcellation, what happened next? A look back at patterns of care and safety a year later

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Objectives: Our multihospital delivery system places patient safety at the forefront of our mission. In response to the US Food and Drug Administration safety communication on April 17, 2014, regarding the use of power morcellation, we banned the use of intracorporeal morcellation effective April 22, 2014. Many clinicians expressed frustration and a concern that patients would be harmed by this action. Specific concerns included an increase in the abdominal hysterectomy rate or percentage, an increase in wound complications, and an increase in length of stay. As a component of our PDCA (*plan, do, check, and act*) safety process, our objective was to review these quality and safety metrics 1 year later, and confirm the benefit of this intervention.

Methods: This is a retrospective evaluation of a prospective institutional decision. Data from our hospital were evaluated in a patient anonymous fashion using Crimson and Optum quality reporting software.

Results: In the year preceding the banning of intracorporeal morcellation (2013), the power morcellator was used in 157 cases. In the 12 months aftr the institutional ban, the wound complication rate, surgical site infections, and length of stay all decreased. The use of morcellation was not replaced by an increase in abdominal hysterectomies, but rather by total laparoscopic hysterectomy and an increase in vaginal hysterectomy.

Conclusions: An institutional ban of intracorporeal and power morcellation resulted in a decrease in the overall number of hysterectomies, including abdominal hysterectomy. Laparoscopic supracervical hysterectomy was replaced by hysterectomies relying on removal of the uterus through the vagina, and an associated decrease in complications and length of stay.

Table 1
Outcomes Before and After Banning Morcellation.

Complication	04/13 – 04/14	04/14 – 04/15	Percent Change
Wound complication/infection	2.4%	1.4%	–41.7%
Surgical site infection (SSI)	24/1,018	13/979	–45.8%
Length of stay	3.93 days	3.25 days	–17.3%
Type of hysterectomy	04/2013 – 04/2014	04/2014–04/2015	
Abdominal	212 (20.8%)	178 (18.2%)	–16.0%
Laparoscopic supracervical	116 (10.2%)	34 (3.5%)	–70.7%
Robot-assisted TLH	204 (20.0%)	211 (21.6%)	+3.4%
Total laparoscopic	232 (22.8%)	286 (29.2%)	+23.3%
LAVH	67 (6.6%)	73 (7.5%)	+14.9%
Vaginal	187 (18.4%)	197 (20.1%)	+5.3%
Total	1,018	979	–3.7%

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Chemo-induced biology of PD-L1 and in vivo combination immune therapy for ovarian cancer

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Objectives: PD-L1 blockade prevents PD-L1/PD-1 interaction and is currently explored as immune therapy for solid tumors. Tumor expression of cyclooxygenase-2 contributes to immune dysregulation but can be inhibited by celecoxib. Ovarian cancer patients receive combination platinum/taxane but chemotherapy effects on tumor PD-L1 expression have only been partially explored. We hypothesize that (1) chemotherapy exposure upregulates PD-L1, and (2) adding PD-L1 blockade with or without celecoxib to cisplatin enhances antitumor immunity.

Methods: Human (OVCA420 and OVCA432) and mouse (2F8 and 2F8-Cis) cell lines were exposed to cisplatin and paclitaxel. PD-L1 expression was analyzed with flow cytometry and Western blot analysis. In vivo, 57 mice were challenged intraperitoneally with 2F8 cells and distributed to different treatment protocols, using combinations of

anti-PD-L1, celecoxib, and cisplatin. Tumor- and ascites-derived cancer cells were analyzed with flow cytometry. RNA was extracted from splenocytes and analyzed with Nanostring using probes for 511 immune genes.

Results: Chemotherapy exposure triggers PD-L1 upregulation in human OVCA420 and OVCA432 cells. Similarly 2F8-Cis, a novel murine cell line derived de novo via gradual in vitro exposure to cisplatin, has increased PD-L1 compared with parental 2F8 cells. In vivo intraperitoneal therapy with single agent anti-PD-L1 or in combination with cisplatin reduced tumor burden (P = .029). Celecoxib reversed the anti-PD-L1 benefits and demonstrated a strikingly different gene signature. Tumor cell culture samples from cisplatin-treated mice expressed more PD-L1, with increased PD-1-expressing cells found among the tumor cells versus cisplatin/anti-PD-L1 treated mice.

Conclusions: Tumor cells upregulate PD-L1 in response to exposure to platinum/taxanes, providing the rationale for PD-L1 blockade in combination with chemotherapy in ovarian cancer. Combination high-dose PD-L1 blockade with cisplatin controls tumor burden, though further optimization of timing and dosage is needed. Celecoxib reduced the survival advantage and cytotoxic gene signature, suggesting limited efficacy in this preclinical model.

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208 - Poster

'When will my cancer be addressed?' A retrospective evaluation of factors that contribute to delay in care for women with ovarian cancer

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Objectives: To characterize the length of time between critical points in the care of women with ovarian cancer and determine the impact of patient demographics.

Methods: A retrospective chart review was performed for all patients diagnosed with ovarian cancer in the past 3 years at a large community hospital. Forty-five patients were identified who met the inclusion criteria for the study. The patient demographics recorded were age at diagnosis, race, insurance type, geographic and driving distance to the hospital, cancer stage, and preoperative CA-125. The critical time points used were date of initial concerning imaging (T1), first gynecologic oncology appointment (T3), initiation of treatment (T4), and adjuvant therapy (T5). Univariate analyses were used to determine associations between specific patient demographics and the time intervals above.

Results: Patient demographics are included in Figure 1. The mean age at diagnosis was 61 years. The mean geographic and driving distance between the patient's home and hospital was 9.2 and 10.9 miles, respectively. Most patients were Caucasian (58%), Medicare enrollees with supplemental insurance (44%), and diagnosed at an advanced stage (63%). Preoperative CA-125 was more than 200 in 62% of the patients. The average time from initial imaging to initiation of treatment was 37.5 days. The time from initial imaging to first office-based visit with a gynecologic oncologist was 18.1 days, and it took an additional 19.4 days to initiate treatment. The average time from surgery to adjuvant chemotherapy was 31.9 days. Conversely, the average time from the start of neoadjuvant chemotherapy to interval cytoreductive surgery was 102.6 days. There were no statistically significant associations between the patient demographics and length of time intervals.

Conclusions: Considering that ovarian cancer is often diagnosed at an advanced stage with low 5-year survival rates, it is important to ensure rapid transit through health care systems to prevent delay in diagnosis and treatment. This study is the first US characterization of health care transit times for patients with ovarian cancer. Additional studies with larger sample sizes and varied health care systems are needed to identify meaningful predictors of transit time to standardize time to treatment.

Table 1
Patient Demographics.

	N	**Mean**	**SD**
Age (y)	45	61.1	14.1
Geo Distance to Hospital (mi)	45	9.2	6.6
Driving Distance to Hospital (mi)	44	10.9	6.4
	N	%	
Early Stage (1&2)	17	37.8	
Advanced Stage (3&4)	28	62.2	
CA- 125 <200	14	37.8	

CA - >200	23	62.2	
African American	1	2.2	
Asian	8	17.8	
Caucasian	26	57.8	
Latino	10	22.2	
Commercial/ PPO	5	11.1	
HMO Only	15	33.3	
HMO with Supplement	1	2.2	
Medicaid Only	1	2.2	
Medicare Only	1	2.2	
Medicare with Supplement	20	44.4	
Self-Pay/Uninsured	2	4.4	

Table 2
Transit Time Intervals.

	N	Mean (d)	Median (d)	SD
Suspicion to First Treatment (T1 to T4)	45	37.5	31	25.5
Suspicion to Initial Gyn Onc Appt. (T1 to T3)	45	18.1	12	15.2
Initial Gyn Onc Appt. to Initial Treatment (T3 to T4)	45	19.4	14	17.0
Primary Cytoreductive Surgery to Neoadjuvant Chemotherapy	32	31.9	30	11.0
Neoadjuvant Chemotherapy to Interval Cytoreductive Surgery	8	102.6	99	29.5

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209 - Poster

The cost-effectiveness of the DISINFECT Initiative (Decreasing the Incidence of Surgical INFECTions) in gynecologic oncology

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Objectives: To evaluate the cost-effectiveness of a quality improvement (QI) project to decrease surgical site infection (SSI) rates after gynecologic cancer surgery.

Methods: We performed a QI project to decrease SSI rates after open and minimally invasive surgery using the following interventions: patient education; preoperative antibacterial soap; appropriate antibiotic prophylaxis with redosing; change of gloves and clean instruments at surgical closure; surgical dressing for 48 hours; and postdischarge phone call to assess for infection. SSI was defined as an infection of the surgical incision or organ space requiring antibiotics. The baseline (BL) SSI rate within 30 days of surgery was obtained from chart review (May 1, 2014 to June 30, 2014) and compared with postintervention (PI) (April 16, 2015 to July 15, 2015) data. SSI rates were compared between groups with the Fisher exact test. Intervention cost was calculated from the hospital perspective and the average cost of SSI treatment was calculated from hospital billing data related to SSI readmissions. The cost of SSI readmission represents a loss to the hospital because readmission for SSI within 30 days of surgery is not reimbursed.

Results: One hundred and sixty-six BL cases were compared with 241 PI cases. The overall SSI rate decreased from BL to PI (12% vs 6.6%, $P = .04$). Rate of SSI by site in the BL and PI groups, respectively, were: superficial (7.8% vs 4.1%), deep (1.2% vs 0.4%), and organ space (OS) (3.6% vs 2.9%). Extrapolating to a year, 35 superficial, 8 deep, and 7 OS SSIs would be avoided. The average intervention cost was $17.23 per case. This included the cost of preoperative soap and changing instruments, gloves, Bovie and suction tip at surgical closure. As educational efforts and staff involvement occurred within scheduled lectures and work duties, no personnel costs were included. The average estimated cost of treatment was $518 for superficial SSI, $5,959 for deep SSI, and $90,481 for OS. The intervention was estimated to save $682,576 per year or $13,652 per SSI avoided. A sensitivity analysis decreasing the SSI cost estimates by one standard deviation still found an overall savings of $119,011 a year or $2,380 per SSI avoided.

Conclusions: Our findings suggest that this intervention significantly decreases SSI rates and lowers hospital costs.

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Primary placement of incisional negative pressure therapy at time of laparotomy for gynecologic malignancies

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Objectives: Wound complications are important causes of postoperative morbidity among patient with gynecologic malignancies. This study evaluates whether the placement of prophylactic negative pressure wound therapy (NPWT) at the time of laparotomy for gynecologic cancer surgery can reduce wound complication rates.

Methods: This is a retrospective analysis of patients treated for gynecologic malignancy at a single academic institution between 2009 and 2013. Women undergoing laparotomy with primary wound closure performed by a gynecologic oncologist were included. The primary intervention examined was placement of prophylactic NPWT dressing. The primary outcome measured was wound complication.

Results: A total of 230 patients were identified. Of these, 208 women received standard wound care, while 22 received NPWT. Groups were similar in age, cancer diagnosis and stage, prevalence of diabetes, tobacco use, and number of previous abdominal surgical procedures. Intraoperative factors including length of procedure, anesthesia type, and transfusion requirement were similar as well. Body mass index (BMI) for patients receiving standard treatment was 30.7 compared to 41.3 for the NPWT group ($P < .001$). Incidence of all postoperative wound complications was 19.7% for those receiving standard treatment versus 27.3% for the NPWT group ($P = 0.4$, see Table). Length of hospital stay was similar between the 2 groups as well (5.2 vs 6.2 days, $P = 0.2$). There were 3 hospital readmissions for wound complications, with none occurring in women with a prophylactic NPWT dressing.

Conclusions: Despite significantly higher BMIs, patients with prophylactic NPWT dressing placement had similar rates of wound complications. The severity of wound complications appeared lower. Our findings suggest a potential benefit with the use of prophylactic NPWT for reducing wound complications in this high-risk gynecologic oncology patient population.

Table 1
Wound complications amongst included patients.

	Control n, (%)	Negative Pressure Wound Therapy Group n, (%)
No Complication	163 (78.4)	15 (68.2)
Wound Complication	45 (21.6)	7 (31.2)
• Home health ordered postop for wound	10 (4.3)	3 (13.6)
• Hospital Readmission for wound complication	3(6.7)	0(--)
Wound separation	25 (55.6)	3 (42.9)
Cellulitis	10 (22.2)	1 (14.2)
Seroma	6 (13.3)	2 (28.5)
Hematoma	3 (6.7)	1 (14.2)
Enterocutaneous fistula	1(2.2)	0 (--)

211 - Poster

Staging lymphadenectomy in low-grade endometrial cancer: A prospective cohort study utilizing a standard algorithm

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Objectives: The role of comprehensive lymphadenectomy in staging of low-grade endometrioid endometrial cancer is controversial. The "Mayo Criteria" incorporate intraoperative evaluation of uterine tumor size, depth of invasion, histology, and grade into an algorithm to guide decision-making. Our institution elected to use this algorithm in 2012. The purpose of this study is to examine adherence to the algorithm.

Methods: Data were prospectively collected between July 2012 and June 2015. Women undergoing primary surgery with a grade 1 or 2 endometrioid adenocarcinoma on preoperative biopsy, and thus potential candidates for deferral of staging according to an algorithm published by authors at the Mayo Clinic, are included in this analysis.

Results: During the study period, 360 consecutive women were eligible for inclusion. Median age and body mass index (BMI) were 62 years (range, 35–89 years) and 35 kg/m^2 (range, 18–66 years), respectively. The surgical approach used was traditional laparoscopy (n = 246), robotic-assisted laparoscopy (n = 46), laparotomy (n = 36), laparoendoscopic single-site (n = 29), and vaginal (n = 3). Intraoperative pathology evaluation was performed in 324 women (90%). The staging algorithm was strictly followed in 220 women (68%). Although the algorithm triaged 99 women (30%) to undergo comprehensive staging, it was performed in only 31 (31%). Pelvic lymphadenectomy alone was performed in an additional 41 women (41%). The algorithm triaged 225 women (70%) to deferral of lymphadenectomy, and it was deferred in 188 women (84%). Age and BMI did not differ significantly between women who were staged and those who were not. Of the 68 women who did not undergo comprehensive staging when the algorithm had dictated such, the factor that prompted staging per the algorithm was tumor size greater than 2 cm, deep myometrial invasion, or grade 3 histology in 61 (90%), 6(9%), or 1 woman (2%), respectively.

Conclusions: Despite widespread acceptance among providers, we observed limited adherence to an algorithm for standardization of approach to staging in women with low-risk endometrial cancer. Limited confidence in the tumor size cutoff as a reliable indicator for risk was most associated with decreased adherence. We are in the process of considering replacement of this algorithm with a sentinel lymph node algorithm for staging.

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Management of type II/high-grade endometrial cancer: A prospective cohort study utilizing a standard algorithm

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Objectives: Type II or high-grade endometrial cancers are more frequently metastatic at the time of diagnosis.The National Comprehensive Cancer Network (NCCN) guidelines do not mandate imaging, but suggest magnetic resonance imaging (MRI)/computed tomograph (CT)/positron emission tomography (PET) “as clinically indicated,” followed by hysterectomy, bilateral salpingo-oophorectomy, comprehensive pelvic and para-aortic lymphadenectomy, and often omental biopsy. Beginning in 2012, we elected to incorporate preoperative PET with concurrent diagnostic-quality torso CT scan (PET-CT) as part of this standard management algorithm. The purpose of this study is to examine how this preoperative imaging affected surgical and adjuvant management.

Methods: Prospective collection of clinical and surgical data in women with preoperative diagnosis including uterine carcinosarcoma, grade 3 endometrioid, clear cell, and serous carcinomas was performed between July 2012 and June 2015. When extrauterine disease was evident on physical examination or PET-CT, the primary treatment was revised at physician discretion.

Results: Median age of 116 women eligible for inclusion was 68 years (range, 43–91 years). Preoperative PET-CT imaging was performed in 85 women (73%), and not performed in 26 women (24%) because of lack of insurance coverage. Of the 85 women studied with PET-CT preoperatively, extranodal metastatic disease was predicted in 11 women (13%) and nodal metastatic disease in 19 women (22%) based on PET-CT findings. Of these, extranodal and nodal disease was confirmed at surgery in 9 and 15 women (81% and 80%), respectively. Surgical approach to hysterectomy involved a minimally invasive approach in 72 patients and laparotomy in 43 patients. Surgical management was modified to debulking surgery in 26 women (31%) based on PET-CT findings. In the 59 women with PET-CT scans suggestive of uterine-confined disease, comprehensive staging was performed in 49 women (83%) and metastatic disease documented in 5 women (10%).

Conclusions: Our data support revising the NCCN guidelines to recommend preoperative PET-CT for type II endometrial cancer patients. In our study, a consistent strategy of preoperative imaging led to important surgical modifications. NCCN approval would likely enable the one- quarter of patients who could not undergo preoperative PET-CT because of insurance coverage to be able to so and in turn optimize their treatment plan from the beginning.

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Panniculectomy morbidity: Using risk score to identify patients for additional care

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Objectives: Panniculectomy at the time of gynecologic surgery is used to improve visualization and prevent major complications in the morbidly obese patient. We examine the role of extended antibiotic prophylaxis in preventing surgical site infections specifically based on patient risk factors (hypertension, diabetes, smoking).

Methods: A prospective study was performed for patients who underwent a combined panniculectomy at the time of gynecologic surgery from 2014 to 2015 at Aultman Hospital. Participants in this study received doxycycline 100 mg orally twice daily for 10 days after surgery as extended antibiotic prophylaxis. These patients were followed postoperatively and examined for wound complications. The characteristics and outcomes of these patients were then compared with those of historical controls from a retrospective chart review at the same institution from 1990 to 2014.

Results: Thirty-eight patients who underwent a panniculectomy at the time of gynecologic surgery received extended antibiotic prophylaxis. Of these, 6 (15.8%) were treated with additional antibiotics for wound infections, which decreased in comparison with 94 of the 300 historical controls (31.3%). Extended antibiotic prophylaxis specifically lowered the incidence of surgical site infections in patients with a history of hypertension (19.2% vs 44.9%) and diabetes (18.8% vs 47.1%) compared with those in the low-risk group.

Conclusions: Panniculectomy at the time of gynecologic surgery is a safe and effective option in obese patients. As with any major operation, there is a risk of surgical site infections. A previous retrospective chart review has shown hypertension, diabetes, and smoking to be predictive factors for surgical site infections. Patients with the risk factors of hypertension or diabetes benefited from an extended course of prophylactic antibiotics to prevent subsequent surgical site infections.

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214 - Poster

Does adjuvant radiation therapy improve overall survival in high-intermediate risk stage I endometrial cancer? A National Cancer Data Base analysis

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Objectives: Adjuvant radiation therapy (RT) improved local control in patients with high-intermediate risk (HIR) stage I endometrial cancer (EC) in randomized trials. Though no differences were found in overall survival (OS), the trials were not well-powered to study this. Using the National Cancer Data Base (NCDB), a population-based analysis was conducted to evaluate the survival impact of adjuvant RT in HIR EC patients.

Methods: The NCDB was queried for patients diagnosed with 1988 FIGO stage I endometrioid adenocarcinoma from 1998 to 2009 who underwent surgery with or without adjuvant RT. Patients with nonsurgical primary therapy, nonendometrioid histology, less than 30 days' follow-up, RT more than 6 months after surgery, and unknown stage/grade were excluded. HIR EC was defined as grade 3 or stage IC with any grade. Lymphovascular invasion was not included because this information is not available in the NCDB prior to 2010. Kaplan-Meier plots with log rank analyses were used to examine the impact of adjuvant RT on OS. Cox proportional regression was performed for multivariable analyses (MVA) of OS (covariates: age, stage, grade, comorbidity, and adjuvant chemotherapy [yes/no]).

Results: Of the 461,307 patients in the EC database, 9,931 patients met our inclusion criteria (Table 1). A total of 5,209 patients (52.4%) underwent surgery alone, 4,722 patients (47.6%) underwent surgery + adjuvant RT. Of patients who received adjuvant RT, 46.3% received external beam RT, 32.8% brachytherapy, 13.5% both, and 7.4% RT nonspecified. Five-year OS was 75.9% for the entire study group, 73.3% for the surgery alone group, and 78.6% for the surgery + adjuvant RT group ($P < .0001$). For patients with stage IC, grade 3 disease (n = 927), 5-year OS was 52.3% with surgery alone vs 68.5% with surgery + RT ($P < .0001$). On MVA, adjuvant RT was independently associated with improved OS versus surgery alone (HR 0.92, 95% CI 0.87–0.97, $P = .0034$).

Conclusions: The results from our study show that surgery + adjuvant RT was associated with a 5.3% improvement in 5-year OS compared with surgery alone in stage I HIR EC. These data along with prior studies suggest that the improvement in local control with adjuvant RT leads to improved OS.

Table 1
Baseline patient and treatment characteristics (n = 9,931).

	All HIR* patients (n = 9,931)	Surgery alone (n = 5,209)	Surgery + RT (n = 4,722)	P-value **
Mean age at diagnosis	66.2	67.1	65.4	<0.0001
Mean Charlson/Deyo Comorbidity Score***	0.29	0.33	0.26	<0.0001
% Lymph Node Dissection Performed	60.7%	60.6%	60.9%	0.0417
% Received Chemotherapy	10.9%	10.1%	11.9%	0.0006
Mean follow-up time (months)	65.8	63.3	68.4	<0.0001

*HIR = High-Intermediate Risk
**t-test to compare means; Chi-square to compare percentages
***"Because of the small proportion of cases with a Charlson Comorbidity score exceeding 2, the [NCDB] data has been truncated to 0, 1, 2 (greater than 1). A score of 0 indicates "no comorbid conditions recorded". Note that the patient's cancer is not directly reflected in the recorded score." http://ncdbpuf.facs.org/?q=content/charlsondeyo-comorbidity-index

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215 - Poster
Racial disparities in survival in malignant germ cell tumors of the ovary
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Objectives: To examine the characteristics of patients presenting with malignant ovarian germ cell tumors (OGCT), and investigate racial disparities with respect to adjuvant treatment and survival.

Methods: The National Cancer Data Base (NCDB) was used to identify women diagnosed with OGCT. Demographic data were abstracted, including stratification by race and histology. Standard univariate and multivariate analyses using logistic regression were performed to describe predictors of adjuvant treatment. Kaplan-Meier and Cox proportional hazards survival methods were used to evaluate racial differences in survival between African American (AA) and white women.

Results: The study population included 2,196 patients, with 1,654 (75.3%) white and 328 AA (14.9%) women. Histologic distribution varied significantly by race ($P < .0001$), with white race being 3.4 times more likely to present with dysgerminoma than AA (CI 2.4–4.7, $P < .0001$) and almost half as likely to present with malignant teratoma (RR 0.7, CI 0.6–0.6, $P < .0001$). In terms of adjuvant treatment, chemotherapy was administered to 1,234 patients (56.2%), and radiation was given to only 27 patients (1.2%). AA women received more chemotherapy than white women (65.5% vs 54.6%, respectively, $P = .008$), but after controlling for histology there was no statistically significant difference in any adjuvant treatment modality. Despite similar treatment and continuing to control for histology, survival varied significantly by race with 5-year survival rate being 91% in white patients (CI 0.89–0.93) compared with 84% in AA patients (CI 0.8–0.89) ($P = .02$). Stratified by stage, the racial disparities were most pronounced in advanced-stage disease, with 5-year survival for stage III disease being 84% (CI 0.79–0.89) in white women compared with 61% (CI 0.48–0.78) in AA women, and for stage IV disease being 54% (CI 0.42–0.68) in white women compared with 14% (CI 0.03–0.71) in AA women.

Conclusions: AA women with OGCT have significantly worse 5-year survival compared with white patients. This disparity persists despite similar rates and modalities of adjuvant treatment.

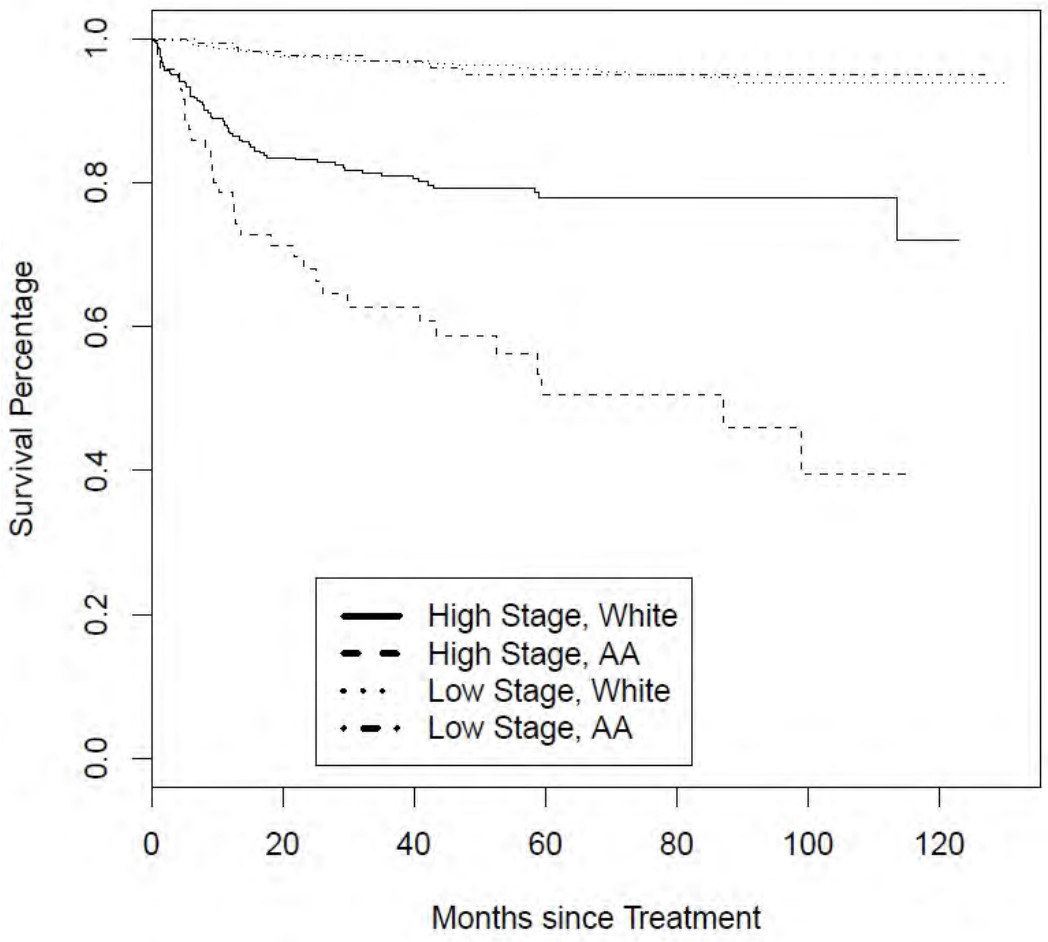

Fig. 1
Five-year Survival Kaplan-Meier Plot by Stage.

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Surgical resection margin including parametrium and vagina significantly correlates with survival of FIGO stage IB cervical cancer patients treated with radical hysterectomy: Multivariate analysis of 360 patients

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Objectives: The aim of this study was to identify the independent clinicopathologic prognostic factors for patients with FIGO stage IB cervical cancer treated with radical hysterectomy (RH) with retroperitoneal lymphadenectomy.

Methods: We retrospectively reviewed clinicopathologic data of 360 patients with FIGO stage IB cervical cancer treated with RH with retroperitonal lymphadenectomy between February 2000 and March 2015. Positive parametrial resection margin and vaginal cuff resection margin were analyzed separately. The disease-free survival (DFS) and overall survival (OS) were estimated using the Kaplan-Meier method. Univariate and multivariate Cox proportional hazard models were applied to analyze prognostic factors.

Results: The median follow-up time was 56 months (range, 3 to 184 months). The 5-year DFS and OS in FIGO stage IB cervical cancer were 91.4% and 97.9% (92.3% in DFS, 98.8% in OS, IB1 vs 74.3% in DFS, 83.2% in OS, IB2). In multivariate analysis, positive parametrial resection margin, tumor grade of 2 or higher, positive vaginal cuff margin, and FIGO stage IB2 were significantly related to DFS. Positive parametrial resection margin (OR 15.041, 95% CI 4.539–49.846, $P < .001$), FIGO stage IB2 (OR 3.533, 95% CI 1.283–9.728, $P = .015$), and tumor grade of 2 or higher (OR 5.466, 95% CI, 1.150–25.983, $P = .033$) were independent prognostic factors for OS.

Conclusions: Surgical resection margin including parametrium and vagina correlates with poor prognosis. The quality of radical parametrectomy and vaginectomy for cervical cancer influences local tumor control and survival. Therefore, it is important to optimize and ensure the quality of surgical management for cervical cancer patients.

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Young women with epithelial ovarian cancer: Prevalence of *BRCA* mutations and clinical correlates

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Objectives: Epithelial ovarian cancer (EOC) is usually diagnosed in postmenopausal women. *BRCA* mutations are frequent in Israeli EOC patients and put carriers at risk of developing disease at a young age. We explored the prevalence of *BRCA* mutations in young EOC patients as well as disease patterns and outcome and their correlation with *BRCA* mutation status in this patient population.

Methods: Consecutive patients diagnosed before age 50 years and treated for EOC at a single institution from 1995 to 2011 were identified. All EOC patients are referred for genetic testing. Medical records were reviewed and cross-referenced with databases at the oncogenetics unit to retrieve demographic and clinical data. Survival data were compared using the Kaplan-Meier method and the association of demographic, genetic, pathologic, and clinical variables with survival was assessed using the Cox proportional hazards method. Statistical analysis was performed with SPSS software.

Results: This analysis included 186 patients diagnosed with EOC before age 50 years. Mean follow-up was 70.2 months. Of 113 patients with documented *BRCA* testing, 49.6% carried germline mutations compared with 29% in the general Israeli EOC population ($P = .001$). *BRCA* mutation carriers had a higher frequency of serous tumors (75% vs 64%, $P = .07$), whereas endometrioid and clear cell histologies were unusually common among young noncarriers (11% and 14%, respectively). Mutation carriers were more frequently diagnosed at an advanced stage (64% vs 52%, $P = .25$), and had higher CA-125 levels at diagnosis (median, 401 vs 157, $P = .001$). *BRCA* mutations, early disease stage, and nonserous histologies were found to be significantly associated with improved disease-free and overall survival on univariate analysis, but *BRCA* status was not found to independently affect survival measures on multivariate analysis (HR 1.032 and 1.13, respectively; not significant). Median overall survival was 85 months and progression-free survival was 29 months for this patient population.

Conclusions: *BRCA* mutations are significantly more frequent in young patients with EOC than in the general EOC population. Mutation carriers typically have serous tumors and present with more advanced disease, but show a trend for later recurrences and prolonged survival, which does not hold up on multivariate analysis. Regardless of mutation status, progression-free and overall survival were extended in this young ovarian cancer patient population.

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Adverse impact of bulky (≥2 cm) pelvic lymph node involvement determined by magnetic resonance imaging in FIGO stage IIB cervical cancer patients treated with primary concurrent chemoradiation therapy

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Objectives: The aim of this study was to identify prognostic factors associated with disease recurrence and survival in patients with FIGO stage IIB cervical cancer treated with primary concurrent chemoradiation.

Methods: Between April 2001 and January 2013, 139 patients with FIGO stage IIB cancer of the uterine cervix were analyzed retrospectively. All patients received weekly concurrent cisplatin chemotherapy with a dose of 40 mg/m^2. Irradiation consisted of external beam pelvic radiation with parametrial boost and high-dose rate brachytherapy. Disease-free survival (DFS), overall survival (OS), and prognostic factors affecting disease recurrence and survival after primary concurrent chemoradiation were evaluated.

Results: The median follow-up time was 43 months (range, 7 to 168 months). The 5-year DFS and OS were 84.1% and 81.4%, respectively. In univariate analysis, pelvic lymph nodes (LNs) greater than or equal to 2 cm in maximum short axis diameter (MSAD) on magnetic resonance imaging (MRI) and pretreatment SCC-Ag/Cyfra 21-1 levels were associated with DFS and OS. In multivariate analysis, pelvic LNs of 2 cm or larger in MSAD on MRI was an independent prognostic factor for distant recurrence, DFS, and OS (OR 4.398, 95% CI 1.187–16.288, $P = .027$). There were significant differences in both 2-year DFS and OS between nonbulky (<2 cm) and bulky (≥2 cm) nodal groups (93.9% vs 47.2% in DFS, 95.0% vs 42.1% in OS). Hematologic toxicities were the most frequent acute toxicities (grade ≥3 neutropenia, 10.8%; grade ≥3 anemia, 8.6%; grade ≥3 thrombocytopenia, 2.9%). Sites of recurrence were within the irradiation field in 8 cases, outside the field in 14 cases, and in both fields in 4 cases.

Conclusions: Bulky pelvic LNs of 2 cm or larger in FIGO stage IIB cervical cancer have an adverse impact on survival. Pretreatment pelvic LN status assessed using MRI might be helpful to predict treatment outcome. Alternative approaches are needed to improve outcomes for such patients.

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219 - Poster

The complex interaction of cancer surgery, complications, and patient-reported outcomes: A single score is not enough

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Objectives: Emerging value frameworks prioritize patient-defined quality of care, but normative data on the quality of life (QoL) journey from the pre- through the postoperative phases are scarce. This study examined the impact of surgery and complications on QoL in a prospective cohort of women at a gynecologic oncology tertiary care center.

Methods: Patients were enrolled preoperatively (October 2013–October 2014), and completed patient-reported outcomes (PROs) assessments at baseline, 1, 3, and 6 months postoperatively. Measures included externally validated instruments of many physical and mental QoL domains. Clinical data were obtained from the medical record. Surgical complications were graded using the validated Clavien-Dindo scale. Bivariate statistics, responder analysis, and multivariate modeling were used.

Results: Of 208 women enrolled, survey completion rates were 88% at 1 month and 83% at 6 months. Uterine (46%), ovarian (13%), cervical (9%), vulvar (2%), other (2%) cancers, and benign disease (28%) were represented. Mean age was 56 years and 24% were ethnic minorities. QoL domains were affected disparately by surgery. From baseline to 1 month, functional wellbeing (20 -> 17.6, $P < .0001$) and work ability (10 -> 7.5, $P < .0001$) decreased, while emotional well-being improved (16.3 -> 20.1, $P < .0001$) and anxiety decreased (54.2 -> 49.0, $P < .0001$). By 6 months, in the absence of severe complications, functional well-being and work ability recovered to baseline, while gains in emotional well-being and anxiety were preserved (Figure).

Postoperative morbidity (PM) occurred in 26% of patients with grade 1 (n = 12), 2 (n = 29), and 3 (n = 6) complications. Changes between baseline, 1-month, and 6-month scores in most QoL measures were similar between PM and no PM with exception of anxiety: patients with PM had more anxiety at 1 month versus baseline (OR 2.5, 95% CI 1.2–5.0). In contrast, those with grade 3 complications had a trend toward sustained decreased QoL (Figure).

Conclusions: For women undergoing gynecologic oncology surgery, temporary decline in functional QoL is balanced by improvements in emotional QoL and anxiety. However, patients with major complications appear to have sustained worsened QoL, indicating that PROs have a role in surgical quality metrics. The timing and choice of PRO instrument will significantly affect the interpretation of quality outcomes.

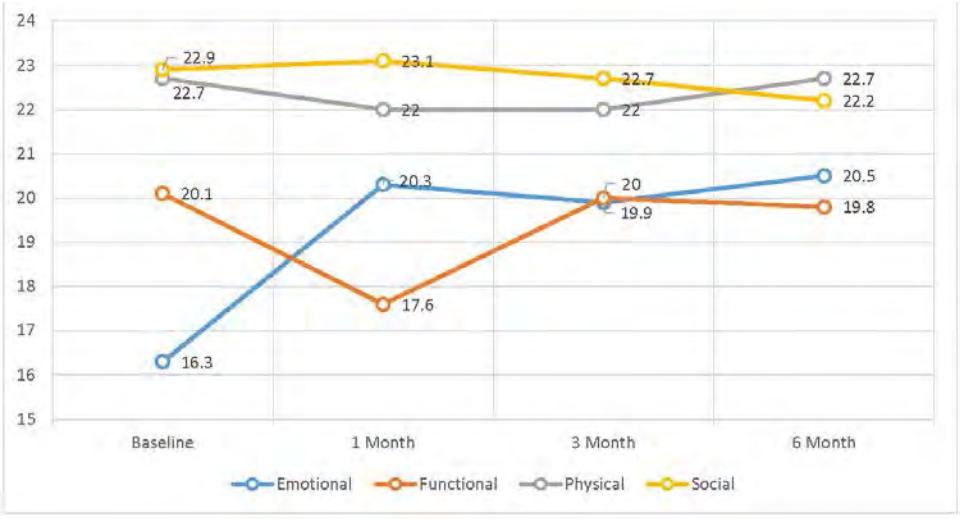

Fig. 1
Functional Assessment of Cancer Therapy (FACT-GP): Subdomains of Quality of Life before and After Surgery (All Patients).

Fig. 2
Fact-GP QOL Score Before and After Surgery: The Impact of Major Complications.

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220 - Poster
Accuracy in determining high-risk endometrial cancer pre- and intraoperatively
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Objectives: To describe our accuracy in determining endometrial cancer high-risk group of lymph node metastasis, using preoperative (magnetic resonance imaging MRI and endometrial biopsy by dilation and curettage D&C) and intraoperative assessments (frozen section).

Methods: This is a prospective study approved by our institutional review board. We included all women with endometrial cancer who were surgically treated at our institution between September 2011 and February 2015. We calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and AUC of MRI and frozen section to detect deep myometrial invasion, and of endometrial biopsy using D&C and frozen section to determine high-grade endometrial cancer histology, considering the final paraffin report as gold standard.

Results: The results from 125 women included in the study are summarized in Table 1. For detection of deep myometrial invasion, the sensitivity, specificity, PPV, NPV, and AUC of MRI were 70.9%, 89.4%, 88.6%, 72.4%, and 0.79, respectively, and of frozen section analysis were 74.6%, 94.3%, 94.3%, 74.6%, and 0.83, respectively. For endometrial biopsy to diagnose high-grade histology, the sensitivity, specificity, PPV, NPV, and AUC using D&C were 53.5%, 91.7%, 88.6%, 72.4%, and 0.72, respectively, and with frozen section analysis, were 45.1%, 97.6%, 95.8%, 58.8%, and 0.69. When the preoperative workup is analyzed in conjunction with MRI and endometrial biopsy of high-risk endometrial cancer, the sensitivity, specificity, PPV, NPV, and AUC were 89.8%, 79%, 86.9%, 83.3%, and 0.85, respectively. In an intraoperative assessment in conjunction, the sensitivity, specificity, PPV, NPV, and AUC were 87.5%, 90.2%, 93.3%, 82.2%, and 0.85, respectively.

Conclusions: Preoperative and intraoperative assessments have adequate accuracy in determining deep myometrial invasion, but do not have good sensitivity and NPV to determine high-grade histology. Used in conjunction, both preoperative and intraoperative assessments have the best accuracy in detecting deep myometrial invasion and high-grade tumors that will reach lymph node metastasis in high-risk patients.

Table 1
Results.

MRI (MI ≥50%)	70.9% (57.1-82.4)	89.4% (76.9-96.5)	88.6% (75.4-96.2)	72.4% (59.1-83.3)	0.79 (0.68-0.91)
D&C (HG Hist)	53.5% (39.9-66.7)	91.7% (80.0-97.7)	88.6% (73.3-96.8)	62.0% (49.7-73.2)	0.72 (0.59-0.84)
Preoperative Assesment	89.8% (79.2-96.2)	79.0% (62.7-90.5)	86.9% (75.7-94.2)	83.3% (67.2-93.6)	0.85 (0,74-0.95)
Frozen Section (MI ≥50%)	74.6% (62.5-84.5)	94.3% (84.3-98.8)	94.3% (84.3-98.8)	74.6% (62.5-84.5)	0.83 (0.73-0.94)
Frozen Section (HG Hist)	45.1% (31.1-59.7)	97.6% (87.1-99.9)	95.8% (78.9-99.9)	58.8% (46.2-70.6)	0.69 (0.57-0.82)
Intraoperative Assesment	87.5% (76.9-94.5)	90.2% (76.9-97.3)	93.3% (83.3-98.2)	82.2% (68.0-92.0)	0.85 (0.75-0.95)

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Prognostic factors for adnexal metastasis in endometrial cancer and its implication for ovarian preservation

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Objectives: To determine the risk factors related to adnexal metastasis in endometrial cancer and its implication for ovarian sparing surgery.

Methods: We analyzed a series of 635 patients treated at AC Camargo Cancer Center from July 1991 to July 2015. Patients who had peritoneal or systemic dissemination (stage IV) were excluded.

Results: Median age was 61.6 years (range, 29–91 years), and 36 (5.8%) patients were younger than 45 years of age, with 5 (0.8%) being younger than 40 years. Pathological characteristics included 37.9% (206/544) with histologic grade 3; 17% (87/512) with lymphovascular space invasion (LVSI); 13.1% with type 2 tumors (79/597); and 38.5% (227/589) with myometrial invasion greater than 50%. Most patients (81.4%) underwent pelvic ± para-aortic lymphadenectomy, with 13.2% pelvic positive nodes and 11.8% para-aortic positive nodes. Fifty-four patients (8.5%) had adnexal involvement, of which 47 (7.4%) were ovarian and 25 (3.9%) tubal metastases. Of patients younger than 45 years, 16.7% (6/36) had adnexal metastasis compared with 7.7% (45/587) among those aged 45 years and older ($P = .10$). Moreover, 20% of patients (1/5) younger than 40 years had adnexal metastasis. However, all 6 patients with adnexal metastasis who were younger than 45 years had high-risk pathological features, with 5 patients having grade 3 tumors ± LVSI and 1 patient having node metastasis. Adnexal metastasis was statistically related to type 2 tumors (22.8% vs 6.8%, $P < .001$), LVSI (26.4% vs 5.9%, $P < .001$), myometrial invasion greater than 50% (14.5% vs 5.0%, $P < .001$), grade 3 tumors (16.0% vs 5.0%, $P < .001$), pelvic node metastasis (27.9% vs 5.6%, $P < .001$), and para-aortic node metastasis (37.5% vs 7.0%, $P < .001$). Considering the uterine prognostic factors, LVSI (HR 3.79, CI 95% 1.85–7.75, $P < .001$) and grade 3 (HR 2.17, CI 95% 1.10–4.30, $P = .025$) were independent risk factors for adnexal metastasis in multivariate analysis.

Conclusions: Presence of LVSI and grade 3 tumors was independently correlated with adnexal metastasis. Our data indicate that ovarian preservation may be considered for young patients with low-risk endometrial cancer (grades 1 and 2 tumors, absence of LVSI, and myometrial invasion <50%).

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Treatment of gestational trophoblastic neoplasia and choriocarcinoma by targeting the endoglin-BMP9 axis

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Objectives: To examine the potential for endoglin (CD105) to be used as a therapeutic target in gestational trophoblastic neoplasia (GTN) and choriocarcinoma.

Methods: In preclinical models, expression of endoglin was measured with qualitative reverse transcriptase polymerase chain reaction, Western blot, and enzyme-linked immunosorbent assay in methotrexate-sensitive and resistant trophoblast cell lines in the presence or absence of methotrexate. Endoglin and BMP9, the ligand for endoglin, were assessed using immunohistochemistry in paraffin-embedded formalin-fixed tissues from women with gestational trophoblastic disease. In a case-control study, serum levels of soluble endoglin and BMP9 were measured in samples from 76 patients with low-risk GTN and then correlated with response to single-agent methotrexate therapy. In a single patient clinical trial, a patient with choriocarcinoma who had failed methotrexate, actinomycin-D, EMA-CO, EMA-EP, ICE, capecitabine, stem cell transplant, radiation, and metastatectomy was treated using a novel drug combination of bevacizumab + TRC105, a monoclonal antibody targeting endoglin.

Results: In vitro, endoglin was expressed in all 3 trophoblast lines. Relative expression of endoglin transcript and protein reflected resistance to methotrexate, with higher endoglin levels correlating with greater chemoresistance. Addition of methotrexate led to an increase in endoglin expression. In histologic sections, immunoexpression of endoglin and BMP9 were seen in the syncytiotrophoblasts of women with GTD, and the relative expressions of the 2 markers were highly correlated. A high correlation was also found between serum endoglin and BMP9 levels in vivo. Both markers were elevated in pretreatment samples of women who went on to develop methotrexate-resistant GTN. As a single marker, BMP9 levels were more predictive of methotrexate resistance than FIGO risk score alone. The patient treated with the novel agent protocol had a complete response with normalization of her human chorionic gonadotropin levels by cycle 4, with tolerable levels of toxicity.

Conclusions: Endoglin is highly expressed in syncytiotrophoblasts and GTN, and its expression is induced by methotrexate. Serum BMP9 may be a useful marker for increased endoglin activity and subsequent methotrexate resistance in patients with GTN. Endoglin-targeted therapy represents a new class of drugs for treatment of this disease.

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Prognostic factors in stage IIIC endometrial cancer
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Objectives: To determine the prognostic factors in stage IIIC endometrial cancer.

Methods: We analyzed a series of 71 patients diagnosed with lymph node (LN) metastasis (stage IIIC) after pelvic ± para-aortic lymphadenectomy at AC Camargo Cancer Center from May 1993 to December 2014.

Results: Median age was 62 years (range, 42-85 years). Of these, 73.2% (50/68) had grade 3 histology, 47% (31/66) had lymphovascular space invasion (LVSI), and 79.4% (54/68) had more than 50% myometrial invasion. Eleven patients (15.5%) had pelvic lymphadenectomy and 60 (84.5%) had pelvic and para-aortic lymphadenectomy. Median pelvic lymph node (PLN) and para-aortic lymph node (PALN) dissected was 27 (range, 1–85) and 15.5 (range, 1–45), respectively. Sixty-four patients (90.1%) had PLN metastasis (median, 2 LNs; range, 1–29), and 36 (50.7%) had PALN metastasis (median, 2 LNs; range, 1–18). The 5-year overall survival (OS) was 59.3%. OS did not correlate with the presence of PALN metastasis ($P = .67$), LVSI ($P = .14$), grade 3 tumors ($P = .92$), deep myometrial invasion (83% vs 51%; $P = .09$), type II tumors ($P = .66$), number of positive LNs (1–3 vs ≥4; $P = .45$), number of resected nodes (≤40 vs >40; $P = .8$), and type of LN dissection (PLN vs PLN + PALN: 38.6% vs 64.9%; $P = .17$). Only adjuvant chemotherapy had a positive effect on 5-year OS (76.6% vs 33.1%; $P = .001$). In multivariate analysis, adjuvant chemotherapy (HR 0.23, CI 95% 0.07–0.72, $P = .012$) was an independent prognostic factor for survival.

Conclusions: Adjuvant chemotherapy correlates with better survival in stage IIIC endometrial cancer.

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Combination metformin and simvastatin treatment synergistically inhibits endometrial cancer cell growth in vitro
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Objectives: Growing evidence suggests that the antidiabetic drug metformin as well as cholesterol-lowering drugs such as simvastatin lower the risk of several cancers including endometrial cancer. Both agents have shown antiproliferative effects on endometrial cancer, but their combined effects are unknown. We sought to evaluate the combined effects of metformin and simvastatin on endometrial cancer cell growth in vitro.

Methods: RL95-2, HEC-1B, and Ishikawa endometrial cancer cell lines were treated with metformin (4 mM) and/or simvastatin (1–8 μM). MTS cell proliferation assays were used to measure growth inhibition after 72 hours of treatment. Synergy was tested using CompuSyn. Apoptosis was evaluated by caspase-3 assay and propidium iodide/annexin V flow cytometry. Polymerase chain reaction (PCR) arrays were used to identify apoptosis-related genes. Treatment effects on the mTOR pathway were investigated with Western immunoblotting using antibodies to phosphorylated (phospho)-AMPK and phospho-S6. Statistical comparisons were made with significance at $P < .05$.

Results: Metformin, simvastatin, and their combination inhibited cell proliferation within 72 hours of exposure in all cell lines; inhibitory effects with combination treatment were synergistic (combination index 0.57–0.75) compared with treatments with individual agents. Combination treatment induced apoptosis in RL95-2 and HEC-1B cell lines; significantly greater caspase-3 activity was demonstrated with combination treatment compared with individual agents ($P < .01$). PCR analysis demonstrated upregulation of BAX, downregulation of BCL-2, and significant changes in several other genes in the death receptor pathway in these 2 cell lines after 24 hours of exposure to combination treatment compared with untreated controls. In all 3 cell lines, Western immunoblot analysis demonstrated that combination treatment increased phospho-AMPK and decreased phospho-S6 within 24 to 48 hours of exposure.

Conclusions: Combination metformin and simvastatin treatment of endometrial cancer cell lines in vitro demonstrates synergistic inhibition of viability, which may be mediated by apoptosis and mTOR pathway inhibition. This combination may have clinical usefulness in the prevention and treatment of endometrial cancer and should be further investigated.

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Sentinel node mapping in endometrial cancer: A Brazilian cancer center experience

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Objectives: The role of sentinel lymph node (SLN) mapping in endometrial cancer is still in debate. Our aim was to determine the detection rate, sensitivity, and negative predictive value of SLN mapping in low- and high-risk (grade 3, serous, clear cell, deep invasion, or angiolymphatic invasion) endometrial cancer.

Methods: We analyzed a series of 91 patients treated at AC Camargo Cancer Center from January 2013 to August 2015 who underwent SLN mapping with cervical injection of blue dye. Forty-nine (53.8%) patients had low-risk tumors and no further lymph node dissection (LND) or only pelvic LND. Forty-two (46.2%) patients had high-risk tumors and received pelvic ± para-aortic LND.

Results: Median age was 59.7 years (range, 37-84 years). Median body mass index (BMI) was 28.1 (range, 18-54). Twenty-one patients (23.1%) had open surgeries and 70 underwent (76.9%) minimally invasive surgeries. Thirty-two patients (36.8%) had pelvic LND, and 27 (28.2%) pelvic + para-aortic LND. The rate of SLN detection was 79.1% overall, and bilateral in 50.5% of cases. The median SLN detected was 2 per patient (range, 1-8). Sixteen patients (18.2%) had histologic grade 3, 17 (18.7%) had angiolymphatic invasion, 8 (8.8%) had serous/clear cell histology, and 22 (24.2%) had deep myometrial invasion. Notably, endometrial cancer was diagnosed after subtotal hysterectomy in 3 cases, and bilateral SLN was detected in all. BMI, age, open surgery, blue dye volume (2 vs 4 mL), and first 30 cases did not influence the detection rate. Four patients (4.4%) had technical difficulty with cervical injection, and in this situation, SLN was detected in only 1 (25%) case. No positive node was found in low-risk cases. In high-risk cases, 4 patients had only SLN with no further LND for medical reasons. In the high-risk group, at least 1 SLN was found in 34 (81%) patients and was positive in 8 (23.5%) cases. Two (5.8%) cases had isolated tumor cells, 1 (2.9%) had micrometastasis, and 5 had (14.7%) macrometastasis. Notably, 3 (37.5%) of 8 SLN metastases were found only on immunohistochemistry. Only 1 patient had false-negative SLNs, with ipsilateral pelvic and para-aortic non–sentinel positive nodes. The sensitivity was 88.9%, negative predictive value was 97.4%, and false-negative rate was 11.1%. Two (25%) patients with positive SLN had also other pelvic and para-aortic positive non-SLN.

Conclusions: Our data suggest that SLN mapping is a safe and accurate technique for high-risk tumors, and increases metastatic detection rate by 8.7% in high-risk tumors.

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Impact of sentinel node mapping in high-risk endometrial cancer staging: A comparative analysis

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Objectives: To determine the impact of sentinel lymph node (SLN) mapping in staging high-risk endometrial cancer. Pathological characteristics considered as high-risk tumors were grade 3 endometrioid histology, type II (serous and clear cell histology), deep myometrial invasion, and angiolymphatic invasion.

Methods: We analyzed a series of 233 patients who underwent lymph node (LN) dissection (group A) and compared the findings with those in 34 patients in whom SLN was detected after blue dye cervical injection (group B). All patients had high-risk tumors treated at AC Camargo Cancer Center and received pelvic ± para-aortic LN dissection.

Results: No differences were found between groups A and B regarding age (group A: median age, 62.7 years; range, 36-91 years; group B: median age, 60 years; range, 48–83 years; *P* = .059), type II tumors, presence of angiolymphatic invasion, deep myometrial invasion, and grade 3 tumors. Median pelvic LNs resected were 25 (range, 1–90) in group A and 23.5 (range, 2-57) in group B (*P* = .40). Group A had higher number of para-aortic LNs resected: median of 9 (range, 0-45) in group A and 2.5 (range, 0–43) in group B (*P* = .041). The overall LN and pelvic LN metastasis rate in group B was higher but not statistically significant. Groups A and B had LN metastasis in 21.9% (51/233) and 26.5% (9/34) cases, respectively (*P* = .55). Pelvic LN metastasis rate for groups A and B were 19.3% (45/233) and 26.5% (9/34), respectively (*P* = .33). Para-aortic LN metastasis rate for groups A and B were 12.6% (22/175) and 12% (3/25), respectively (*P* = 1.0).

Conclusions: Our data suggest that SLN mapping identified more pelvic LN metastasis compared with only LN dissection; however, it did not achieve statistical significance. Moreover, in the group that had SLN mapping, one-third of pelvic LN metastasis cases were detected only after immunohistochemistry.

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Unanticipated 30-day readmission following rectosigmoid resection at the time of cytoreductive surgery in patients with advanced-stage ovarian cancer

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Objectives: To analyze the rates and reasons for readmission of patients with advanced-stage ovarian cancer undergoing rectosigmoid resection as a part of cytoreductive surgery.

Methods: A retrospective review was conducted of all patients with primary ovarian cancer who underwent rectosigmoid resection as part of cytoreductive surgery between July 2003 and July 2014. The timing and reasons for unanticipated hospital readmission within 30 days of discharge were recorded. Readmission for planned chemotherapy was excluded. Univariate and bivariate analyses identified rates and reasons for readmission.

Results: Between July 2003 and July 2014, a total of 285 charts were identified, with 50 patients eligible for analysis. Among this cohort, the unanticipated 30-day readmission rate was 18% (n = 9). Of those readmitted less than 30 days from date of discharge, 3 were readmitted more than once, for a total of 14 readmissions (28%) during the study period. A total of 21 indications for readmission were reported in the reviewed records. The most common indication for readmission was infectious morbidity (i.e., pyelonephritis, infected pelvic hematoma) (23.8%, n = 5), followed by thromboembolic events (19%, n = 4) and severe protein calorie malnutrition requiring parenteral support (14.3%, n = 3). The remaining readmissions (n = 9) were attributed to cytopenia, anastomotic complications, weakness/nausea, wound dehiscence, and abdominal pain with ascites. Mean time to readmission was 13.0 days (range, 2–26; standard deviation, 8.59). Preoperative platelet level less than $150 \times 10^3/\mu L$ ($150 \times 10^9/L$) was associated with readmission within 30 days of discharge (OR 6.0, 95% CI 0.97–36.99). There were no deaths within 30 days of surgery in the cohort.

Conclusions: Unanticipated 30-day readmission remains a common problem among this population, with infectious morbidity and thromboembolic events being the most common causes for readmission. Further study of this population is needed to identify risk factors for early readmission, and potentially develop interventions to prevent this adverse outcome.

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The impact of body mass index on surgical outcomes of total laparoscopic radical hysterectomy

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Objectives: Minimally invasive procedures are associated with less surgical morbidity than equivalent procedures performed via laparotomy. We sought to compare surgical outcomes among ideal body weight, overweight, and obese women who underwent a total laparoscopic radical hysterectomy (TLRH).

Methods: TLRHs performed between June 2012 and May 2015 were reviewed. Data collected included body mass index (BMI), stage of malignancy, operating room (OR) time, estimated blood loss (EBL), length of hospitalization, length of bladder catheterization, intra- and postoperative complications, and pathology. Comparison between groups was performed with analysis of variance (ANOVA) or Fisher exact test with $P < .05$ considered statistically significant.

Results: Thirty-one patients underwent TLRH. Twenty-nine were treated for early-stage cervical cancer (stage IA1 = 3; IA2 = 3; IB1 = 22; IB2 = 1), 1 for stage II endometrial cancer, and 1 for suspected adenoma malignum. The median clinical cervical tumor diameter was 2.0 cm (0–6 cm). All but 1 patient, who had microscopic positive parametria, had negative surgical margins. Four patients had positive lymph nodes. The median BMI was 29.2 (range, 20.5–39.7). Twenty-three percent of patients had ideal body weight (BMI <25), 42% were overweight (BMI 25–30), and 35% were obese (BMI >30). Mean total OR time was similar among ideal weight, overweight, and obese patients (364 vs 368 vs 392 minutes; $P = .49$). There was no difference in EBL between the 3 groups (146 mL vs 133 mL vs 143 mL; $P = .92$). The mean number of lymph nodes removed was 22.8, 17.2, and 19.4 in women with ideal, overweight, and obese BMI, respectively ($P = .40$). The mean duration of hospitalization was 1 day and bladder catheterization was 13.9 days for all patients, with no significant difference between the 3 BMI groups. No patients suffered intraoperative bowel, bladder, or ureteral injury. Postoperative complications included infected lymphoceles (n = 2) and cuff cellulitis (n = 2), with no significant differences between BMI groups. Eleven patients required postoperative adjuvant therapy, with no significant difference between nonobese and obese patients (45% vs 22%; $P = .41$).

Conclusions: TLRH in overweight and obese women did not confer increased morbidity or need for adjuvant therapy, relative to women with normal BMI. Overweight and obese BMI should not preclude laparoscopic radical hysterectomy.

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Postoperative complications and return of bowel function among patients with advanced-stage ovarian cancer following rectosigmoid resection with reanastamosis

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Objectives: To analyze postoperative complications and return of bowel function in patients with advanced-stage ovarian cancer following rectosigmoid resection with reanastamosis as a part of cytoreductive surgery.

Methods: A retrospective review was conducted of all patients with primary ovarian cancer who underwent rectosigmoid resection as part of cytoreduction between July 2003 and July 2014. Postoperative complications, bowel regimens used, and return of bowel function data were recorded. Univariate and bivariate analyses identified reasons and rates for postoperative complications as well as time to return of bowel function.

Results: Between July 2003 and July 2014, a total of 285 charts were identified, with 50 patients eligible for analysis. Among this cohort, 74% (n = 37) experienced 30-day postoperative morbidity. The most common morbidities included ileus (27%, n = 10), wound infection or cellulitis (24%, n = 9), infectious morbidity (i.e., *Clostridium difficile* infection, urinary tract infection) (16%, n = 6). Patients took nothing orally (NPO) for a mean of 4 days (n = 50; range, 1–14; standard deviation [SD], 3.02). On average, diet was advanced to *regular diet* on postoperative day 4 (n = 49; range, 1–14; SD, 2.80), flatus was passed on postoperative day 5 (n = 44; range, 2–11; SD, 1.94), and bowel movement was passed on postoperative day 6 (n = 36; range, 2–13; SD, 2.43). Following surgery, patients were assigned to either a strict NPO regimen until postoperative day 5 (n = 12) or were able to advance diet as tolerated (n = 38). No significant difference was found between the 2 cohorts in postoperative length of stay ($P = .103$), or postoperative complications, including infectious or bowel morbidity ($P = .858$). There were no 30-day mortalities in the study group.

Conclusions: Postoperative complications are common in the 30 days immediately after cytoreductive surgery involving rectosigmoid resection and reanastamosis. Delayed initiation of enteral nutrition is not associated with a reduction in postoperative morbidity, supporting data in the colorectal literature.

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High complexity cytoreductive surgery for disseminated ovarian cancer in a UK setting: Challenges and possibilities

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Objectives: To assess outcomes of ultraradical cytoreductive surgery (UCS) in patients with advanced epithelial ovarian cancer (EOC) in a UK tertiary center.

Methods: This was a prospective monocentric analysis of surgical morbidity and mortality at the West London Gynecological Cancer Centre, Imperial NHS Trust, UK. A systematic evaluation was performed to assess surgical and clinical outcomes as well as anesthetic and perioperative care on all primary or relapsed stage-IIIc/IV EOC patients who underwent UCS over a 2-year period.

Results: A total of 118 patients, with a median age of 63 years (range, 19–91 years), were eligible. The patient characteristics are described in Table 1. Total macroscopic tumor rate was 89%. Median duration of surgery was 247 minutes (range, 100–540 minutes). Median surgical complexity score was 10 (range, 5–15) consisting of bowel resection (71%), stoma formation (13.6%), diaphragmatic stripping/resection (67%), liver/liver capsule resection (39%), splenectomy (20%), resection stomach/lesser sac (26.3%), pleurectomy (17%), and celiac trunk/subdiaphragmatic lymphadenectomy (8%). Major surgical complication rate was 18.6% (n = 22), with 28-day and 3-month mortality rates of 1.7% and 3.4%, respectively. The rate of anastomotic leak was 0.8%; fistula/bowel perforation, 3.4%; thromboembolism, 3.4%; and reoperation, 4.2%. Median length of intensive care unit and hospital stay were 1.7 days (range, 0–104 days) and 8 days (range, 4–118 days), respectively. The mean time between surgery and the first cycle of postoperative chemotherapy was 38 days (95% CI 36.17–41.16).

Conclusions: UCS for EOC when performed within a specialized setting of surgical and anesthetic expertise with adequate infrastructure is associated with acceptable morbidity in the presence of high multivisceral resections and total macroscopic clearance. Despite the high rate of bowel resections, bowel-related morbidity such as anastomotic leak was low, with comparably low rates of stoma formation. Furthermore, only a small proportion of patients failed to proceed to systemic adjuvant treatment within the intended time window of 8 weeks. The results from this series are encouraging for advocating an ultraradical surgical approach for this group of patients in an appropriate setting and correlate to similar American analyses in advanced EOC.

Table 1
Characteristics of Patients Who Underwent Ultraradical Debulking Surgery.

Variable	Patients (N = 118)	Variable	Patients (N = 118)
Median Age [years]	63 (range: 19 - 91)	**Median BMI** [kg/m^2]:	25 (range: 11-46)
FIGO-stage at initial diagnosis		**Postoperative tumour residuals**	
▪ IIIc	82 (69.5%)	▪ none	105 (89.0%)
▪ IV	36 (30.5%)	▪ ≤0.5 cm	10 (8.5%)
Grade 1/2	13 (11.0%)	▪ <1 cm	2 (1.7%)
Grade 3	105 (89.0%)	▪ >2 cm	1 (0.8%)
Ethnicity		**Type of surgery**	
▪ Caucasian	87 (73.7%)	▪ Upfront primary	67 (56.8%)
▪ Asian Indian	21 (17.8%)	▪ Interval debulking	27 (22.9%)
▪ Black	6 (5.1%)	▪ Secondary debulking	22 (18.6%)
▪ Chinese	2 (1.7%)	▪ Tertiary debulking	2 (1.7%)
▪ Arabic	2 (1.7%)		
Pleural effusion	34 (28.8%)		
Histology		**Median pre-op CA125** [U/L]	369 (range: 23-8586)
▪ serous-papillary	106 (89.8%)	**Median post-op CA125** [U/L]	17 (range: 3-569)
▪ carcinosarcoma	9 (7.6%)		
▪ endometrioid	1 (0.8%)	**Median preop hospital stay [**days]	1 (range: 0-11)
▪ clear cell	2 (1.7%)		
Intraoperative ascites		**Median postoperative hospital stay** [days] (range)	8 (4-118)
▪ none	40 (33.9%)	**Median ICU stay** [days] (range)	1 (0-104)
▪ <500 ml	22 (18.6%)	**Median surgical complexity score** (range)	10 (5-15)
▪ ≥500 ml	56 (47.5%)	**Median duration of surgery [min]** (range)	247 (100-540)
Median preop albumin [g/dl]	35 (range: 9-45)	**ECOG 0/1**	77 (65.3%)
		ECOG 2/3	41 (34.8%)

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CA-125 and grade 1 endometrial cancer: Analyzing the risk of metastases
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Objectives: To relate preoperative serum CA-125 levels to risk of nodal metastases in women with grade 1 endometrial cancer that was fully surgically staged.

Methods: Charts were reviewed to determine all patients with preoperative grade 1 endometrial carcinoma and a serum CA-125 level, undergoing complete surgical staging. Charts were also reviewed for final stage, grade, and site of metastases. All serum CA-125 levels were measured within 3 weeks of definitive surgery.

Results: Analysis was completed on 737 patients with grade 1 endometrial cancer. The mean age of the population was 61.9 years (95% CI 61.3–62.4). Extrauterine disease was found in 14.7% of patients and nodal disease in 12.6%. A significant difference in body mass index was seen between those without lymph node metastases (mean 38.7 kg/m^2; 95% CI 38.1–39.3) and those having positive nodes (mean 35.3 kg/m^2; 95% CI 34.3–36.3) ($P < .001$). The mean CA-125 level for the cohort was 25.6 mIU/mL (95% CI 22.0–29.2). No patients with preoperative grade 1 disease and CA-125 levels less than 15 mIU/mL (0/239) had nodal disease at surgical staging, whereas 18.7% (93/498) with a CA-125 level greater than 15 mIU/mL had nodal metastases ($P < .001$).

Conclusions: In patients with grade 1 endometrial adenocarcinomas, CA-125 can be used to identify patients who need full surgical staging, with the risk of missing nodal-positive patients being minimal.

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Identification of target and cytotoxicity of novel monoclonal antibody NEO-201 in ovarian and uterine cancer subtypes
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Objectives: Given the heterogeneity of ovarian cancer, it is imperative to identify subtype-directed treatments. The novel antibody NEO-201 targets a specific tumor-associated antigen (TAA) expressed on some ovarian and uterine malignancies, providing a tumor-directed approach. Here, we aimed to identify the cancer subtypes that express the NEO-201 target and demonstrate its cytotoxic effects.

Methods: NEO-201 is a genetically humanized novel monoclonal antibody developed through vaccines with TAAs. This antibody targets malignant tissues with tumor-specific mutations in membrane-anchored proteins CEACAM-5 and CEACAM-6. We performed immunohistochemistry (IHC) on tissue microarrays from formalin-fixed paraffin-embedded subtyped ovarian and uterine cancers to estimate the incidence of cancers expressing the NEO-201 target. Ovarian and uterine cell line pellet arrays were stained with IHC to identify in vitro models. We examined the cytotoxicity of NEO-201 in 3 high- and 3 low-expressing cell lines using XTT cell viability assays alone and with interleukin 2 (IL2)–stimulated human peripheral blood mononuclear cells (PBMC).

Results: IHC of NEO-201 in Accumax microarrays demonstrated 51% and 12% reactivity in uterine and ovarian samples, respectively. Similar expression patterns were identified in representative cell lines with IHC and Western blot. NEO-201 killed cell lines expressing its target in the range of 0.5 to 20 μg/mL. Over 3 weeks, treatment of tumor-bearing mice demonstrated control of tumor growth with 3 doses of 250 μg NEO-201 and tumor regression with 100 μg in combination with IL2-stimulated PBMC. Studies are ongoing to identify the mechanism of tumor cell death and the target epitope of NEO-201.

Conclusions: NEO-201, a novel monoclonal antibody, specifically targets epithelial malignancies including ovarian and uterine cancer. This potentially therapeutic antibody demonstrates tumor-specific cytotoxicity in cancer cell lines, expressing its

target in vitro and in xenograft mice with IL2-stimulated PBMC. This suggests that both antibody-dependent cell-mediated cytotoxicity (ADCC) and direct cytotoxicity mechanisms are involved in tumor inhibition and regression. These studies lay the groundwork for future examination of TAA-directed therapy for ovarian or uterine malignancies.

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Antimicrobial prophylaxis in the DISINFECT initiative: Decreasing the incidence of surgical INFECTions in gynecologic oncology

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Objectives: To evaluate the use of antimicrobial prophylaxis as part of a bundled intervention on surgical site infection (SSI) rates after gynecologic cancer surgery.

Methods: A quality improvement (QI) project to decrease SSI rates after abdominal surgeries was initiated in the Department of Gynecologic Oncology. SSI was defined as an infection of the surgical incision or organ space requiring antibiotics. Components of the bundled intervention included appropriate antibiotic prophylaxis and redosing based on the 2013 American Society of Health-System Pharmacists, Infectious Diseases Society of America, Surgical Infection Society, and Society for Healthcare Epidemiology of America guidelines and the use of a preoperative order set (cefoxitin 2 g or cefazolin 2 g [3 g if ≥120 kg], and for patients with penicillin allergies clindamycin 600 mg [900 mg if >70 kg] and ciprofloxacin 400 mg). The baseline (BL) SSI rate within 30 days of surgery; use of the preoperative order set; antibiotic dose and redose; and administration within 60 minutes of incision (60–120 minutes for ciprofloxacin) were obtained from retrospective review (May 1, 2014, to June 30, 2014) and compared with prospectively collected postintervention (PI) data (April 16, 2015, to July 15, 2015). The Fisher exact test was used to test for decrease in SSI rates from BL to PI and to assess similarity of these 2 groups.

Results: A total of 166 BL cases were compared with 241 PI cases. Overall SSI rate decreased from BL to PI (12% vs 6.6%, P = .04). The rate of penicillin-allergic patients remained similar (15% for BL vs 12% for PI, P = .38). Use of the institutional preoperative order set increased from BL to PI (22% vs 51%, P < .001). In both groups, 88% of patients received preoperative antibiotics, including cefazolin (43% BL vs 55% PI), cefoxitin (25% BL vs 15% PI), clindamycin (13% BL vs 14% PI), ciprofloxacin (<1% BL vs 13% PI), and other (8% BL vs 7% PI). Overall appropriate antibiotic prophylaxis did not change, 69% BL vs 75% PI, P = .13. However, appropriate antibiotic prophylaxis for penicillin-allergic patients improved (5% BL vs 95% PI, P < .001). Appropriate antibiotic redosing improved from 87% BL to 94% PI (P = .02).

Conclusions: This interim analysis of an ongoing QI project found a decrease in SSI rates and an increase in the use of a preoperative antibiotic order set, appropriate prophylaxis for penicillin-allergic patients, and antibiotic redosing.

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Fertility preservation in young patients with epithelial ovarian tumors of low malignant potential: How does it impact disease outcome?

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Objectives: Borderline ovarian tumors (BOT) are typically indolent neoplasms. Many are diagnosed in younger women, therefore fertility conservation is an important consideration. Our objective was to identify features affecting recurrence and survival in a series of BOTs, and to assess the safety of a fertility-sparing approach.

Methods: This is a historical cohort of consecutive BOTs treated at a single institution over 30 years (1981–2011). Data on surgical approach (fertility sparing or otherwise) as well as disease stage, CA-125 levels, histologic features, and implant type (invasive vs noninvasive) were collected. Associations with recurrence and survival were assessed using the Kaplan Meier and Cox proportional hazards models.

Results: A total of 213 cases with sufficiently complete data were identified. Mean follow-up was 75 months. Mean age at diagnosis was 39 years. The majority of tumors (n = 140, 67%) had serous histology, and 28 (20%) of these had a micropapillary pattern. In 133 patients (65%), the disease was confined to the ovaries—stages 1a to 1b. Of 41 patients with peritoneal disease, 11 (27%) had invasive implants. Of 132 women of age 40 years and below at diagnosis, 112 (85%) had a fertility-sparing procedure and 60 (46%) had conservation of an uninvolved ovary. A total of 42 patients went on to achieve 72 pregnancies. Fifty patients (24%) developed recurrences, of whom 48 were treated surgically. Thirty-one patients had a single recurrence, 15 patients had 2 recurrences, and 4 patients had 3 or more. On univariate analysis, fertility preservation, ovarian conservation, cyst rupture at surgery, advanced stage (1c and above), peritoneal implants, and serous histology were all associated with shorter disease-free survival. Multivariable regression analysis found only fertility preservation (HR 2.8; CI 1.1–6.9; *P* = .024) and advanced stage (HR 3.7; CI 1.6–8.5; *P* = .002) to be independently associated with recurrence. Twenty patients (9%) died of their disease. Fertility preservation was not associated with overall survival.

Conclusions: BOTs carry a good prognosis overall, though the recurrence risk is higher for advanced-stage disease. Fertility preservation is also associated with a higher risk of disease relapse; however, perhaps because many recurrences are cured with repeat surgery, overall survival is not compromised.

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Implementation of indocyanine green and near-infrared fluorescence sentinel lymph node mapping in endometrial and cervical cancer at a community-based academic hospital

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Objectives: Indocyanine green (ICG) and near-infrared (NIR) fluorescence imaging for sentinel lymph node (SLN) mapping has been incorporated in the National Comprehensive Cancer Network (NCCN) guidelines for endometrial and cervical cancer staging. Our objective was to evaluate the implementation and performance characteristics of ICG and NIR fluorescence SLN mapping at a community-based academic hospital.

Methods: This was an observational quality control study approved by the institutional review board. Patients who had robotic hysterectomy for endometrial or cervical cancer between October 2014 and September 2015 were included. All patients had SLN dissection using the NCCN algorithm with SLN ultrastaging. Complete lymphadenectomy (CND) was performed in patients with cervical cancer or high-risk endometrial cancer. Statistics were performed with R (version 2.2.2).

Results: Sixty-three patients (58 endometrial, 4 cervical, and 1 both) were included; median age was 61 years and body mass index was 33. SLNs were identified in all patients, and bilateral SLNs were detected in 87.3% (55/63). Median SLNs sampled per patient was 5. Metastatic nodal disease was identified in 19% (12/63). Of 36 patients with low risk endometrial cancer who underwent only SLN mapping, 1 had positive SLNs. Twenty-seven patients underwent both SLN and bilateral CND. Eleven of these (40.7%) had metastatic nodal disease. SLN biopsy achieved a sensitivity of 63.6% and specificity of 100%. In 5 (45.4%) of 11 patients with nodal disease, metastases were found only in the SLNs. Two (18.2%) of 11 patients had metastases in both SLN and CND. In 4 of 11 patients, metastases were found only in the CND and not in the SLNs, and in 2 of these patients, the metastases were isolated to the periaortic dissection. This represents a false-negative nodal disease diagnosis rate of 36.4% (4/11), and a negative predictive value of 80%.

Conclusions: Implementing ICG and NIR fluorescence imaging for SLN mapping at a community-based academic hospital is feasible with detection rates that equate those in the literature. SLN mapping with ultrastaging identifies metastases in low-risk patients that otherwise may go undiagnosed. Adopting the SLN algorithm as the only method of surgical staging in high-risk patients warrants caution.

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Laparoscopic staging for stage I epithelial ovarian cancer: Analysis of the National Cancer Data Base

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Objectives: To evaluate the association between laparoscopic staging with survival among women with stage I epithelial ovarian cancer.

Methods: We used the National Cancer Data Base to identify women who underwent staging surgery for stage I epithelial ovarian cancer diagnosed in 2010 and 2011. The exposure of interest was laparoscopic surgery and the primary outcome was overall survival. We used propensity score methods to compare similar patients based on observed characteristics. We estimated propensity to undergo laparascopic surgery based on demographic, socioeconomic, and clinical characteristics using logistic regression. We used an optimal 1:1 matching algorithm to match 566 women who underwent laparoscopic staging with 566 women who underwent staging laparotomy. Survival analysis used the Kaplan-Meier method and log-rank test. Secondary outcomes included extent of lymphadenectomy, readmission within 30 days of discharge, and death within 90 days of surgery.

Results: Of the 3,044 patients who met study criteria, 566 (18.6%) underwent laparoscopic staging. Patients who underwent laparoscopic staging were younger, more often privately insured, resided in wealthier zip codes, and more often had serous histology compared with those who underwent staging laparotomy. After propensity score matching, we found no difference in overall survival between women who underwent laparoscopic staging and those who underwent staging laparotomy (P = .12, Figure 1). Three-year survival was 95.2% (95% CI 92.2–98.3) and 93.9% (95% CI 91.5–96.3) for patients undergoing laparoscopy and laparotomy respectively. There were no significant differences in the number of lymph nodes excised (P = .36), 30-day readmission rate (P = .70), or rate of death within 90 days of surgery (P = .85) between these groups.

Conclusions: Women who underwent laparoscopic staging for stage I epithelial ovarian cancer had equivalent survival to those who underwent staging laparotomy.

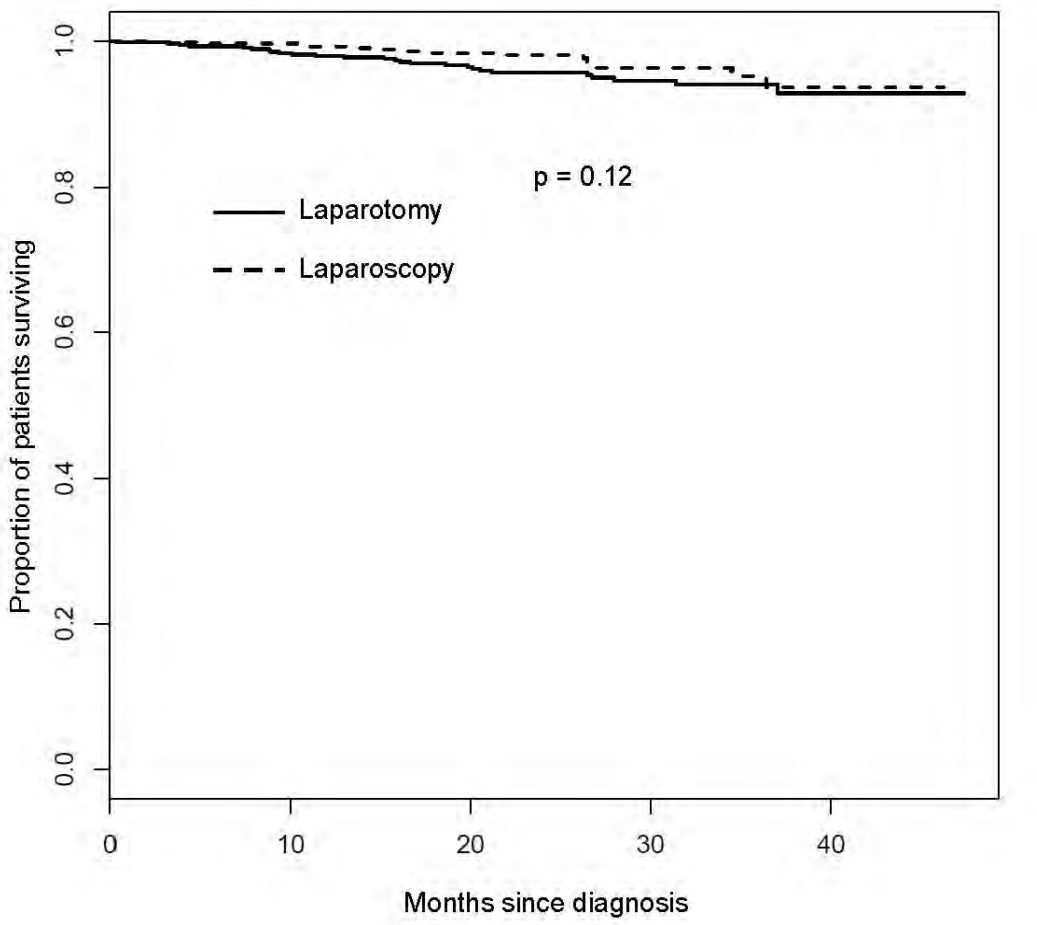

Fig. 1
Kaplan-Meier Survival Curves for Stage 1 Epitheial Ovarian Cancer by Mode of Surgery (n = 1,132).

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Involuntary weight loss between surgery and chemotherapy impairs overall survival of high-grade serous ovarian cancer patients

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Objectives: High-grade serous ovarian cancer (HGSOC) is the most common, aggressive histologic type of this neoplasm. Most patients require platinum-based chemotherapy after primary surgical treatment. This study aimed to assess the prognostic value of involuntary weight changes between surgery and first cycle of chemotherapy.

Methods: Of 73 patients surgically treated for HGSOC, 64 received adjuvant chemotherapy. Prognostic value of several clinicopathologic features was assessed, including change of body weight and body mass index between the day of primary debulking surgery and first cycle of chemotherapy. Survival analyses included the Kaplan-Meier method, log-rank test, and Cox proportional hazards model.

Results: The median follow-up was 45.89 months (range, 17–79 months). Median change of body weight in the group of 64 patients who received chemotherapy was –3.5 kg (range, –33 kg to +5 kg). Higher weight loss values (median, –5 kg; range, –1 to –33 kg) were observed in platinum-resistant patients (n = 21) compared with platinum-sensitive patients (n = 43) (median, –3.0 kg; range, –14 to +5 kg) (*P* = .03). Weight loss between primary surgery and first cycle of chemotherapy was found to be an independent prognostic factor for decreased overall survival (HR 3.8, CI 95% 1.15–12.53, *P* = .029) and progression-free survival (HR 3.35, CI 95% 1.40–8.02, *P* = .0123).

Conclusions: Prevention of weight loss and nutritional wasting in HGSOC patients who are to receive adjuvant chemotherapy might improve treatment results. Further prospective trials are needed on the nutrition of this group of patients.

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The novel application of plasma energy as a tissue-preserving treatment modality for vulval and perianal intraepithelial neoplasia

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Objectives: To investigate the use of plasma energy using the PlasmaJet® system as a treatment for vulval intraepithelial neoplasia (VIN) and perianal intraepithelial neoplasia (PAIN).

Methods: This was a case series of 8 patients with VIN/PAIN treated with PlasmaJet at West London Gynecological Cancer Centre, Imperial NHS Trust, UK.

Results: Demographic data and background medical and surgical history are displayed in Table 1. All 8 patients had macroscopic recurrence, confirmed histologically, following previous treatment. All patients had multifocal high-grade lesions. Three patients had localized vulval disease, 2 had isolated perianal lesions, and 3 had disease extending across both areas. Three patients had periclitoral involvement. All patients underwent uncomplicated PlasmaJet treatment, 7 of which were undertaken using general anesthesia and one using regional anaesthesia. There were no immediate postoperative complications and the treatments were well-tolerated. One patient reattended with urinary retention and, after temporary indwelling catheterization for 7 days, had an uncomplicated recovery. Postoperatively, 2 patients remained asymptomatic, with no further evidence of disease. Six patients required repeat PlasmaJet therapy because of histologically proven evidence of further disease. One patient required a third treatment. At the time of writing, all 8 patients have had excellent macroscopic and symptomatic improvement, after a median follow-up period of 269 days (range, 105–483 days).

Conclusions: Current treatments for VIN may be limited by either efficacy or adverse effects. Excision often necessitates reconstructive surgery, and has the potential for major physical and psychological sequelae. In this series of high-grade recurrent disease cases not responding to medical treatment or unsuitable for surgical treatment, these initial data show that the use of plasma energy could be an effective and acceptable treatment modality. It may be particularly useful in PAIN where tissue preservation may prevent iatrogenic sphincter damage and in sexually active women with periclitoral disease. Given the 5% risk of coexistent invasion, preoperative biopsies are essential, as is close postoperative follow-up. Long-term follow-up and patient satisfaction studies are required.

Table 1
Patient demographics, previous medical history, areas affected and number of treatments needed.

Patient	Age	Ethnicity	Previous medical history	Previous surgical	Previous medical	Areas affected	Number of treatments
1	51	Afro-Caribbean	HIV positive, Hypertension	Excision VIN X 2	Imiquimod	PAIN	2
2	46	Black British	Hypertension	Nil	Podophyllotoxin	VIN	2
3	54	Caucasian	Rheumatoid Arthritis	Radical Vulvectomy	Imiquimod	PAIN	2
4	40	Caucasian	Factor V Leiden deficiency	Excision VIN	Imiquimod	VIN + PAIN + peri-clitoral	3
5	29	Caucasian	Chronic Neutropenia	Excision VIN X 3	Nil	VIN + PAIN	1
6	51	Caucasian	Previous bone marrow	Excision of PAIN +	Nil	VIN + PAIN	2
7	55	Afro-Caribbean	Type 1 Diabetes, HIV	Nil	Imiquimod	VIN + peri-clitoral	2
8	49	Afro-Caribbean	HIV positive, Asthma	Nil	Imiquimod	VIN + peri-clitoral	1

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Clinical comparison of robotic, laparoscopic, and open hysterectomy procedures for endometrial cancer patients
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Objectives: Management of endometrial cancer has changed with the introduction of minimally invasive techniques. New York State endometrial cancer surgery data from 2011 indicate that 48% of procedures were abdominal hysterectomy, 15% were laparoscopic, and 35% were robotic. Conflicting data have been reported when comparing outcomes for these techniques, and the inherent bias in patient selection is a major confounder. The goal of the current study is to investigate whether specific patient demographic, comorbidity, and severity variables are associated with the type of hysterectomy procedure performed and compare outcomes for the procedures.

Methods: A retrospective cohort study was performed of women with endometrial cancer scheduled for open, laparoscopic, or robotic hysterectomy from October 2008 to September 2012. Preoperative characteristics and surgical outcomes were compared between the 3 procedure types using descriptive and comparative analyses.

Results: A total of 150 open, 187 laparoscopic, and 353 robotic hysterectomies were performed for preoperative diagnosis of endometrial cancer. Preoperative characteristics showed that body mass index, comorbidities, American Society of Anesthesiology category, and number of prior abdominal surgeries were higher in patients undergoing open surgery. Uterine

size was also significantly greater in the open group. Patients with open procedures were more likely to have higher stage and grade and underwent para-aortic node dissection more frequently. Estimated blood loss was significantly higher in open procedures than laparoscopic or robotic. Although laparoscopic procedures had the shortest surgical times, they also resulted in significantly fewer pelvic and para-aortic nodes than either open or robotic cases. Both postoperative complications and 30-day readmission rates were higher in patients undergoing open hysterectomy.

Conclusions: Patients undergoing open hysterectomy show significant differences when compared with patients undergoing robotic or laparoscopic hysterectomy for endometrial cancer. Robotic and laparoscopic surgery shows similar outcomes with the exception that robotics results in improved lymph node yields.

Table 1
Preoperative, Perioperative and Postoperative Characteristics and Outcomes.

Preoperative characteristic	**Open**	**Laparoscopic**	**Robotic**	**p-value**
Age, mean (SD)	62.89 (11.12)	62.75 (10.73)	62.97 (10.88)	0.9761
BMI, mean (SD)	38.41 (10.93) [b]	34.33 (8.81) [a]	35.51 (9.48) [a]	0.0005
Prior Abdominal Surgeries, *n* (%)				
0	59 (39.86)	88 (51.76)	151 (44.54)	
1	40 (27.03)	53 (31.18)	104 (30.68)	
≥2	49 (33.11) [b]	29 (17.05) [a]	84 (24.78) [a]	0.0077
Co-morbidities				
Hypertension, *n* (%)	104 (71.23) [b]	83 (48.26) [a]	192 (54.39) [a]	0.0001
Diabetes, *n* (%)	55 (37.41) [b]	39 (22.67) [a]	86 (24.36) [a]	0.0041
Hypercholesterolemia, *n* (%)	61 (42.36) [c]	36 (20.93) [a]	107 (30.31) [b]	0.0002
CAD/CHD, *n* (%)	20 (13.79) [b]	9 (5.23) [a]	27 (7.65) [a]	0.0182
Other Cancer, *n* (%)	16 (10.96)	13 (7.51)	30 (8.50)	0.5362
Tobacco History, *n* (%)	52 (34.67)	63 (34.81)	96 (27.2)	0.1021
Perioperative and postoperative characteristics and outcomes	**Open**	**Laparoscopic**	**Robotic**	**p-value**
Hysterectomy/BSO, *n* (%)	60 (40)	24 (13)	69 (20)	
Hysterectomy/BSO and Pelvic lymph node dissection, *n* (%)	44 (29)	143 (76)	234 (67)	
Hysterectomy, Pelvic lymph node and Paraaortic lymph node dissection, *n* (%)	46 (31) [b]	20 (11) [a]	48 (14) [a]	<0.0001
Uterine weight, mean (SD)	175.51 (142.85) [b]	121.56 (102.12) [a]	110.85 (74.11) [a]	<0.0001
Uterine Diameter, mean (SD)	8.85 (2.62) [b]	8.04 (2.33) [a]	7.74 (2.36) [a]	<0.0001
Lymphatic/vascular invasion, *n* (%)	65 (45.45) [b]	58 (31.52) [a]	95 (28.44) [a]	0.0013
Metastasis, *n* (%)	7 (4.67)	5 (2.67)	6 (1.73)	0.1713
Grade 3, *n* (%)	52 (38.81) [b]	40 (22.35) [a]	58 (17.42) [a]	<0.0001
ASA 1 or 2, *n* (%)	50 (39.06) [b]	115 (68.45) [a]	208 (61.18) [a]	<0.0001
FIGO Stage 1, *n* (%)	92 (64) [a]	156 (83) [b]	307 (92) [c]	<0.0001
FIGO Stage 2, *n* (%)	6 (4)	6 (3)	4 (1)	
FIGO Stage 3, *n* (%)	26 (18)	16 (9)	18 (5)	
FIGO Stage 4, *n* (%)	19 (13)	9 (5)	6 (2)	
Operative Time Incision To Close, mean (SD)				
Hysterectomy/BSO	128.9 (47.7) [c]	73.2 (35.6) [a]	99.8 (32.2) [b]	<0.0001
Hysterectomy/BSO, PLND	118.9 (29.8) [b]	75.8 (29.3) [a]	125.6 (32.8) [b]	<0.0001
Hysterectomy/BSO, PLND, PAND	151.9 (42.7) [b]	106.1 (24.5) [a]	162.1 (34.0) [b]	<0.0001
Estimated Blood Loss, mean (SD)	400.67 (307.82)	115.32 (125.82)	99.61 (109.59)	
Estimated Blood Loss >100 ml *n* (%)	133 (89) [b]	24 (13) [a]	40 (12) [a]	<0.0001
Pelvic lymph nodes total, mean (SD)	18.322 (9.69) [b]	12.75 (6.51) [a]	21.95 (9.54) [c]	<0.0001
Pelvic lymph nodes positive, mean (SD)	0.43 (1.15) [b]	0.24 (0.97) [a]	0.14 (0.89) [a]	0.0007

Paraaortic lymph nodes total, mean (SD)	8.18 (5.67) [b]	3.75 (3.39) [a]	9.56 (7.96) [b]	0.0011
Paraaortic lymph nodes positive, mean (SD)	0.27 (0.72)	0.35 (0.75)	0.36 (1.47)	0.4943
Postoperative complications during the surgical admission, *n* (%)	13 (8.67) [b]	2 (1.07) [a]	7 (1.98) [a]	0.726*
Conversion to open, *n* (%)		1 (0.53) [a]	22 (6.23) [b]	0.001*
Readmitted in 30 days, *n* (%)	12 (8.00) [b]	2 (1.07) [a]	8 (2.27) [a]	0.506*
SD standard deviation; *ASA* America Society of Anesthesiologists physical status classification; notations a, b, and c: means or percentages designated with the same letter are not significantly different at α=0.05; * p-values for robotic – laparoscopic comparison				

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Use of immunotherapy and radiation for treatment of mucosal melanomas of the lower genital tract

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Objectives: To report our experience using ipilimumab, a monoclonal antibody targeting CTLA-4, in combination with radiation therapy in women diagnosed with mucosal melanoma of the lower genital tract.

Methods: We retrospectively identified all patients who received ipilimumab and concurrent radiation for treatment of mucosal melanoma of the lower genital tract at Memorial Sloan Kettering Cancer Center between July 2012 and March 2014. Various clinicopathologic data and treatment responses were abstracted and analyzed. Appropriate statistical tests were used.

Results: Four patients were identified. Median age was 61.5 years (range, 44–68 years). Three patients were diagnosed with vaginal melanomas and 1 patient was diagnosed with a cervical melanoma. Two patients were noted to have multifocal lesions and all were deemed unresectable at initial diagnosis. Median size of lesions was 5 cm (range, 3.3–5 cm). All melanomas were in Ballantyne stage I. Median number of doses of upfront ipilimumab received was 4 (range, 3–4). Diarrhea related to ipilimumab use occurred in 2 (50%) of 4 patients and was grade 1/2 by CTCAE v4. No patients experienced any CTCAE grade 3/4 complications. All patients received external beam radiation therapy: up to 3,000 cGy in 3 patients and 6,020 cGy in 1 patient. A complete radiographic response was achieved in 3 (75%) of 4 patients. The remaining patient had a complete local response but was noted to have lung metastasis on follow-up imaging. Postradiation surgical resection was performed in 3 (75%) of 4 patients, with 1 (33%) of 3 achieving a complete pathologic response. One patient with a complete radiographic response received an additional year of treatment with maintenance ipilimumab. Disease recurrence was seen in 2 patients at 9 and 10 months after the initial diagnosis (mediastinum and lung) and 2 patients remain disease free at 17 and 36 months after the diagnosis.

Conclusions: Mucosal melanoma of the lower genital tract is rare and data-driven treatment strategies remain limited. Immunotherapy has been shown to be effective in the treatment of cutaneous melanomas with durable effects. Our small case series demonstrates a favorable response to combined therapy with ipilimumab and radiation. Larger studies are necessary to validate these promising results.

Table 1

	Induction IpilimumabDoses	**Radiation therapy**	**Post-RT surgical resection**	**Response**
Patient A	4	EBRT 3000 cGy	Vaginectomy	Complete
Patient B	4	EBRT 6020 cGy	WLE	Complete local
Patient C	4	EBRT 3000 cGy	n/a	Complete
Patient D	3	EBRT 3000 cGy	Hysterectomy, vaginectomy	Complete

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Molecular characterization of mucinous ovarian cancer
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Objectives: Mucinous ovarian carcinoma (MOC) is a rare, chemoresistant tumor known to share pathologic features with gastrointestinal and pancreaticobiliary tumors. To better understand the genomic and proteomic landscapes of invasive MOCs, we evaluated somatic mutations and protein expression and compared these results with data from The Cancer Genome Atlas (TCGA) tumor projects.

Methods: Twenty-six primary invasive MOCs with available paired tumor and normal tissue were identified between July 2001 and July 2012. Extracted DNA underwent next-generation sequencing with a combination of a candidate gene assay (37 genes), the MSK-IMPACT assay (341 genes), transcriptome sequencing, and whole exome sequencing. Copy number alterations (CNAs) were identified using data from the MSK-IMPACT assay, whole exome sequencing, or Affymetrix SNP 6.0 arrays. Immunohistochemistry (IHC) was performed to confirm the diagnosis of MOC (ER, PR, CK7, CK20, CDX-2, PAX8) and to correlate protein expression with mutation status and CNAs (p53, ARID1A[Baf250a], PTEN, PMS2, MSH6, HER2, p16). Mutation data for other tumor types were obtained from the cBio Cancer Genomics Portal (cbioportal.org).

Results: Somatic *TP53* and *KRAS* mutations were the most common and were identified in 18 (69%) cases each, with a comutation rate of 50% (13/26). Other commonly mutated genes include *ARID1A* and *PIK3CA*. *CDKN2A* homozygous deletions were found in 27% (7/26). *ERBB2* alterations were identified in 19% (5/26). Mutations in at least 1 potentially targetable gene were identified in 50% of tumors (13/26). IHC and sequencing results were concordant in 154 (85%) of 182 stained cases. Comutations of *KRAS* and *TP53* occur most commonly in pancreatic (67%) and colorectal (21%) carcinomas. *CDKN2A* deletions are found at a similar frequency in pancreatic adenocarcinomas (30%). Compared with TCGA data, mutation rates of the 11 most commonly mutated genes in our cohort were most similar to pancreatic adenocarcinoma and least similar to high-grade serous ovarian cancer.

Conclusions: MOC is characterized by frequent *KRAS* and *TP53* mutations, *ERBB2* alterations, and *CDKN2A* deletions. The mutational landscape of MOC shares similarities with that of pancreatic adenocarcinoma. This suggested shared molecular pattern offers the potential to guide future therapeutics.

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242 - Poster
Pelvic exenteration for recurrent vulvar squamous cell carcinoma
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Objectives: Pelvic exenteration is a radical procedure that can be indicated for women with local recurrence of vulvar squamous cell carcinoma, especially in cases in which the tumor involves the lower urinary and gastrointestinal tracts. We sought to review and characterize our experience with pelvic exenteration for recurrent vulvar squamous cell carcinoma over the past 25 years.

Methods: All patients who underwent an exenterative procedure for recurrent vulvar squamous cell carcinoma from January 1, 1990, to September 1, 2015, were identified. Pertinent demographic and treatment data, including age, race, body mass index (BMI), and medical, surgical and treatment history, were abstracted. Survival was calculated using the log-rank and Kaplan-Meier tests.

Results: A total of 467 patients received treatment for vulvar squamous cell carcinoma at our institution during the study period; 16 of these patients underwent an exenterative procedure. Mean age at the time of exenteration was 68 years (range, 54–85 years), and mean BMI was 32.5 kg/m^2 (range, 21.1–63.3 kg/m^2). Median progression-free survival after the exenterative procedure was 22 months (95% CI 15.9–28.1 months), and median overall survival was 30 months (95% CI 17.6–42.4 months) (Figure). Two patients (12.5%) achieved an overall survival of more than 5 years, though median follow-up

time for the cohort was 24.5 months. Of 16 patients, 6 (37.5%) underwent anterior exenteration, 3 (18.75%) underwent posterior exenteration, and 7 (43.75%) underwent total pelvic exenteration. Seven of 16 patients had major complications in the immediate postoperative period, including pelvic abscess (12.5%), thromboembolic event (6.25%), wound breakdown (18.75%), and death (6.25%). Median number of excisional procedures preceding exenteration was 2 (range, 0–4). Fourteen (87.5%) of 16 patients had undergone some form of radiation therapy before exenteration, and 2 (12.5%) had intraoperative radiation therapy at the time of exenteration.

Conclusions: Although associated with considerable perioperative morbidity, exenterative procedures often represent the only curative option for many patients with locally recurrent vulvar squamous cell carcinoma.

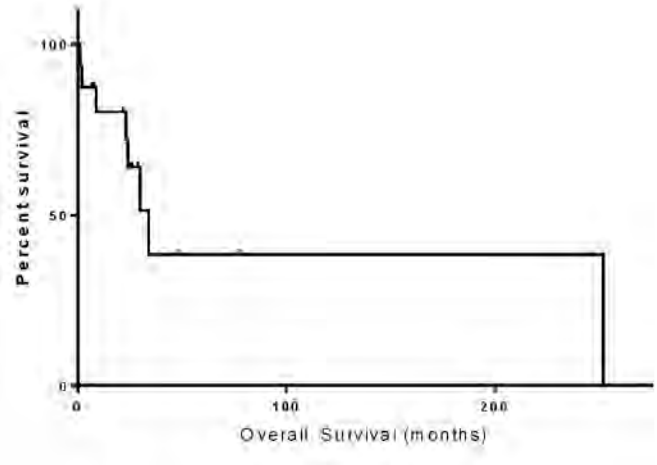

Fig. 1
OS from Time of Exenterative Procedure.

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243 - Poster
Obesity does not influence the decision between neoadjuvant chemotherapy and upfront cytoreductive surgery in advanced ovarian cancer
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Objectives: To assess whether body mass index (BMI) may influence the decision of initial treatment in advanced ovarian cancer.

Methods: A consecutive series of all patients with stage IIIB or higher ovarian cancer who received primary treatment at our institution from June 2009 to June 2015 were identified. Retrospective chart review gathered demographic and clinical variables including age, race, BMI, cancer stage, CA-125 levels, imaging findings, American Society of Anesthesiology (ASA) level, Eastern Cooperative Oncology Group (ECOG) performance status, and medical comorbidities. SPSS software was used for analysis, with the *t* test used to evaluate continuous variables and χ^2 test for categorical variables; significance was set at $P < .05$.

Results: A total of 197 women met our inclusion criteria: 85 (43.1%) received neoadjuvant chemotherapy (NACT) and 115 women (56.9%) underwent primary debulking surgery. The average age of the cohort was 64.2 years (range, 27–89 years), and the majority were white (86.3%), with an average BMI of 28.4 kg/m^2 (range, 18–50 kg/m^2). There was no difference in the mean age at diagnosis for women undergoing NACT compared with primary debulking (67.6 vs 61.5 years, $P = .251$). Median BMI was similar between the 2 groups, at 27 kg/m^2. There was also no difference in primary treatment of those with a BMI greater than 35 kg/m^2, with these women equally likely to receive NACT or primary debulking. Similarly, race was not significantly associated with primary treatment. Of the clinical factors examined, higher stage, higher CA-25 level, higher ASA level, lower ECOG performance status, presence of ascites, omental disease, or splenic involvement on computed tomography, as well as active anticoagulation were all significantly associated with higher likelihood of having NACT as primary treatment (Table 1).

Conclusions: Age, BMI, and race did not seem to influence initial treatment of advanced ovarian cancer. The high number of stage IV cases and patients with ASA level 3 likely contributed to our high rate of NACT. NACT utilization was influenced by multiple clinical variables, including imaging results and performance status. The lack of consensus about the role of NACT in the management of ovarian cancer makes it difficult to determine if inherent biases affect clinical management.

Table 1
Demographic and clinical factors associated with initial treatment modality for advanced ovarian cancer patients.

	Neoadjuvant Chemotherapy N = 85 (43.1%)	Primary debulking N = 112 (56.9%)	*P*-value
Mean age (yrs)	67.6 ± 11.3	61.5 ± 10.0	0.251
Race			
White	71 (83.5)	99 (88.4)	0.113
African American	12 (14.1)	9 (8.0)	
Hispanic	0 (0)	2 (1.8)	
Asian	0 (0)	2 (1.8)	
Other	2 (2.4)	0 (0)	
BMI			0.451
<35	17 (20.2)	18 (16.1)	
≥35	67 (79.8)	94 (83.9)	
Stage			**<0.001**
IIIB	2 (2.4)	14 (12.5)	
IIIC	53 (62.4)	80 (71.4)	
IVA	19 (22.4)	6 (5.4)	
IVB	11 (12.8)	12 (10.7)	
ASA			**0.004**
1	0 (0)	4 (3.6)	
2	23 (41.8)	71 (64.0)	
3	32 (58.2)	34 (30.6)	
4	0 (0)	2 (1.8)	
ECOG Performance Status			**0.004**
0	20 (40.0)	23 (42.6)	
1	21 (42.0)	28 (51.9)	
2	0 (0)	3 (5.6)	
3	9 (8.7)	0 (0)	
CA 125			**0.009**
<500	32 (37.6)	62 (59.6)	
500-1000	10 (11.8)	10 (9.6)	
>1000	43 (50.6)	32 (30.8)	
CT findings			
Ascites	63 (74.1)	64 (57.7)	**0.017**
Omental disease	73 (85.9)	70 (63.1)	**<0.001**
Mesenteric disease	4 (4.7)	5 (4.5)	0.598
Retroperitoneal adenopathy	25 (29.4)	25 (22.5)	0.273
Diaphragm disease	4 (4.7)	2 (1.8)	0.222
Liver involvement	3 (3.5)	2 (1.8)	0.372
Splenic involvement	7 (8.2)	1 (0.9)	**0.012**
Medical Co-morbidities			
Diabetes	16 (18.8)	15 (13.4)	0.300
Coronary artery disease	6 (7.1)	5 (4.5)	0.432
Active Anticoagulation	14 (16.5)	2 (1.8)	**<0.001**
Hypertension	45 (52.9)	53 (47.3)	0.435
Congestive heart failure	3 (3.5)	0 (0)	0.079

244 - Poster

Ultrasound surveillance intervals based on resolution for persistent ovarian abnormalities consistently observed as cysts, septated cysts, cysts with solid structure, or solid structures

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Objectives: To follow ovarian abnormalities that persist as only a single type to estimate a surveillance interval based on time to resolution.

Methods: Ovarian abnormalities that either resolved (n = 1,800) or persisted (n = 2,634) as a single type of structure throughout their entire existence were identified from 44,475 individuals who had received 270,302 ovarian screening tests with transvaginal ultrasonography, representing 264,623 screening years.

Results: A total of 1,800 resolving ovarian abnormalities that persisted as a single type of structure throughout their entire existence (cysts = 1,288, cysts with septation(s) = 1,790, cysts with solid areas = 581, solid abnormalities = 154) were selected to determine how long each type of abnormality existed before resolving. Considered together, all structure types that resolved received a total of 8,764 scans with transvaginal sonography so that each type of ovarian abnormality received approximately 4 to 6 scans, as shown in the Table. Cyst resolution was longer than the resolution of cysts with septations or cysts with solid areas (significant; $P > .02$, α 2-tailed) whereas the difference was not significant for solid abnormalities because of the small sample size. Half of the abnormalities consistently appearing as cysts resolved in 17 months whereas more than 75% resolved in just over 3 years and the remainder took over 5 years. Half of the abnormalities consistently appearing as cysts with septations resolved in approximately 14 months whereas more than 75% resolved in approximately 3 years, with the remainder taking more than 5 years to resolve. Half of the abnormalities consistently appearing as cysts with solid areas resolved in approximately 8 months, whereas more than 75% resolved in just under 3 years with the remainder taking more than 5 years to resolve. Half of the abnormalities consistently appearing as solid structures resolved in approximately 12 months, whereas more than 75% resolved in just over 3 years and the remainder took well over 5 years to disappear.

Conclusions: In cases in which an ovarian abnormality retains its originating sonographic structure throughout its existence, half will resolve within 18 months regardless of complexity. Half of the rest will resolve with a 3-year surveillance plan. However, the remainder will persist for more than 5 years before resolving and should be subject to continuing annual surveillance.

Table 1
Resolution Time.

Type of Structure	***Cyst***	***Cyst & Septation***	***Cyst & Solid***	***Solid***
Scans, n=	6239	1790	581	154
Structures, n =	1288	366	122	24
Average Scan Number	4.8	4.9	4.8	6.4
Mean ± SEM (months)	31.0+0.97	26.5±1.6	23±2.7	26.4±7.2
Range (months)	0.3-287.6	0.5-182.5	0.8-207	0.5-123.3
Median (months)	17	14.1	8.3	12.7
75th percentile	38.4	36.0	33.8	38.7
90th percentile	70.9	64.5	64.3	93.8

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245 - Poster

Language as a barrier to cancer clinical trial accrual: Assessing consenting team knowledge

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Objectives: Cancer therapeutic studies involve a complex consenting process. In large and culturally diverse institutions, low English fluency (LEF) is a common problem, contributing to scarce minority accrual. Institutions provide research staff access to interpretation services and have working guidelines and best practice education available. The purpose of this study was (1) to assess knowledge of proper consenting procedures among team members when obtaining consent from LEF patients; and (2) to compare the percentage of index cancer cases by language preference with percentage of research participants enrolled in clinical therapeutic trials by language preference.

Methods: Institutional review board approval for this study was obtained. An anonymous web-based survey was distributed to investigators, research staff, and interpreter services to assess knowledge of consent procedures. Patient enrollment data were retrieved from the clinical trials enrollment tracking system from January 2011 to October 2014 and matched with patient registration data indicating preferred language (n = 1,521). The number and type of cancer cases for the same period were retrieved from the institutional cancer registry and matched to patient registration data indicating preferred language.

Results: Although there are many organizational in-person and web-based training programs focused on the requirements for obtaining consent from LEF patients, only 64.8% (34/53) of participants responded to the survey correctly. There were no significant differences between research staff and investigators. The enrollment rates were similar to the percentage of index cancer cases for Spanish (2.6%) and Armenian (0.5%) speakers, whereas the rates of participation in clinical trials among English-speaking participants (92%) were higher than the percentage of index cancer cases (74%). Chinese- and Korean-speaking participants had higher rates of participation (19%), with representation in clinical trials being almost twice the percentage of index cancer cases. Populations speaking Russian and Arabic were underrepresented in clinical trials compared with index cancer cases. There were no differences among types of cancer diagnosis.

Conclusions: To increase enrollment in clinical trials, institutions must provide continuous training opportunities for research staff, engage interpreters, and adopt recruitment and study materials in different languages.

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246 - Poster

Age as a prognostic factor in cervical cancer: A 10-year review of patients treated at a single institution

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Objectives: The effect of age on cervical cancer outcomes remains controversial. The objective of this study was to explore the effect age at diagnosis on overall survival (OS) in cervical cancer patients treated at a single institution over a 10-year period.

Methods: A retrospective chart review of all patients diagnosed with cervical cancer from January 1, 2003, to December 31, 2012, at an academic institution was conducted. Records were reviewed for demographics, cancer characteristics, treatment course, recurrence, and long-term outcomes. Young patients (age <40 years) were compared with older patients (age ≥40 years) for comorbidities, histology, disease stage, and treatment. Univariate analyses of potential factors associated with OS were conducted using Cox regression models. A multivariate model to assess effect of age at diagnosis on OS was conducted, adjusting for confounding factors.

Results: A total of 447 patients were included and had a median age of 48.6 (±14.0) years at diagnosis. Most had early-stage disease (71.3% stage I or II) and squamous cell histology (71.9%). Compared with older women, younger women were significantly less likely to have advanced-stage disease ($P < .0001$) and were therefore more likely to undergo surgery and less likely to receive definitive radiation therapy ($P < .0001$). Age (<40 years vs ≥40 years) was not significantly associated with OS in univariate analysis ($P = .25$). Advanced-stage disease ($P < .0001$), rare histology ($P < .0001$), and treatment with radiation ($P < .0001$) were associated with significantly poorer OS in our population. Cancer history, advanced-stage disease, adenocarcinoma histology, and treatment with either surgery or radiation alone compared with surgery and radiation remained significantly associated with poorer OS after adjusting for potential confounders. After adjusting for race, presence of diabetes, hypertension, history of other cancer, disease stage, histology, and treatment, younger age at diagnosis was significantly associated with poorer OS (OR 1.90, 95% CI 1.04–3.50, $P = .04$).

Conclusions: In this single institution study, age less than 40 years at diagnosis of cervical cancer was an independent prognostic factor for worse OS. Further investigation into tumor characteristics of young women is warranted to determine why stage for stage they had a more virulent course.

Table 1
Multivariate Cox regression model for overall survival.

	OR (95% CI)	p-value
Age Category		**0.038**
<40 years	1.90 (1.04-3.50)	
40+ years	1.00	
Cancer History		**0.028**
Yes	3.06 (1.13-8.30)	
No	1.00	
Stage		**0.002**
IA1	1.00	
IA2/IB1	2.51 (0.30-21.11)	
IB2	15.40 (1.30-181.89)	
II	25.54 (1.94-336.88)	
III	52.95 (3.94-710.73)	
IV	74.97 (5.27-1067.10)	
Histology		0.162
SCC	1.00	
Adenocarcinoma	2.00 (1.05-3.82)	
Neuroendocrine	2.39 (0.51-11.12)	
Adenosquamous cell	5.24 (0.57-48.04)	
Other	2.09 (0.27-16.12)	
Treatment		**0.003**
Surgery alone	30.54 (3.84-243.09)	
Radiation alone	9.57 (2.16-42.47)	
Surgery + Radiation	1.00	

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247 - Poster
Adherence to hematologic hold parameters in dose-dense chemotherapy for ovarian malignancies: A survey of the National Comprehensive Cancer Network (NCCN) sites
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Objectives: To determine adherence to published hematologic hold parameters for dose-dense paclitaxel and carboplatin in patients with ovarian, fallopian tube, or primary peritoneal cancers.

Methods: All 26 member sites of the National Comprehensive Cancer Network (NCCN) were contacted electronically. Hematologic hold parameter values for absolute neutrophil count (ANC) and platelet count for cycle days 1, 8, and 15 were queried. These institutional hold parameters were compared with those in published literature that support the use of dose-dense chemotherapy in ovarian cancer. Descriptive statistics were used to analyze the data.

Results: Overall survey response rate was 81% (n = 21). Of the responding sites, 24% (n = 5) were fully adherent to all published hematologic hold parameters, 66% (n = 14) had hold parameter for ANC or platelets that differed from published data, and 10% (n = 2) did not have center-specific hold parameters (Figure 1). For ANC on cycle day 1, 52% (n = 11) did not adhere to the published hold parameters, and for cycle days 8 and 15, 43% of centers (n = 9) were nonadherent. Regarding platelets, 52% of centers (n = 11) were nonadherent for day 1 parameters and 57% (n = 12) were nonadherent on days 8 and 15 of each cycle.

Conclusions: Our study found that 66% of NCCN sites use higher cutoffs for ANC and platelet count than the hold parameters in published data. By requiring higher blood counts for treatment, a greater percentage of patients may experience treatment delays or dose reductions, thereby functionally decreasing dose density. Further research is necessary to determine the optimal strategy to increase individual site adherence to published protocols.

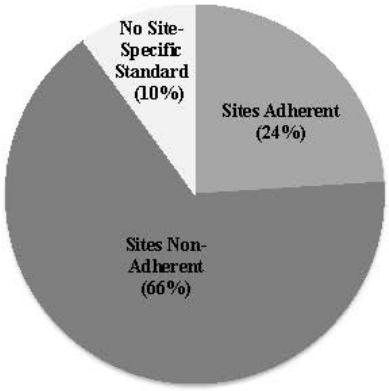

Fig. 1
NCCN Sites Adherence to Hematologic Hold Parameters.

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248 - Poster
Should elderly patients with epithelial ovarian cancer be treated standardly?
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Objectives: To compare intraoperative and postoperative data, and oncological outcome of elderly patients with epithelial ovarian cancer treated according to standard cytoreductive surgery and chemotherapy versus other treatment. Predicting factors leading to a deviation to standard surgical treatment will be assessed.

Methods: We conducted a retrospective, bicentric study in patients older than 70 years with surgical treatment for an epithelial ovarian cancer between January 2005 and January 2014. Two groups were compared: patients with standard cytoreductive surgery following neoadjuvant chemotherapy or not, and patients with other treatment. We studied pretherapeutic data of patients, their treatment, and their outcome. Patients were compared using univariate and multivariate analysis.

Results: The study included 222 patients, of whom 93 (41.7%) had standard cytoreductive surgery and 129 (58.1%) had incomplete surgery or chemotherapy. The causes encountered for deviation from standard care were spread of the disease in 87 cases (67.4%), toxicity of chemotherapy in 44 cases (34.1%), medical refusal because of comorbidities in 36 cases (27.9%), surgical complications in 19 cases (14.7%), patient refusal in 15 cases (11.6%), and familial refusal in 2 cases (1.6%). An oncogeriatric assessment was performed in 22% of cases in the group with standard surgical treatment and in 38% in the group with minimal surgery ($P = .02$). When the oncogeriatric analysis did not promote a standard treatment, no patient had a standard treatment. Perioperative complications were not increased despite more aggressive surgery in the group with standard treatment. Patients without deviation had an extended survival (HR 0.23 (0.14–0.39), $P < .001$). We did not identify predicting factors leading to a deviation from standard care.

Conclusions: Elderly patients with ovarian cancer should have standard cytoreductive surgery whenever possible.

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249 - Poster

Impact of surgical staging on prognosis in patients with borderline ovarian tumors: A meta-analysis

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Objectives: To quantify the effect of complete surgical staging (CSS) on prognosis in borderline ovarian tumor (BOT) patients through a meta-analysis.

Methods: We systematically reviewed published studies comparing CSS with incomplete surgical staging (ISS) in BOT patients through April 2015. Endpoints were recurrence and mortality rates. Study design features that possibly affected participant selection, recurrence/death detection, and study publication were assessed. For pooled estimates of the effect of CSS on recurrence/death, random- or fixed-effects meta-analytic models were used after assessing cross-study heterogeneity.

Results: Eighteen observational studies (CSS: 1,297 patients; ISS: 1,473 patients) met our search criteria. Fixed-effects model–based meta-analysis indicated a reduced recurrence risk among CSS patients (odds ratio [OR] 0.64; 95% CI 0.47–0.87, $P < .05$, $I^2 = 25.6$). However, no significant between-group difference in mortality was observed (OR 0.98, 95% CI 0.42–2.29, $P = .97$, $I^2 = 0$). In subgroup analysis, CSS was associated with a reduced recurrence risk in 16 studies of all histologic types (OR 0.66, 95% CI 0.48–0.91, $P < .05$, $I^2 = 31.9$) but not in 2 studies of only mucinous disease (OR 0.41, 95% CI 0.13–1.30, $P = .13$, $I^2 = 0$). In subgroup analyses of 4 studies with recurrence data according to fertility-sparing surgery, no significant association was found (OR 0.51, 95% CI 0.18–1.43, $P = .20$, $I^2 = 0$). There was no evidence of publication bias.

Conclusions: In this meta-analysis based on observational studies, CSS appeared to significantly reduce recurrence among BOT patients. No survival impact was observed. Longer-term randomized controlled trials could verify this relationship but appear unfeasible for this rare tumor.

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250 - Poster

Application of topical imiquimod for treatment of cervical intraepithelial neoplasia in young women: A preliminary result of a pilot study

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Objectives: In young, especially nulliparous women, it is not easy to decide on excisional therapy for cervical intraepithelial neoplasia (CIN). We aimed to evaluate how effective topical imiquimod is in the treatment of high-grade CIN so that excisional therapy can be avoided in young women.

Methods: Patients with CIN were allocated to this pilot study. They did not want excisional therapy and agreed with topical imiquimod therapy, which required once-a-week hospital visit for 8 weeks for the application of imiquimod to the cervix by a gynecologic oncologist. If the lesion got worse during treatment, it was decided to convert imiquimod therapy to excisional therapy.

Results: A total of 36 patients with a median age of 29 years (range, 22–41 years) agreed to receive topical imiquimod therapy. Of these, 32 patients (88.9%) were positive for high-risk human papillomavirus (HR HPV). Twenty-five patients (69.4%) had low-grade squamous intraepithelial lesion (LSIL), and 11 (30.6%) had high-grade squamous intraepithelial lesion (HSIL) on their initial LBC. Twenty-eight patients underwent punch biopsy, which showed CIN 1 in 7 (19.4%), CIN 2 in 11 (30.6%), and CIN 3 in 10 (27.8%) patients. Twenty patients finished the 8-week imiquimod therapy. Among them, 14 patients had CIN 2 or 3, and 6 patients had CIN 1. HR HPV was positive in 12 patients. On the last examination, 14 patients (70.0%) had negative intraepithelial lesions, 3 (15.0%) had atypical squamous cells of undetermined significance, and 1 (5.0%) had LSIL. Two patients had persistent HSIL: 1 patient underwent loop electrosurgical excision procedure, resulting in CIN 3 with positive resection margin, and the other patient underwent punch biopsy, resulting in intermediate cells and restarted imiquimod therapy. Only 7 patients were negative for HR HPV.

Conclusions: This study showed that topical imiquimod therapy was effective for the treatment of high-grade CIN, with a histologic regression rate of 85.7% (14/20) and HPV eradication rate of 25.0% (8/32). Based on our findings, topical imiquimod therapy might have a successful therapeutic effect in young women with CIN 2-3 so that they can avoid excisional

therapy. In addition, it could be a more reassuring treatment option for CIN 1 than just follow-up after few months. To confirm its efficacy, a phase II study with larger cohort would be needed.

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251 - Poster

Postsurgical readmissions among women with gynecologic malignancies

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Objectives: We sought to determine 30-day postsurgical readmission rates, as well as pre- and postoperative risk factors for readmission among women with gynecologic malignancies.

Methods: We identified patients who underwent surgical intervention for gynecologic malignancy (uterine, cervical, ovarian and other gynecologic cancers) in the National Surgical Quality Improvement Program database from 2006 to 2012. Data collected included surgical procedure, operative time, 30-day readmission, comorbidities, preoperative condition, and serious postoperative complications. Descriptive statistics and multivariable logistic regression analyses were performed.

Results: Of patients who underwent gynecologic cancer surgery, 5% (654/13,093) were readmitted. Readmission rates were highest for ovarian cancer (7.1%; 195/2,765), followed by uterine (4.3%; 290/6,728), cervical (4.3%; 102/2,373), and other gynecologic cancers (5.5%; 67/1,227) ($P < .01$). Ovarian cancer patients were more likely to have comorbidities, worse preoperative condition, and more major complications including surgical site infection, deep vein thrombosis/pulmonary embolism, need for ventilation for more than 48 hours, sepsis, and septic shock ($P < .01$). Overall, independent factors for readmission for gynecologic cancer surgery included worse preoperative condition (OR 1.33, CI 1.14–1.54), complex surgery (OR 1.67, CI 1.23–2.25), and major complications (OR 2.71, CI 2.44–3.01), all $P \leq .001$. For uterine cancers, complexity of surgery ($P = .002$), operative time ($P = .015$), and major complications ($P < .0001$) remained significant factors for readmission. For ovarian cancer, the only independent factor for readmission was major complications ($P < .001$). For cervical cancer, only operative time ($P = .005$) and major complications ($P < .001$) remained significant in adjusted models.

Conclusions: The 30-day postsurgical readmission rate for gynecologic cancer patients is 5% overall, with the highest rates seen among patients with ovarian cancer (7%). Major complications remained an independent factor for readmission among all types of gynecologic cancer surgery. Efforts to improve preoperative surgical status and lower complication rates may reduce surgical readmission and morbidity. The effect of such efforts on overall cancer outcome and survival remain unknown.

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Robotic-assisted surgery for colorectal procedures in a gynecologic oncologic setting: Analysis of initial outcomes

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Objectives: To review the intraoperative data and short-term oncologic outcomes in a series of patients managed with robotic-assisted colorectal surgery in a gynecologic oncologic setting.

Methods: Retrospective review of all robotic-assisted colorectal cases performed by a single gynecologic oncologist from June 2011 to July 2015

Results: Twelve patients who had 13 robotic-assisted colorectal procedures were identified (Table 1). Demographic data included mean age of 56.3 years (range 41–75 years), body mass index 26.9 (range 19–32.2). Nine patients (75%) had undergone a previous hysterectomy. Surgery indication varied; 5 (42%) of 12 presented with rectovaginal fistula after previous gynecologic cancer surgery, 5 (42%) presented with primary disease, and 2 (16%) presented with recurrent

rectosigmoid disease after previous gynecologic cancer surgery. Five patients (42%) received previous radiation therapy to the pelvis. Robotic procedures included formation of end sigmoid colostomy (n = 5), sigmoid/transverse colon resection with primary anastomosis, (n = 4), low anterior resection with end-to-end anastomosis (n = 3) and cecectomy (n = 1). Mean operative time was 136.3 minutes (range 80–181 minutes), estimated blood loss 83.3 mL (range 50–200 mL), and length of stay 2.4 days (range 1–6 days). No intraoperative complications occurred. One patient had postoperative ileus that resolved with supportive care.

Conclusions: As our specialty transitions toward proficiency in less invasive surgeries, the need for gynecologic oncologists to adapt and learn how to perform minimally invasive colorectal procedures is of paramount importance. Our data indicate that robotic-assisted colorectal rectal procedures in a gynecologic oncology setting are feasible, safe, and offer good short-term outcomes. These data support the concept that gynecologic oncologists can embrace and become proficient in minimally invasive colorectal techniques.

Table 1
List of patients with colon procedures.

Patient	Surgical Indication	Robotic Procedure
1	Metastatic Primary Peritoneal Carcinoma	Transverse Colectomy
2	Pelvic Pain, Stage IV Endometriosis	Sigmoid Resection with Primary Anastomosis
3	Stage IBI Cervical Cancer Recurrence to colon, Rectovaginal Fistula	End Sigmoid Colostomy
4	Stage IV, Grade 3 Endometrial Cancer, Radiation Therapy Rectovaginal Fistula	End Sigmoid Colostomy
5	Stage 1B1 Endometrial Cancer, Radiation Therapy Recurrence to Rectum	Low Anterior Resection with Primary Anastomosis
6	Stage IIIB Vaginal Cancer, Radiation Therapy Rectovaginal Fistula	End Sigmoid Colostomy
7	Pelvic Mass with Colonic Lesion (Final Pathology Metastatic Colon Adenocarcinoma)	Sigmoid Resection Low Anterior Resection
8	Carcinoma of cervical stump, Radiation Therapy, and status post anterior exenteration for persistent disease, Presenting with Recto-Vaginal Fistula	End Sigmoid Colostomy
9	Stage 1A Papillary Serous Endometrial Cancer, Radiation Therapy, with Focal Recurrence to Large Bowel	Low Anterior Resection with Primary Anastomosis
10	Stage IIIB Ovary and Stage 1A grade 3 Endometrial Cancer Focal Recurrence to Large Bowel	End Sigmoid Colostomy
11	Pelvic Pain Stage IV Endometriosis	Sigmoid Resection with Primary Anastomosis
12	Pelvic Pain, Stage IV Endometriosis	Cecectomy

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253 - Poster

Significant, unexplained regional variation in fertility-sparing surgery among reproductive-age women with early epithelial ovarian cancer

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Objectives: To describe associations between histologic and demographic factors and performance of hysterectomy at the time of initial surgery for early epithelial ovarian cancer (EOC).

Methods: A retrospective cohort study was conducted using the National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) 18 dataset. Women younger than 40 years with localized EOC diagnosed between 2000 and 2012

who had primary surgery were included. Multivariate logistic regression was performed to evaluate associations with performance of hysterectomy at the time of initial surgery. Variables included in the analysis were age, race, marital status, geographic region, tumor grade, cell type, and concomitant performance of lymph node dissection (LND). SEER registries were combined into 4 geographic regions (North, South, East, West).

Results: A total of 847 women were included, of whom 401 underwent hysterectomy. Age-adjusted relative 5-year survival was not significantly better for women who underwent hysterectomy (96.7%, 95% CI 93.6%–98.3%) compared with those who did not (95.5%, 95% CI 92.3%–97.4%). Univariate analysis revealed significant associations between hysterectomy and all of the clinical or demographic variables described above, with the exception of tumor grade. In multivariate logistic regression analysis, geographic region, age, cell type, and LND were significantly ($P < .05$) and independently associated with hysterectomy at the time of initial surgery. Adjusted odds ratios for hysterectomy are presented in Table 1.

Conclusions: NCCN guidelines recommend treatment of early EOC with hysterectomy, but acknowledge the appropriateness of fertility-sparing surgery based on patient age and reproductive goals. Higher odds of hysterectomy in patients older than 30 years likely reflect changing reproductive goals with age. After adjusting for relevant cofactors, we observed significant regional variation in fertility-sparing surgery. SEER does not include data on parity or access to gynecologic oncologist subspecialty care, so additional investigation may be of value. Primary surgical management of women with early invasive EOC could represent an opportunity for improving the quality of healthcare delivery outcomes by measures directed at reducing unexplained regional variation in practice.

Table 1
Multiple Logistic Regression Model Describing the Relationship between Geographic Region and Hysterectomy at the Time of Initial Surgery for Reproductive-age Women with Early Stage Epithelial Ovarian Cancer, Adjusting for Clinical and Demographic Variables.

		No Hysterectomy n (%)	Hysterectomy n (%)	Total n (%)	Adjusted OR for Hysterectomy (95% CI)	P-value
Total		446 (52.7)	401 (47.3)	847 (100)		
Geographic Region						
	West (CA, NM, HI, UT, WA)	294 (65.9)	215 (53.6)	509 (60.1)	1.0 (reference)	
	North (IA, MI)	34 (7.6)	35 (8.7)	69 (8.1)	1.3 (0.7-2.2)	0.393
	South (GA, KY, LA)	65 (14.6)	94 (23.4)	159 (18.8)	1.9 (1.3-2.9)	0.001
	East (CT, NJ)	53 (11.9)	57 (14.2)	110 (13.0)	1.3 (0.8-2.0)	0.257
Age						
	<20	36 (8.1)	3 (0.7)	39 (4.6)	1.0 (reference)	
	20-29	160 (35.9)	55 (13.7)	215 (25.4)	3.8 (1.1-13.2)	0.033
	30-39	250 (56.1)	343 (85.5)	593 (70.0)	13.6 (4.1-45.8)	<0.001
Histology						
	Serous	72 (16.1)	57 (14.2)	129 (15.2)	1.0 (reference)	
	Endometrioid	84 (18.8)	144 (35.9)	228 (26.9)	1.8 (1.1-2.9)	0.017
	Mucinous	226 (50.7)	136 (33.9)	362 (42.7)	0.9 (0.6-1.4)	0.588
	Other	64 (14.3)	64 (16.0)	128 (15.1)	1.0 (0.6-1.7)	0.953
Lymph Node Dissection						
	No	200 (44.8)	101 (25.2)	301 (35.5)	1.0 (reference)	
	Yes	246 (55.2)	300 (74.8)	546 (64.5)	2.3 (1.7-3.2)	<0.001
Grade						

	Low Grade	260 (58.3)	249 (62.1)	509 (60.1)		NS
	High Grade	45 (10.1)	48 (12.0)	93 (11.0)		
	Unknown	141 (31.6)	104 (25.9)	245 (28.9)		
Race						NS
	White	343 (76.9)	319 (79.6)	662 (78.2)		
	Black	19 (4.3)	30 (7.5)	49 (5.8)		
	Other	84 (18.8)	52 (13.0)	136 (16.1)		
Married						NS
	No	256 (57.4)	168 (41.9)	424 (50.1)		
	Yes	190 (42.6)	233 (58.1)	423 (49.9)		

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A population-based study of rare malignant trophoblastic neoplasms: Epithelioid trophoblastic tumor and placental site trophoblastic tumor

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Objectives: To present the first population-based study of 2 rare malignant trophoblastic tumors.

Methods: Patients were identified from the National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) 18 dataset. Differences in means were evaluated with the Student *t* test, differences in proportions were evaluated with the X^2, and relative survival using the Kaplan-Meier method was calculated in SEERstat. Incidence rates per 100,000 were standardized to the 2000 US population, and annual age-adjusted incidence rates per 100,000 (AAIR) were determined.

Results: Sixty-one patients had epithelioid trophoblastic tumor (ETT), with an average age of 34.4 years (range 16-53 years). Fifty patients had placental site trophoblastic tumor PSTT, with an average age of 32.7 (range 17-52). The AAIR of ETT was 0.0058 (95% CI 0.0044-0.0074) and was higher in black women (rate ratio 2.2, 95% CI 1.1-4.4, *P* = .02). The AAIR of PSTT was 0.0034 (95% CI 0.0024-0.0046) and was higher in Asian women (rate ratio 2.8, 95% CI 1.1-7.0, *P* = .04). Frequency of localized disease was higher among those with ETT relative to PSTT (39% vs 19%, *P* = .03). Patients with ETT more frequently had surgery (69% ETT vs 48% PSTT, relative risk 1.4, 95% CI 1.0-2.0, *P* = .026). Seven patients (11%) with ETT and 2 (4%) with PSTT had died at the time of last follow-up. The relative survival at 5 years for ETT was 86.9% (95% CI 73.7%-93.8%) and for PSTT was 95.7% (95% CI 82.8%-99.0%). Age greater than 40 years was associated with worse survival compared with those younger than 40 years in patients with ETT (relative survival 62.9% [95% CI 33.8%-82.0%] vs 97.4% [95% CI 82.5-99.6%]) and PSTT (relative survival 82.4% [95% CI 44.1%-95.5%)] vs 100%). Metastatic disease was associated with worse survival in patients with ETT, with relative survival of 93.5% (95% CI 75.3%-98.4%) compared with 100% in those with localized disease.

Conclusions: Despite a common origin in intermediate trophoblast, ETT and PSTT are distinguished by histologic findings and, we may now begin to make observations regarding distinct clinical features. Demographic and prognostic factors, as presented here, may be helpful in clarifying diagnosis and recommending treatment. This study provides the only population-based description in the literature, and provides new insights into the descriptive epidemiology of these rare neoplasms.

255 - Poster

Weight loss outcomes following referral of obese women with endometrial cancer and complex atypical hyperplasia to a bariatric specialist

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Objectives: To report weight loss outcomes following the referral of obese women with endometrial cancer (EC) or complex atypical hyperplasia (CAH) to bariatric specialists.

Methods: Women with stage I-II EC or CAH with a body mass index (BMI) higher than 30 kg/m^2 were offered a medical bariatric referral (BR); if their BMI was higher than 35 kg/m^2 with an obesity-related comorbidity or higher than 40 kg/m^2 they were also offered a surgical BR. Descriptive statistics and 2-sided *t* tests were used.

Results: Of 156 women approached, 6 were already seeing a bariatrician and 18 declined. Of the remaining 132, 11 had CAH and the rest had stage IA (n = 102), IB (n = 13), or II (n = 6) endometrioid adenocarcinoma. Mean BMI was 42.8 kg/m^2 (95% CI 41.2–44.4 kg/m^2). Mean follow-up was 10.7 months (95% CI 9.8-11.5 months) from the time of their BR. Seventy-eight (59.1%) reported any weight loss attempt (WLA): 51 (38.64%) initiated a self-guided WLA, in the form of diet (n = 40) and/or exercise (n = 28), 7 (5.3%) joined a commercial weight loss program, and 24 (18.2%) initiated a physician-guided WLA which included physician-supervised diet (n = 21), medications (n = 2), nutritionist visits (n = 17), therapy (n = 2), and surgery (n = 2). Compared with the remaining cohort, at 3 months, physician-guided WLA resulted in a mean loss of 4.8 versus 0.8 lbs (*P* = .0173) and initiating any WLA was associated with a weight loss of 3.3 lbs versus gain of 0.7 lbs (*P* = .0215). However, at 6 months, 12 months, and last recorded weight, neither the group initiating any WLA nor the group initiating a physician-guided WLA had lost more weight than the remaining cohort. Self-guided diet was not associated with significant weight loss at any point, but those who reported exercise lost more weight at 6 months than those who did not (6.9 vs 2.0 lbs, *P* = .0161). Only 2 women had bariatric surgery. At 3, 6, and 12 months and last follow-up, they lost a mean of 5.3, 4.0, 30.2, and 61.5 lbs compared with the remaining cohort who lost 1.8, 3.0, 1.2, and 0.3 lbs at those time points.

Conclusions: Most EC and CAH survivors will initiate a WLA after a BR is offered, but very few use surgery. Both self- and physician-guided WLA are associated with short-term weight loss, but this effect diminishes over time. Exercise may help keep weight off for a few more months, but also fails to result in long-term weight loss. Although the small numbers limit our ability to demonstrate statistical significance, bariatric surgery results in the most profound and durable weight loss.

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Quality of life, function, and symptom scores following referral of obese women with endometrial cancer and complex atypical hyperplasia to a bariatric specialist

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Objectives: To report changes in quality of life (QOL), function, and symptoms 1 year after the referral of obese women with endometrial cancer (EC) and complex atypical hyperplasia (CAH) to a bariatric specialist.

Methods: Obese women with stage I-II EC or CAH were offered a bariatric referral (BR). Validated QOL questionnaires (EORTC QLQ-C30 and EN24) were administered at the time of BR and 12 months later. Descriptive statistics and 2-sided *t* tests were used.

Results: Both baseline and 12-month surveys were completed by 51 (38.6%) of 132 participants. Mean age was 54.4 years (95% CI 51.9–56.8 years) and body mass index (BMI) was 41.4 kg/m^2 (95% CI 39.1–43.7) kg/m^2. Most had early-stage EC (37 IA, 4 IB, 4 II), but 6 (11.8%) had CAH. Forty (78.4%) initiated a WLA: 12 (23.5%) complied with a BR (10 medical, 2 surgical), 29 (72.5%) initiated self-guided weight loss attempts (SG-WLA), 4 (7.8%) joined a commercial program, 32 (62.7%) started a diet, and 25 (49.02%) exercised. Twelve months after referral, women who initiated any WLA or a SG-WLA demonstrated a greater improvement in global health QOL scores than those did nothing (+5.4 vs –8.3, *P* = .0306; +5.5 vs –8.3, *P* = .0341). Compared with those who did nothing, women who complied with a BR did not demonstrate significantly changed QOL, function, or symptom scores at 12 months. However, trends suggested that women who complied with a BR experienced improvement in poor body image symptoms (–28.8 vs –5.6, *P* = .0584) but more financial difficulties (+16.7 vs –4.4, *P* = .0501) compared with the remaining cohort. Women who went on a diet as part of their WLA reported an improvement in global health QOL (+7.3 vs –5.7, *P* = .0258) and a greater reduction in fatigue (–8.7 vs +2.9, *P* = .0410), gastrointestinal (–7.5 vs –1.4, *P* = .0023), and poor body image symptoms (–15.7 vs –0.9, *P* = .0252). Exercise was associated with a greater increase in sexual activity at 12 months (+9.1 vs –8.7, *P* = .0179).

Conclusions: Twelve months after a BR, initiation of a WLA, even if self-guided, is associated with improved global health QOL. Dieting is associated with improved fatigue, gastrointestinal symptoms, and body image. Exercise resulted in greater sexual activity. Compliance with a BR may cause financial strain for obese survivors and providers should remain sensitive to this barrier to weight loss.

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Vulvar and vaginal melanoma: A distinct subclass of melanoma based on a comprehensive molecular analysis of 51 cases

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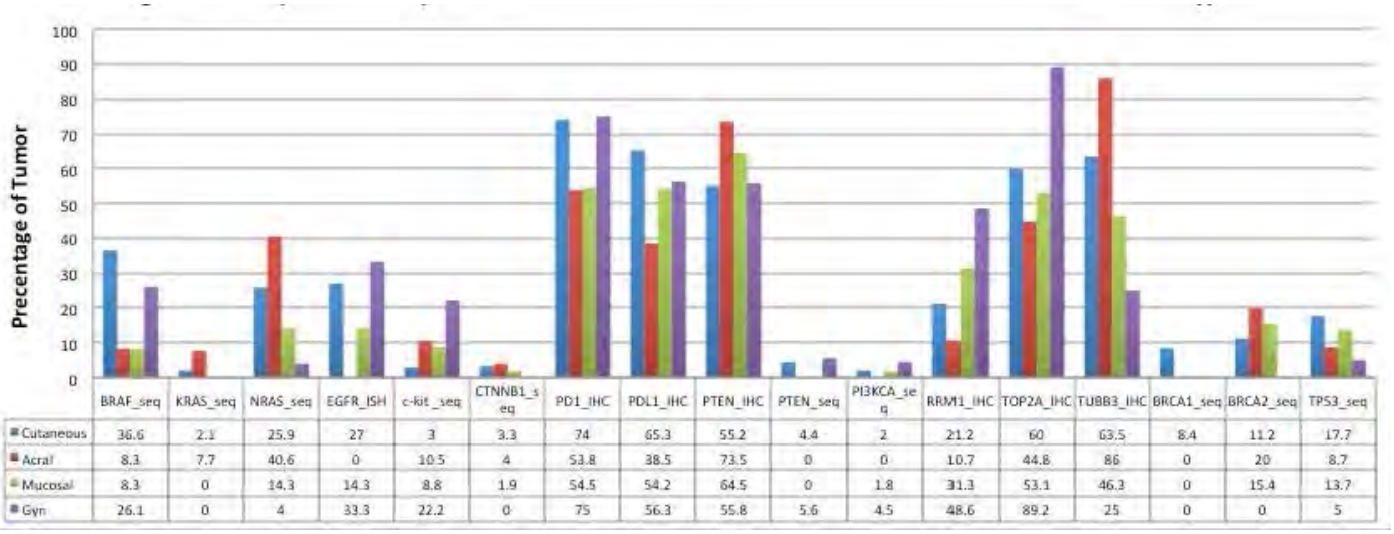
Objectives: Vulvar and vaginal melanomas are rare cancers that are biologically aggressive. These tumors may harbor distinct molecular characteristics compared with cutaneous and mucosal melanoma of other sites. We analyzed the patterns of molecular, genomic, and protein changes in vulvar/vaginal melanoma (VM), and compared these changes with those of a large cohort of melanoma of non-gynecologic origin.

Methods: A total of 2,304 cases of melanoma submitted for molecular profiling from 2009 to 2015, including 51 VM cases, were reviewed. All tumors were analyzed using Illumina TruSeq Amplicon Cancer panel to search for sequence variants in genes commonly implicated in carcinogenesis. In situ hybridization and immunohistochemistry were also used to assess copy number and protein expression, respectively, of selected genes.

Results: Of 51 cases of malignant VM, 14 originated from the vagina, 37 from the vulva. Figure 1 summarizes the frequency of biomarkers of interest in VM, and NGM, which are further classified into cutaneous, acral, and mucosal based on site of origin. *BRAF* is most frequently mutated in VM (26%), compared with 36.6% in cutaneous melanoma and 8.3% (P = .008) in mucosal melanoma. However, *BRAF* mutations in VM are significantly less likely to include known responders to *BRAF* inhibitors than those from NGM tumors (P = .011). The *c-KIT* mutation rate in VM (22%) is significantly higher than cutaneous (3%, P < .001) and mucosal (8.8%, P = .05) melanoma. The majority (60%) of *c-KIT* mutations in VM are also known to be sensitive to inhibitors of tyrosine kinase receptor. *NRAS* mutations are rare in VM (4%) compared with cutaneous (25.9%, P = .009) and acral (40.6%, P = .002) melanoma. VMs express biomarkers of cytotoxic sensitivity more commonly than NGM, including increased TOP2A and RRM1, markers of anthracycline and gemcitabine resistance, respectively (P = .0001, 0.006). PDL1 is expressed frequently in both VM and NGM (56%, 63.5%), *PI3KCA*mutations, and ER/PR receptor expression are rare.

Conclusions: Our findings suggest VM may represent a unique subclass of melanoma. VMs are unlikely to harbor mutations sensitive to existing *BRAF* inhibitors. Tyrosine kinase inhibitors or MEK inhibitors targeting *c-KIT* and *NRAS* may be of therapeutic benefit. PDL1 inhibitors warrant further exploration in patients with vulvovaginal melanoma.



	BRAF_seq	KRAS_seq	NRAS_seq	EGFR_ISH	c-kit _seq	CTNNB1_seq	PD1_IHC	PDL1_IHC	PTEN_IHC	PTEN_seq	PI3KCA_seq	RRM1_IHC	TOP2A_IHC	TUBB3_IHC	BRCA1_seq	BRCA2_seq	TPS3_seq
Cutaneous	36.6	2.1	25.9	27	3	3.3	74	65.3	55.2	4.4	2	21.2	60	63.5	8.4	11.2	17.7
Acral	8.3	7.7	40.6	0	10.5	4	53.8	38.5	73.5	0	0	10.7	44.8	86	0	20	8.7
Mucosal	8.3	0	14.3	14.3	8.8	1.9	54.5	54.2	64.5	0	1.8	31.3	53.1	46.3	0	15.4	13.7
Gyn	26.1	0	4	33.3	22.2	0	75	56.3	55.8	5.6	4.5	48.6	89.2	25	0	0	5

Fig. 1

Comparative Frequencies of Alteration in Biomarker of Interest across Melanoma Subtypes.

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Progestin-based therapy for complex atypical hyperplasia: Does body habitus matter?

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Objectives: Although progestins can effectively treat women with complex atypical hyperplasia (CAH) who desire future fertility or are poor surgical candidates, the effect of body habitus on treatment outcome is not well studied. This study examines the association between body mass index (BMI) and progestin treatment outcomes.

Methods: This was a retrospective cohort study of patients who received a biopsy diagnosis of hyperplasia between 2003 and 2011. For each patient, demographics, medical history, BMI, hormonal therapy, and histologic treatment response were abstracted. Patients with CAH were included if they had no previous/current diagnosis of endometrial cancer, had not taken progestin therapy within a month before diagnosis, had documented progestin treatment after diagnosis, and had follow-up histology. The rates of complete response (normal endometrium on follow-up biopsy) were examined across collected variables.

Results: Of the 623 hyperplasia patients identified, 114 had CAH and satisfied the inclusion criteria. Median age was 34 years and nearly two-thirds (63%) were nulliparous. Mean BMI was 41. Eighty-five percent were obese (36% with BMI of 30–39.9 and 49% with BMI ≥40). Ninety-one percent received systemic progestin therapy and 9% received progestin intrauterine devices. Forty-seven patients (41%) had a complete response to progestin-based therapy. BMI had no effect on the rate of complete response. The proportions of CAH patients with complete response to hormonal therapy were as follows: 47% with BMI less than 30, 38% with BMI of 30 to 39.9, and 39% with BMI of 40 or higher (P = .66). Age (43% ≤30 years vs 41% >30 years, P = .81) and treatment type (40% systemic vs 50% local, P = .74) also had no effect on the rate of complete response. Obese patients were more likely than nonobese to receive progestin intrauterine devices (0% with BMI <30, 3% with BMI of 30–39.9, and 17% with BMI ≥40; P = .03).

Conclusions: In this predominantly obese population, response to progestin therapy was generally low; body habitus did not have an effect on progestin treatment outcome for CAH.

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Increased efficacy of metformin corresponds to differential metabolic effects in ovarian tumors in obese versus lean mice

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Objectives: We assessed the metabolic anti-tumorigenic effects of metformin in a genetically engineered mouse model of serous ovarian cancer (OC) under obese and lean conditions.

Methods: We used the K18-gT121+/-; p53fl/fl; Brca1fl/fl (KpB) OC mouse model. KpB mice were subjected to 60% calories derived from fat in a high-fat diet to mimic diet-induced obesity versus 10% calories from fat in a low-fat diet. Mice were treated with placebo or metformin orally (200 mg/kg per day) following tumor onset for 4 weeks (n = 8–10 mice per group). Tumor size and volume were recorded weekly. Global, untargeted metabolomics was used to identify obesity-dependent effects of metformin in the ovarian tumors.

Results: Metformin inhibited tumor growth in lean and obese KpB mice. In the obese mice, metformin decreased tumor growth by 60%, whereas tumor growth was only decreased by 32% in the lean mice (P = .003) compared with placebo-treated mice. The OCs from obese mice had evidence of impaired mitochondrial complex 2 function and energy supplied by fatty acid oxidation rather than glycolysis compared with lean mice. However, in obese mice treated with metformin, glycolysis was stimulated, suggesting an obesity-specific switch in substrate from fatty acids to glucose. Succinate was depleted and fumarate and malate accumulated in metformin-treated OCs in obese versus lean mice, consistent with metformin's inhibition of complex 1. Finally, n3 and n6 fatty acids increased with metformin treatment in OCs of obese mice but not lean mice, indicating an inability to oxidize fatty acids when mitochondrial complex 1 and 2 were inhibited by metformin and obesity, respectively.

Conclusions: Metformin has increased anti-tumorigenic efficacy in obese versus lean mice. Detected metabolic changes may underlie why ovarian tumors in obese mice have heightened susceptibility to metformin, i.e., ovarian tumors in obese mice have impaired complex 2 function at baseline. When combined with metformin's inhibition of complex 1, obese OCs display profound impairment of mitochondrial oxidative phosphorylation, leaving glycolysis as the sole option for ATP production. In sum, improved efficacy of metformin corresponds with inhibition of mitochondrial complex 1 and fatty acid oxidation, and stimulation of glycolysis in only the OCs of obese mice.

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A population-based study of malignant neuroendocrine tumors of the female genital tract

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Objectives: To present the descriptive epidemiology of malignant neuroendocrine tumor (MNET) of the female genital tract (FGT).

Methods: Data were collected from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database between 1973 and 2012. Simple descriptive statistics were calculated. SEER*Stat 8.2.1 was used to calculate age-adjusted annual percent change in incidence per 100,000, estimated annual percent change in incidence (EAPC), and age-standardized relative survival. Cox proportional hazard and multivariate logistic regression analysis were performed using SPSS version 23.0.

Results: A total of 1,098 patients of ages 14 to 85+ years old with female genital MNET diagnosed between 1973 and 2012 were identified. Descriptive statistics are shown in Table 1. The incidence of MNET increased at a rate of 3.1% (95% CI 1.5–4.8) between 2000 and 2012. The EAPC for carcinoids was 2.0% (95% CI 1.3–5.4) and noncarcinoids 3.9% (1.4–6.5). Median survival was 70 months for carcinoids and 11 months for non-carcinoids ($P < .001$). Overall, the 1- and 5-year relative survival was 87% and 78% in patients with carcinoids, and 47% and 24% in patients with non-carcinoid, respectively. Noncarcinoid had a greater risk of cause-specific mortality than carcinoids, even when adjusted for age, site, race, stage, primary surgery, and adjuvant radiation therapy (RT) (HR 4.5, 95% CI 3.076–6.641). On multivariate analysis, localized disease, non-black race, carcinoid histology, having primary surgery, and not having RT were independently associated with better cause-specific survival; primary site of the tumor was not associated with survival. See table for more details.

Conclusions: Although they remain rare tumors, incidence of MNET of the FGT is increasing, specifically among white and non-Hispanic populations. Carcinoids are the most common individual cell type, but comprise less than half of MNETs. Patients with carcinoids most frequently have an ovarian primary, are diagnosed early, and have favorable prognosis. Patients with non-carcinoid histology more frequently present with advanced stage and have worse prognosis. Those with non-carcinoid histology have a worse cause-specific survival, even when adjusted for site, race, stage, having primary surgery, or adjuvant RT. Familiarity with the distinct clinical features and natural history of these rare tumors can result in more accurate diagnosis, refine prognosis, and may result in improved outcomes.

Table 1

Baseline characteristics and hazard ratios in MNET by carcinoid and non-carcinoid histology in the FGT.

Baseline characteristics	Overall	Carcinoid	Non-Carcinoid	p-value[a]
N	1,098	454	644	
Mean/Median age (y)	54/54	53/52	56/56	
Age ≥ 50	62%	59%	64%	0.090
Race				0.003
White	77.3%	76.2%	78.1%	
Black	13.2%	16.5%	10.9%	
Asian	8.7%	6.2%	10.6%	
Other	0.7%	1.1%	0.5%	

Site				<0.001
Cervix	24.3%	1.8%	40.2%	
Uterus	13.1%	0.4%	22.0%	
Ovary	56.6%	96.0%	28.7%	
Other	6.0%	1.8%	9.0%	
Histology				
Neuroendocrine, NOS	45.6%	---	77.8%	
Carcinoid	41.3%	100%	---	
Large Cell carcinoma with neuroendocrine features	6.0%	---	10.2%	
Epithelial-Myoepithelial carcinoma	1.2%	---	2.0%	
Merkel Cell carcinoma	0.5%	---	0.8%	
	5.4%	---	9.2%	
Stage				<0.001
Localized	47.9%	82.8%	23.6%	
Regional/Distant	52.1%	17.2%	76.4%	
Primary Surgery	75.0%	95.1%	61.1%	<0.001
Adjuvant RT	19.8%	1.5%	32.8%	<0.001
1-year Survival (%, 95%	78.0 (57.5-65.8)	87.0 (79.9-91.8)	46.9 (41.7-51.9)	
5-year Survival (%, 95%	45.0 (40.1-49.7)	78.0 (67.7-85.4)	24.2 (19.2-29.4)	
Hazard Ratio (95% CI) [c]				
Carcinoid[d]	4.52 (3.076-6.641)			<0.001
Age[e]	0.889 (0.714-1.108)	1.818 (0.728-4.542)	0.831 (0.660-1.046)	
Site[f]	1.044 (0.786-1.386)	3.254 (0.509-20.815)	0.975 (0.632-1.502)	
Stage[g]	5.089 (3.686-7.027)	24.375 (10.728-55.385)	3.309 (2.388-4.584)	
Race[h]	1.396 (1.006-1.939)	1.356 (0.479-3.844)	1.384 (0.978-1.957)	
Primary Surgery[i]	2.704 (2.166-3.376)	2.007 (0.621-6.488)	2.886 (2.296-3.628)	
Adjuvant	1.649 (1.297-2.097)	0.306 (0.067-1.393)	1.646 (1.292-2.098)	

[a] P-value calculated using Pearson's Chi-Squared Test using SPSS v 23.0
[b] Relative age standardized mean survival analyzed using SEER*STAT 8.2.1
[c] Hazard Ratios were calculated through Cox proportional regression in SPSS v 23.0
[d] Carcinoid vs. non-carcinoid histology
[e] age <50 vs. age >50
[f] Ovary vs. cervix vs. uterus vs. other
[g] Localized vs. regional/distant
[h] Black vs. other races
[i] Primary surgery vs. no surgery
[k] Adjuvant RT vs. no RT
[l] $p<0.05$

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Prognostic values of metabolic parameters measured by 18F-FDG PET/CT in patients with uterine carcinosarcoma

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Objectives: We evaluated the relationship between the metabolic parameters measured with 18F-FDG positron emission tomography (PET)/computed tomography (CT) and oncological outcomes in patients with uterine carcinosarcoma.

Methods: From September 2006 to May 2015, 55 patients with uterine carcinosarcoma had undergone 18F-FDG PET/CT as a preoperative disease evaluation. For each patient, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of primary tumor lesion were measured. The receiver operating characteristics (ROC) curves were used to determine the cutoff value for predicting recurrence or death. The effect of these metabolic parameters on recurrence and survival was evaluated using the Cox proportional hazard model.

Results: The numbers of patients with FIGO stages were as follows: 20 with stage I; 4 with stage II; 22 with stage III; and 9 with stage IV disease. At a median 26 months of follow-up, 19 patients (34.5%) experienced the recurrence of disease, and 23 patients (41.8%) died of their disease. The area under the ROC curve after discriminating for recurrence using MTV (≥36.70 mL) and TLG (≥192.49 g) as cutoff values were 0.648 (95% CI 0.502–0.793) and 0.640 (95% CI 0.495–0.786). The area under the ROC curve after discriminating for death using MTV (≥36.70 mL) and TLG (≥192.49 g) as cutoff values were 0.692 (95% CI 0.546–0.837) and 0.670 (95% CI 0.520–0.820). The median recurrence-free survival and overall survival were 18 months (range, 2–107 months) and 26 months (range, 2–107 months). Univariate analyses showed that hazard ratios for recurrence based on MTV (≥36.70 mL) and TLG (≥192.49 g) were 2.586 (95% CI 1.010–6.623, *P* = .048) and 2.536 (95% CI 1.004–6.410, *P* = .049). Hazard ratios for death using MTV (≥36.70 mL) and TLG (≥192.49 g) were 2.461 (95% CI 1.039–5.828, *P* = .041) and 3.058 (95% CI, 1.282–7.298, *P* = .012).

Conclusions: MTV and TLG of primary tumor lesion could be prognostic predictors of recurrence or death in patients with uterine carcinosarcoma.

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miR-200C inhibits growth of uterine carcinosarcoma cells by driving a mesenchymal-to-epithelial transition

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Objectives: To investigate the importance of epithelial-mesenchymal transition (EMT) in the evolution of uterine carcinosarcoma (UCS) and to explore the role of the miR200 family as a driving force for mesenchymal-epithelial transition (MET) in UCS.

Methods: Endometrioid adenocarcinoma (EAC) cells, Ishikawa and MFE-280, were depleted of miR-200b/c using targeted inhibitors. UCS cells, SNU685 and JHUCS1, were stably transfected with miR-200c expression or control vectors. Gene expression was measured using TaqMan assays. Immunoblotting was performed to assess the protein expression of the EMT markers ZEB1, ZEB2, E-cadherin, N-cadherin, and vimentin. Cell adhesion and in vitro cell proliferation were measured using commercially available assays. In vivo tumor growth of subcutaneously injected JHUCS1 miR-200c-overexpressed or control cells was measured in xenografted mice.

Results: Compared with EAC cells, USC cell lines had undetectable miR-200c expression. Depletion of miR-200b/c in EAC cells resulted in expected increased ZEB1 and decreased E-cadherin expression. Although cell adhesion was decreased, the lack of increased N-cadherin, vimentin, and morphologic changes, even in the presence of exogenous tumor growth factor beta, suggests partial EMT induction. Overexpression of miR-200c in UCS cells resulted in full MET, with decreased expression of ZEB1, ZEB2, N-cadherin, and vimentin and increased expression of E-cadherin. Increased cellular adhesion was observed along with typical MET morphologic changes, whereby cells transitioned from elongated and spindle-shaped to cobblestone and cuboidal. miR-200c overexpression led to inhibited UCS cell proliferation and metabolic activity. Overexpression of miR-200c in vitro resulted in substantially smaller tumors compared with mice bearing control UCS cells.

Conclusions: Ishikawa and MFE-280 EAC cells were resistant to complete EMT, suggesting that additional mechanisms are necessary for the evolution of UCS from EAC according to the conversion theory. SNU685 and JHUCS1 UCS cells, however, readily undergo robust MET in the setting of increased miR-200c expression. These findings suggest that miR200 overexpression through advanced microRNA therapeutics may lead to new options for the treatment of uterine carcinosarcoma.

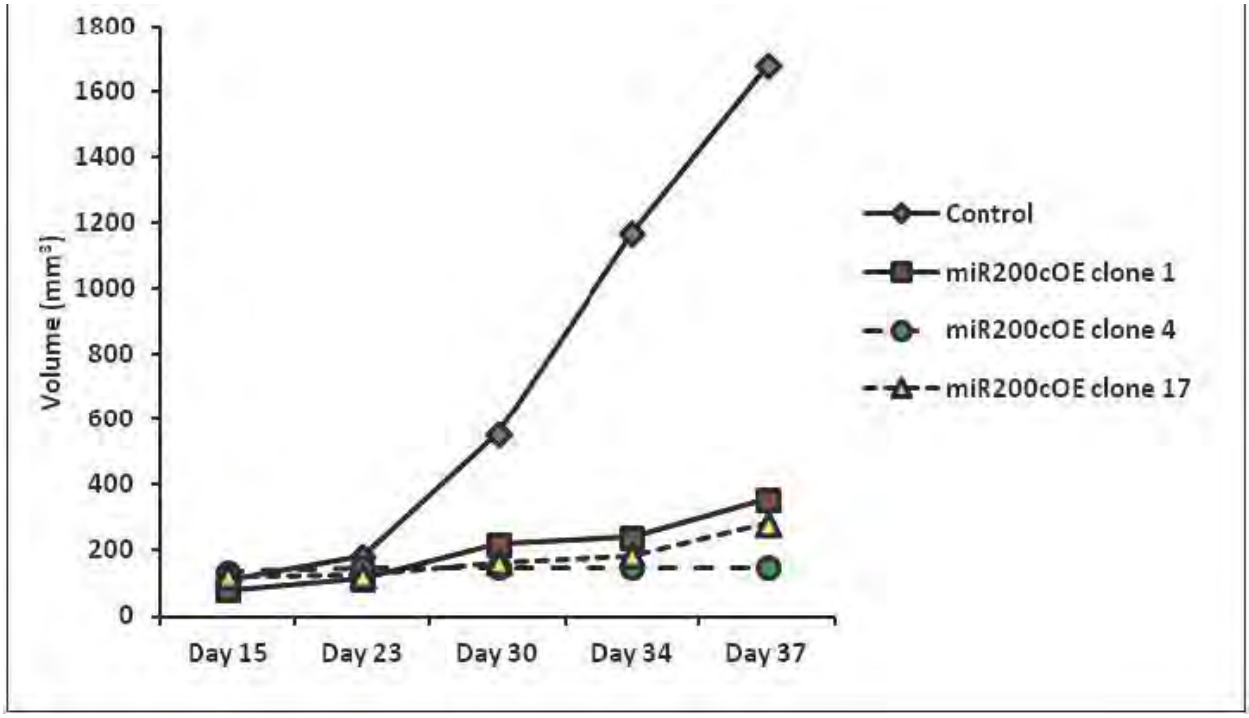

Fig. 1
JHUCS-1 Uterine Carcinosarcoma: Tumor Growth in Control vs. miR-200c Overexpressed Cells.

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Use and efficacy of adjuvant chemotherapy for stage I ovarian cancer
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Objectives: Women with early-stage epithelial ovarian cancer (EOC) generally have a favorable prognosis. Although the standard of care for high-risk patients (IC or any grade 3 tumor) is chemotherapy, the value of chemotherapy for patients with stage IA/IB, grade 1 and 2 tumors is uncertain. We examined utilization and efficacy of chemotherapy in women with stage I ovarian cancer.

Methods: The National Cancer Data Base (NCDB) was used to identify women with stage I EOC who underwent surgery from 1998 to 2012. Patients were classified into 3 groups based on grade and stage: stage IA or IB, grade 1 (low risk); stage IA or IB, grade 2 (intermediate risk); stage IA or IB, grade 3 or any stage IC (high risk). Multivariable generalized estimating equations to adjust for facility-level clustering were used to examine predictors of chemotherapy use while survival was explored using marginal Cox proportional hazards models.

Results: A total of 21,758 patients were identified including 4,245 low-risk, 4,057 intermediate risk, and 13,456 high-risk patients. Use of chemotherapy within the groups was 15.9%, 41.4%, and 70.0%, respectively ($P < .0001$). In a series of separate multivariable models for each group, use of chemotherapy increased with increasing tumor grade and stage, was more frequent in women with clear cell tumors, and less frequent in those with mucinous carcinomas and in older patients ($P < .05$ for all). Among low-risk patients, use of chemotherapy had no effect on survival (HR 1.10, 95% CI 0.85–1.43), whereas chemotherapy was associated with reduced mortality for high-risk (stage IC or any grade 3) patients (HR 0.78, 95% CI 0.71–0.86). For intermediate risk (stage IA/IB, grade 2), chemotherapy was associated with improved survival (HR 0.74; 95% CI 0.63–0.88). The association between chemotherapy and improved survival in these patients remained significant when limited to only patients who underwent staging lymphadenectomy (78.5% of patients, HR 0.78, 95% CI 0.63–0.96).

Conclusions: Although there is some variation in use of chemotherapy for women with early-stage ovarian cancer, chemotherapy usage aligned with known clinical risk factors. Chemotherapy was not associated with survival for patients with stage IA/IB, grade 1 tumors, but was associated with improved survival for stage IA/IB, grade 2 patients.

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Is surgical management associated with sexual dysfunction in women undergoing treatment for gynecologic cancer?

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Objectives: Disruptions to sexual function occur in many women after treatment for gynecologic cancer. Surgical management can alter sexual function by shortening of the vagina, damage to pelvic nerves, orgasmic disruption, sexual arousal difficulty, decreased vaginal lubrication, and early menopause. We hypothesized that patients with open hysterectomy, lymphadenectomy, and longer operative times would have worse postoperative sexual function.

Methods: A cross-sectional study of women with gynecologic cancer was conducted using a survey of validated instruments to assess sexual dysfunction. A subanalysis was performed of women having surgical management to compare outcomes of sexual function. Sexual dysfunction was measured by a change in prediagnosis to post-treatment scores using the Female Sexual Function Index (FSFI) score. A significant decline in sexual function was determined to be a decrease of 5.8 points using a Reliable Change Index Statistic (RCIS). The X^2, Student *t* test, and logistic regression analyses were used to analyze predictors of sexual dysfunction.

Results: A total of 171 patients were included in the primary study (mean age 54.3 ± 12.2 years); 155 (90.1%) had surgical management. Sexual dysfunction rates were similar for those who had surgery and those who did not (40% vs 50%). Hysterectomy was performed for 80% (n = 123) of the surgical cases; 67% (n = 82) had total abdominal hysterectomy (TAH) and 33% (n = 41) had minimally invasive surgery (MIS) via robotic-assisted laparoscopic hysterectomy or total laparoscopic hysterectomy. Women with TAH reported greater sexual dysfunction compared with those with MIS (50% vs 22%; OR 3.6, 95% CI 1.5–8.4), were more likely to be younger than 50 years (36.6% vs 14.6%; OR 3.4, 95% CI 1.3–8.9), have longer operating times (270 ±108 minutes vs 230 ± 49 minutes; *P* = .024), and have more lymph nodes removed (15.9 ± 6.2 vs 12.2 ± 9.8; *P* = .05). Body mass index and lymphadenectomy were not found to be associated. In logistic regression, both TAH and age less than 50 years were independent predictors of sexual dysfunction.

Conclusions: Women undergoing TAH and those younger than 50 years of age are more likely to experience sexual dysfunction after surgical treatment for gynecologic cancer. Providers should discuss these possible effects of treatment with their patients and provide resources for coping.

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The efficacy of mTORC1/2 inhibition on ovarian cancer stem cells

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Objectives: Ovarian cancer is the most lethal gynecologic malignancy. Following the initial response to platinum drugs, most patients experience recurrence of resistant disease, necessitating development of durable new treatments. Resistance to treatment is centered on cancer stem (initiating) cells (CSCs) and the AKT pathway. AKT regulates mTOR complex (mTORC1/2), downstream mRNA translation, cell proliferation, survival, and angiogenesis in tumorigenesis. Rapalogs are clinically approved inhibitors of mTORC1 but have no effect on mTORC2. We investigate a clinical experimental dual mTORC1/2 inhibitor on platinum-resistant ovarian CSCs.

Methods: Platinum-resistant ovarian OVCAR3 cells were treated with vehicle, carboplatin, or INK128/MLN128, (mTORC1/2 inhibitor). CSCs were identified with flow cytometry or isolated using fluorescence-activated cell sorting using CD133+/CD44+. The CSC population was quantified using non-adherent spheroid growth assays. Cell viability was determined by colony formation assays with spheroids for carboplatin re-sensitization by mTORC1 or mTORC1/2 inhibition. Doxycycline-

inducible shRNA silencing cell lines were generated from OVCAR3 cells to inhibit Raptor (mTORC1) or Rictor proteins (mTORC2).

Results: CSCs comprise 4.9% of untreated OVCAR3 cells, confirmed by stem cell markers Oct4 and Sox2, and AKT/mTORC1 activation by phosphorylated-4E-BP1. Surprisingly, INK128 treatment increased the platinum-resistant CSC population by 2-fold (Figure 1, $P < .005$), whereas carboplatin alone had no effect. INK128-treated cells formed fewer colonies compared with vehicle controls (mean colony number 36.3 + 23.8 vs 83.3 + 32.1, $P < .001$) and smaller colonies (mean cell number 5,260 + 835.8 vs 6,907 + 702.4, $P < .0002$). NS- and Raptor-silenced cells were unchanged in all assays, whereas Rictor silencing reduced CSCs by half (Figure 2, $P < .002$) and formed fewer colonies by approximately 5-fold ($P < .03$).

Conclusions: The PI3K/AKT/mTOR pathway promotes platinum resistance in ovarian cancer cells, and supports the CSC population, but can be overcome by pharmacologic inhibition of mTORC1/2. Drugging mTORC1/2 does not selectively inhibit CD133+/CD44+ ovarian CSCs, but appears to target non-CSCs and "stem-like" cells based on functional data. Targeting mTORC1/2 sensitizes the resistant CSC population and should be clinically explored.

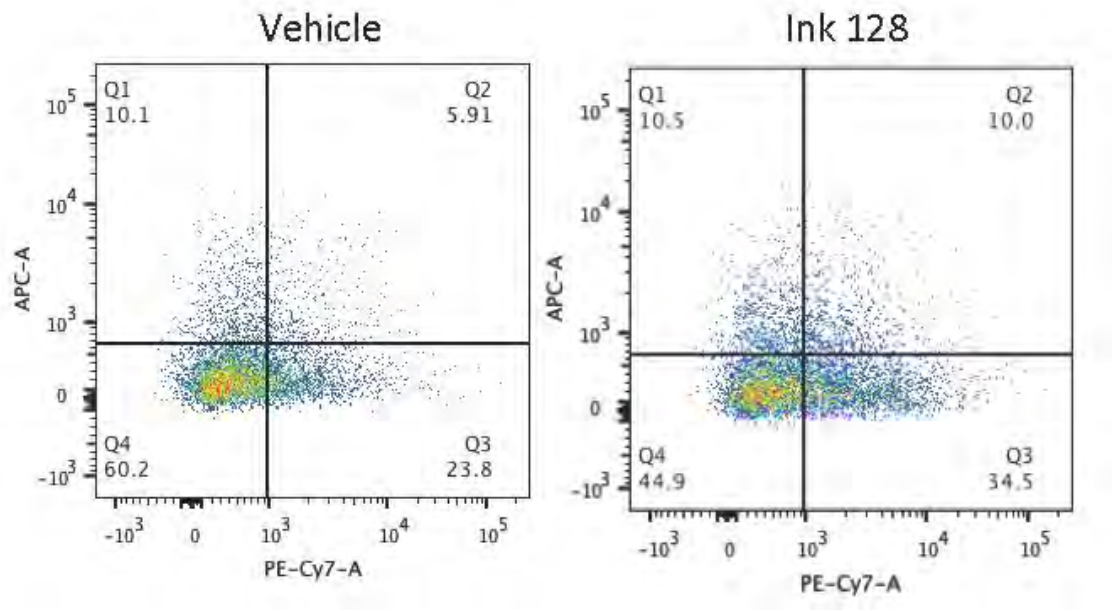

Fig. 1
CSCs Population after Treatment of OVCAR Cells with Ink128.

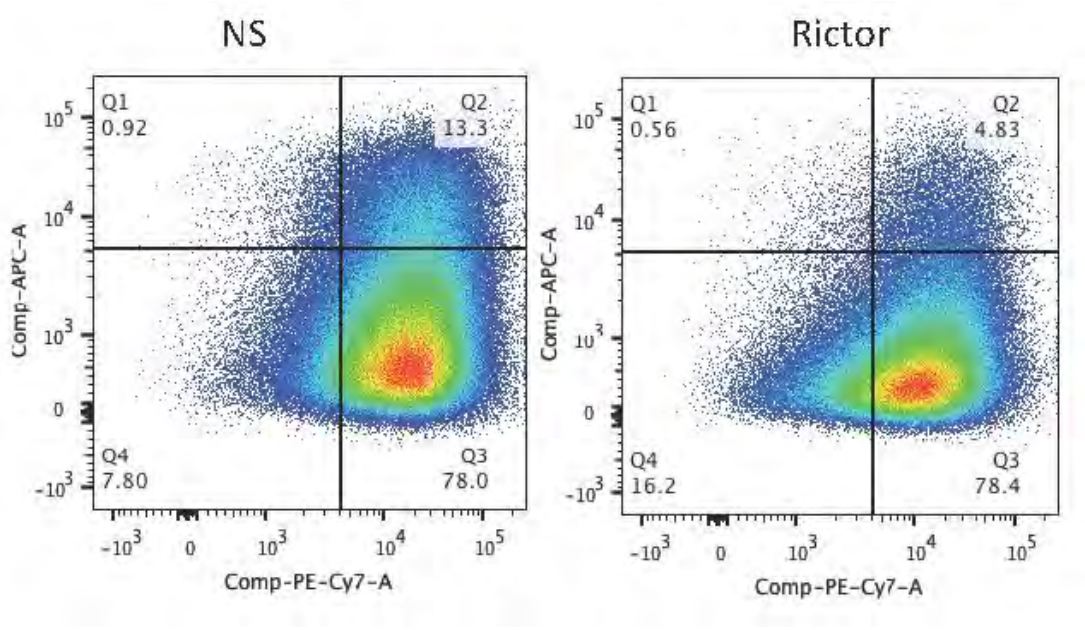

Fig. 2
Identification of CSCs in Non-silenced vs. Rictor-silenced cells.

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Risk of 30-day readmissions after robotic surgical management for endometrial cancer: A multicenter retrospective chart review

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Objectives: Since its widespread release, robotic surgery has become increasingly prevalent in endometrial cancer staging procedures. We sought to determine the risk factors and readmission rate 30 days after robotic surgery for endometrial cancer.

Methods: Patients with endometrial cancer who underwent a robotic surgical staging by gynecologic oncology at 2 large academic institutions between January 2010 and April 2015 were identified. Demographic information, intraoperative and postoperative data, and reasons for readmission were collected. The Student *t* and Fisher's exact tests were used to compare patients readmitted within 30 days with those who were not readmitted.

Results: A total of 212 patients were identified. Average body mass index (BMI) for this population was 35 (range, 19–63). Medical comorbidities identified in this cohort included endocrine, cardiac and hematologic issue, smoking status, and the prevalence of other cancer diagnoses. Fourteen patients (6.6%) were readmitted within 30 days of discharge, usually for ileus/small bowel obstruction (n = 3) or fever/infection (n = 6). The median BMI for readmitted patients was 42 (range, 32–48), compared with 34.5 (range, 19–63) for those were not readmitted (*P* = .026). Thirteen readmitted patients had an endocrine disorder, which was significantly higher (*P* = .004). We did not identify an association with cardiac conditions (*P* = .26), hematologic abnormalities (*P* = 1.0), other cancer diagnoses (*P* = .57), or smoking status (*P* = 1.0).

Conclusions: Robotic surgical management for endometrial cancer was associated with a 6.6% 30-day readmission rate. Higher rates of readmission were seen in women who were morbidly obese and those with endocrine disorders. Preoperative informed consent should acknowledge this risk.

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Multiplatform tumor-profiling of 43 malignant Sertoli-Leydig cell tumors of the ovary reveals therapeutic opportunities

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Objectives: Sertoli-Leydig cell tumors (SLCTs) of the ovary are a rare subtype of sex cord–stromal tumor accounting for less than 0.5% of ovarian malignancies. Their management largely relies on surgery followed by adjuvant chemotherapy for high-grade and advanced-stage tumors; however, the drugs of choice for treatment of initial and recurrent disease remain unknown. We aim to systematically evaluate biomarkers from a relatively large cohort of SLCTs to explore therapeutic opportunities for this rare subtype of ovarian tumor.

Methods: SLCTs profiled between 2009 and 2015 with multiple platforms including immunohistochemistry and sequencing were included.

Results: We identified 43 SLCTs: 14 from the ovary and 29 from metastatic sites. The average age of patients was 34.5 years. Hormone receptors ER, PR, and AR were overexpressed in 26%, 49%, and 35% of tumors, respectively, suggesting the potential use of hormonal therapies. Overexpression of EGFR, TOPO2A, TOPO1, TLE3, and cMET were seen in 88%, 67%, 34%, and 3% of tumors, suggesting possible benefit from EGFR-targeted agents, anthracyclines, topotecan, taxanes and cMET-targeted therapies, respectively. Low expression of ERCC1, MGMT, RRM1, PTEN, and TS was seen in 85%, 65%, 64%, 37%, and 29% tumors, suggesting benefit from platinums, temozolomide, gemcitabine, mTOR inhibitors, and fluoropyrimidines, respectively. High Pgp was seen in 11%, showing potential resistance to agents including etoposide. Tumor expression of PD-L1 was not seen (0 of 10); PD-1 expression on tumor-infiltrating lymphocyte was seen in 1 of 10 tumors evaluated. NextGen sequencing of 16 tumors showed one mutation in KRAS (G12C), AKT1 (E17K), TP53 (C277F) and BRCA2 (S3366frameshift), respectively, revealing opportunities for targeted therapies. Variants of unknown significance were seen on STK11, MPL, MLH1, JAK3 and GNA11 in one case each. In addition, Sanger sequencing on KRAS and BRAF on 8 tumors revealed a KRAS Q61H and BRAF G466V (exon 11) mutation.

Conclusions: Molecular profiling of 43 rare SLCTs suggested therapeutic opportunities including commonly used agents such as platinums/taxane, as well as additional cytotoxic, targeted, and biological agents that would not be otherwise considered.

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Unraveling the etiology of ovarian cancer racial disparity in the Deep South: Is it nature or nurture?

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Objectives: Multiple etiologies have been proposed as contributing to cancer racial healthcare disparities, such as differences in clinical features, treatment, environment, and tumor biology. Our objectives were to evaluate a possible racial healthcare disparity in black patients in the Deep South with ovarian cancer.

Methods: A retrospective study of ovarian cancer patients from 2007 to 2014 was performed. Medical records were used to abstract demographic, treatment, and survival data. Socioeconomic status (SES) was obtained using US Census block data and compared using Yost Index scores. Comparisons were made between the 2 groups of black and white patients using standard statistical approaches.

Results: A total of 393 patients were evaluated, 325 (83%) white and 68 (17%) black. Groups were similar in age, performance status, stage, grade, and histology. Surgical approaches were similar between groups (primary debulking vs interval debulking surgery; $P = .09$). However, compared with whites, black patients had lower optimal debulking rates (89% vs 71%, respectively; $P = 0.001$) with lower IP chemo accordingly (19% vs 10%, $P = .01$). Compared with whites, black patients demonstrated lower SES of percentage with college degree (31% vs 25%, $P = .02$); mean household income ($49,047 vs $33852, $P < .001$); and percentage under 200% poverty level (6% vs 12%, $P < .001$). These factors and others contributed to the lower global Yost Score SES of 1 (17% vs 41%, $P < .001$). When controlling for these factors using the Cox regression analysis, a survival disadvantage was seen in black patients for both progression-free survival (16 vs 27 months, $P = .003$) and

overall survival (42 vs 88 months, *P* < .001). Platinum resistance (progression-free survival <6 months) was more common in black patients (35%) compared with whites (14%), with an odds ratio for black patients of 2.7, (95% CI 1.5–4.4, *P* < .001).

Conclusions: Despite controlling for differences in clinical features, treatment, and environmental factors, a survival disadvantage was still observed in black patients with ovarian cancer. Based on these data, tumor biology plays a role in ovarian cancer racial disparity, and continued research is needed for determining the cause of this racial disparity.

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Prognostic value of loss of MMR protein expression in endometrial carcinoma in African American and White women

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Objectives: The effect of MMR loss on the prognosis of endometrial cancer (EC) is controversial. Correlations between MMR-related protein expression and clinicopathologic factors of EC in African American (AA) versus white women were analyzed.

Methods: A retrospective review of EC (n = 578) between 1995 and 2013 was conducted to analyze clinicopathologic parameters (Table 1). Immunohistochemical evaluation of MMR protein expression (MLH1, PMS2, MSH2, and MSH6) was performed on tumor tissue microarray. Absence of nuclear staining of any of the 4 proteins in tumor cells with positive lymphocytes (internal control) was considered as MMR loss. Data were analyzed using the Fisher's exact test and Kaplan-Meier survival analysis.

Results: MMR loss was identified in 116/578 patients (20%) with the highest frequency of loss in both MLH1 and PMS2 (47%), PMS2 (30%), MSH6 (14%), and both MSH2 and MSH6 (9%). White women with MMR loss had significantly higher-grade cancer and shorter disease-free interval (187 vs 594 months). AA women with MMR loss had endometrioid histology (*P* = .001), higher grade (*P* = .042), tumor size of 2 cm or greater (*P* = .019), and tendency toward myometrial invasion compared with AA women with intact MMR. Disease-free interval was similar for AA and white women with MMR loss (190 vs 187 months).

Conclusions: Although EC is reported to have worse prognosis in AA than white women, our study showed no difference between AA women and white women who had MMR loss.

Table 1

	AA MMR Loss (n=46)*	**AA Intact MMR (n=194)***	***P* value**	**EA MMR Loss (n=70)***	**EA Intact MMR (n=268)***	***P* value**
Age: <50 years	6 (13.0%)	23 (11.9%)	0.804	8 (11.4%)	46 (17.2%)	0.163
≥50 years	40 (87.0%)	171 (88.1%)		62 (88.6%)	222 (82.8%)	
Histology: Endometrioid	41 (89.1%)	109 (56.2%)	**0.001**	56 (80.0%)	225 (84.0%)	0.267
Nonendometrioid	5 (10.9%)	85 (43.8%)		14 (20.0%)	43 (16.0%)	
Histology:Type 1	41 (89.1%)	109 (56.2%)	**0.001**	58 (82.9%)	228 (85.1%)	0.384
Type 2	5 (10.9%)	85 (43.8%)		12 (17.1%)	40 (14.9%)	
FIGO Stage: I-II	34 (73.9%)	141 (73.1%)	0.534	53 (76.8%)	216 (81.8%)	0.219
III-IV	12 (26.1%)	52 (26.9%)		16 (23.2%)	48 (18.2%)	
FIGO grade : Grade 1	7 (16.7%)	44 (27.7%)	**0.042**	11 (16.9%)	94 (37.8%)	**0.007**
	20 (47.6%)	44 (27.7%)		35 (53.8%)	102 (41.0%)	
	15 (35.7%)	71 (44.7%)		19 (29.2%)	53 (21.3%)	

Grade 2 Grade 3						
Tumor size: <2cm ≥2cm	14 (36.8%) 24 (63.2%)	103 (58.9%) 72 (41.1%)	**0.019**	12 (19.4%) 50 (80.6%)	61 (27.5%) 161 (72.5%)	0.128
MI Inner 1/2 Outer 1/2	26 (60.5%) 17 (39.5%)	138 (72.3%) 53 (27.7%)	0.300	48 (68.6%) 22 (31.4%)	178 (70.6%) 74 (29.4%)	0.422
DFI (months)*	190	170	0.327	187	594	0.230

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270 - Poster

HPV vaccination rates and attitudes: A cross-sectional survey of college men and women

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Objectives: Human papillomavirus (HPV) vaccination rates remain low, especially among young adults. The objective of the study was to measure the rate of HPV vaccination among college men and women, and to assess attitudes toward HPV vaccination and their association with vaccination status and intent.

Methods: A random sample of 3,000 college men (18–21 years) and women (18–26 years) were asked to complete an online survey including questions about HPV vaccination status and intention and the modified Carolina HPV Immunization Attitudes Scale (CHIAS).

Results: Overall, 67.6% of students had received at least 1 HPV vaccination; this proportion was higher for women (74.7%) than for men (51.0%). Male and female attitudes toward vaccination were not significantly different for 14 of 17 CHIAS items. Barriers score was the factor most strongly associated with vaccination intent "today" and also strongly associated with vaccination intent for "the next 6 months." In contrast to the other factors, higher Barriers scores were actually associated with greater vaccination intent both "today" and "in the next 6 months."

Conclusions: The rate of HPV vaccination among college students was higher than expected, with rates double the national average for 18- to 26-year-old women (74.7% vs 34.5%) and 20 times higher than the national average for 18- to 21-year-old men (51.0% vs 2.4%). Men and women report similar attitudes to HPV vaccination. Even among a college population, barriers remain a significant factor in non-vaccination. Decreasing cost and access barriers is essential to improving HPV vaccination rates among young adults. Additional studies are needed to validate CHIAS among male populations.

Table 1

CHIAS Barrier Factor Items.

It would be hard to find a provider or clinic that would be easy to get to for getting vaccinated against HPV.
It would be hard to find a provider or clinic where I could afford the HPV vaccine.
It would be hard to find a provider or clinic that has the HPV vaccine available.
I am concerned that the HPV vaccine costs more than I can pay.
It would be hard to find a provider or clinic where I don't have to wait a long time to get an appointment to be vaccinated.

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271 - Poster
Identification of molecular targets in vulvar cancers
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Objectives: Vulvar cancer may comprise only 5% of gynecologic malignancies but its incidence has been increasing. Given its rarity, there is a paucity of data surrounding treatment guidelines and targets for new therapies. We retrospectively examined a database of molecularly profiled patients for insight into the molecular alterations that contribute to vulvar pathogenesis with the hopes of identifying molecular targets for this rare disease.

Methods: A total of 143 vulvar cancer patients were included in the study and tested at a central laboratory (Caris Life Sciences, Phoenix, AZ). Tests included 1 or more of the following: gene sequencing (Sanger or next-generation sequencing [NGS]), protein expression (immunohistochemistry [IHC]), and gene amplification (chromogenic/fluorescence in situ hybridization [ISH]). The 2-tailed Fisher's exact test was performed to test where proportions of positive results were different by subgroup ($P \leq .05$).

Results: The study cohort had a median age of 65 years, consisted of 84% (120/143) squamous (SCC) and 16% (23/143) adenocarcinoma (ADC) histologies, and 46% of patients had metastatic disease (stage IV). Targeted hot-spot sequencing identified variants in the following genes, in descending order of frequency: *TP53* (34%), *PIK3CA*/*BRCA2* (8% each), *HRAS*/*FBXW7* (5%-6% each) and *ERBB4*/*GNAS* (3% each). Mutations in *AKT1*, *ATM*, *FGFR2*, *KRAS*, *NRAS*, and *BRAF* also occurred (n = 1 each). Specific protein changes for targetable genes included clinically pathogenic mutations commonly found in other cancer types (e.g., *PIK3CA*: exon 9 [E545K]; *RAS*: G13D, Q61L; *BRCA2*: S1667X; *BRAF*: R443T; and *FBXW7*: E471fs). Additional drug targets are identifiable using IHC and ISH methodologies, including cMET (32% IHC, 2% ISH), PDL1 (16%), PTEN loss (45%), HER2 (6% IHC, 2% ISH), and hormone receptors (AR, 6%; ER, 11%; PR, 4%). Comparisons between SCC and ADC identified differential rates for AR, ER, HER2, and GNAS, with an increased presence in ADC ($P < .05$ for all).

Conclusions: Molecularly guided precision medicine could provide alternative, targeted treatment options for vulvar cancer patients especially because of the easy accessibility for repetitive biopsy.

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272 - Poster
Is intraperitoneal chemotherapy as effective within the elderly population for the treatment of epithelial ovarian cancer?
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Objectives: Intraperitoneal (IP) chemotherapy for the treatment of epithelial ovarian cancer (EOC) has been shown to provide a substantial advantage in overall survival, and is now considered the standard of care. As the US population ages, evaluating these treatments, specifically for patients with this condition, is of utmost importance. This study aims to compare the toxicity and benefits of IP chemotherapy in patients of ages 70 years and older with those younger than 70 years.

Methods: We performed a single institution retrospective review of patients diagnosed with stage IIA-IIIC EOC from 2000 to 2013 who received IP chemotherapy. Clinicopathologic characteristics were extracted, and survival was calculated. SAS version 9.3 was used for descriptive statistics and multivariate analyses.

Results: A total of 133 patients were included, with 100 patients being younger than 70 years and 33 patients aged 70 years or older. Race, stage, histology, and performance status were similar. Residual disease did not differ ($P = .23$). All patients received a platinum/taxane doublet for frontline chemotherapy. Clinical trial enrollment was similar (89% vs 90%, $P = 1.00$) despite age. In trial-enrolled patients, older patients received statistically fewer cycles of therapy (6.4 vs 5.8, $P = .002$) but had similar dose delays (0.9 vs 0.3, $P = .17$) and dose modifications (1.00 vs 0.93, $P = .91$). Median progression-free survival (27 vs 31 months) and overall survival (71 and 62 months) were not statistically different. Grade 4 heme toxicities ($P = 1.0$), and grade 3 and higher non-heme toxicities (6.1% vs 6.7%, $P = 1.0$) were similar between groups. Although not statistically significant, neuropathy grade higher than 2 trended higher in the older group (100 vs 86%; $P = .18$). Upon multivariate analysis for overall survival, age less than 70 years (HR 0.697, 95% CI 0.36–1.26, $P = .23$) was not predictive, but stage (IIIC vs

lower: HR 3.95, 95% CI 1.55–10.10, *P* = .004) and residual disease (HR 2.67, 95% CI 1.29–5.52, *P* = .008) were significant factors.

Conclusions: Older EOC patients completed fewer cycles of IP/intravenous chemotherapy without any significant increase in toxicity, dose delays or dose modifications, and comparable survival to younger patients. The numeric increase in neuropathy higher than grade 2 is a point of concern, especially in a more vulnerable population. The population of older patients receiving IP chemotherapy in this study were on clinical trial and likely to be healthier than the general elderly population. IP chemotherapy appears well tolerated and effective among older patients and is likely underutilized outside clinical trials.

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273 - Poster

The evolution of estrogen receptor signaling in the progression of endometriosis to endometriosis-associated ovarian cancer

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Objectives: To investigate estrogen receptor (ER) signaling as a potential mechanism of malignant transformation of endometriosis into endometriosis-associated ovarian cancer (EAOC).

Methods: Tissue samples of normal endometrium (n = 23), and benign (n = 19), atypical (n = 11), and concurrent (n = 9) endometrioisis and endometriosis-associated cancers (n = 20) were collected. To evaluate ER signaling, a 236-gene signature of estrogen-regulated genes (the "E2sig") was developed. RNA was isolated from each tissue specimen and expression of the E2sig was measured on the NanoString nCounter platform. Analysis of variance (ANOVA) and unsupervised clustering were used to identify differentially regulated genes and distinct gene expression profiles across samples. These profiles were compared with gene expression datasets of estrogen regulation using Gene Expression Omnibus (GEO). Gene Set Enrichment Analysis (GSEA) against the Molecular Signatures Database was performed to assess whether the pattern of gene expression was consistent with ER activity.

Results: ANOVA revealed 158 differentially expressed genes ($q < 0.05$) and unsupervised clustering of this subset identified 4 distinct gene clusters. Cluster 1 includes genes with increasing expression from benign endometriosis to EAOC and best represents genes involved in malignant transformation. The most notable genes in this cluster are FGF18 and ESR2 (ER □). Clusters 2 and 3 include genes that are highly expressed and underexpressed in EAOC compared with endometriosis, respectively. Cluster 4 includes genes with an incremental decrease in expression from benign endometriosis to EAOC and includes ESR1 (ER □) and several downstream ER targets (e.g., PGR, GREB1). Compared with datasets of classic ER signaling profiles identified in GEO, profiles of EAOC differed significantly. Likewise, GSEA analysis did not identify any ER-related signatures activated in EAOC and among those ownregulated genes, GSEA identified signatures consistent with endocrine resistance and loss of ER function.

Conclusions: Gene expression data suggest classic ER signaling decreases in the progression of endometriosis to EAOC. The gene expression pattern in EAOC is more consistent with profiles of endocrine resistance. FGF18 and ESR2 may play an important role in malignant transformation.

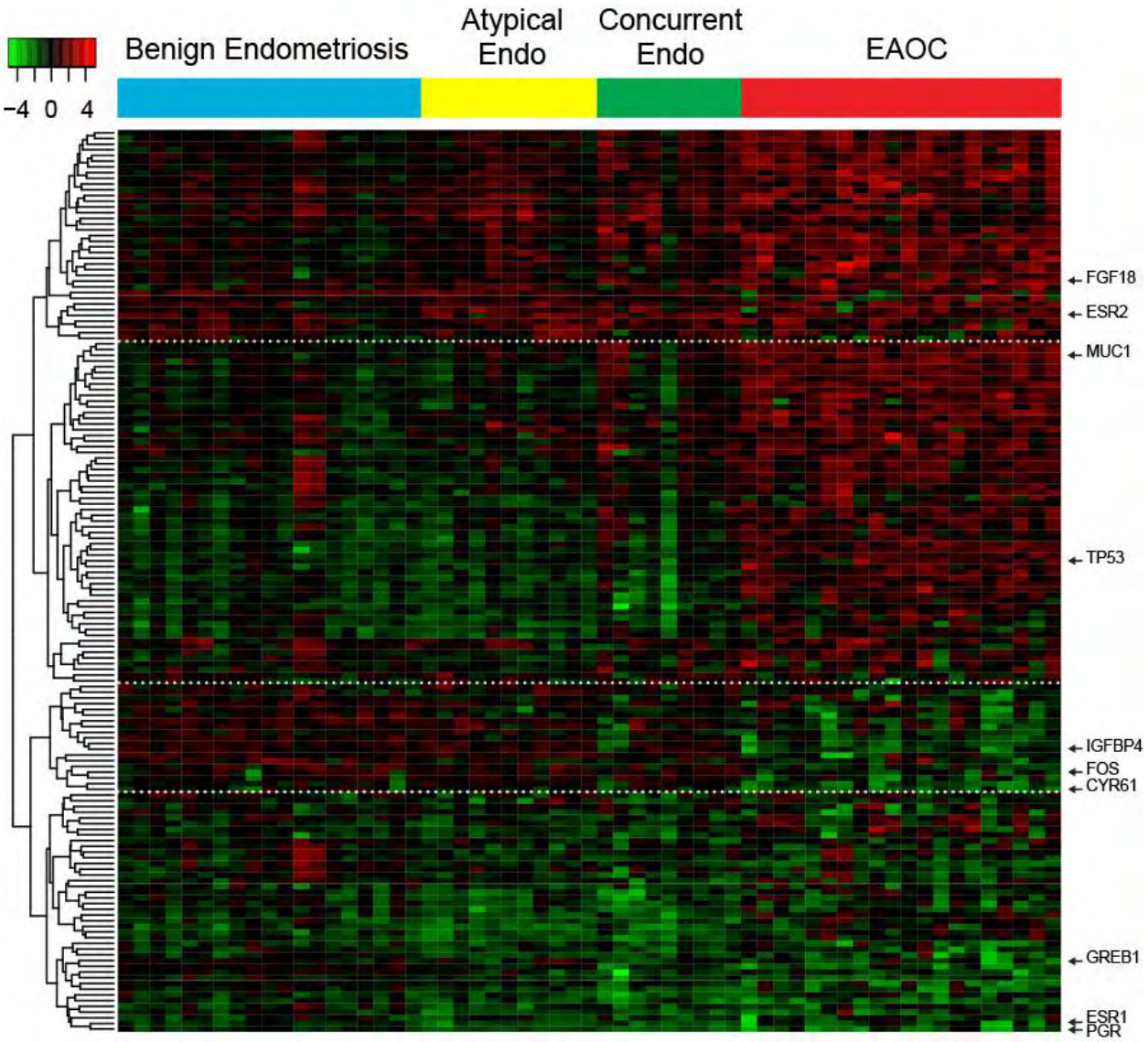

Fig. 1

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274 - Poster

Cost-effectiveness of perioperative thromboprophylaxis in women undergoing laparoscopic surgery for a gynecologic malignancy

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Objectives: To evaluate the costs associated with perioperative thromboprophylaxis with sequential compression devices (SCD) alone or in combination with single-dose low-molecular-weight heparin (LMWH) versus no prophylaxis in women undergoing laparoscopic surgery for a gynecologic malignancy.

Methods: A decision-tree model was constructed to evaluate the cost of perioperative prophylaxis with SCD +/- LMWH versus no prophylaxis in women undergoing laparoscopic surgery for a gynecologic malignancy. Transition probabilities were estimated from the current published peer-reviewed literature. Quality adjusted–life years (QALY), number of venous thromboembolic events (VTE) averted, number of pulmonary embolisms (PE) averted, and costs were modeled over a horizon

of 12 months. Assuming a US public payer perspective, incremental cost-effectiveness ratios (ICER) were evaluated as the incremental cost per QALY gained as well as the incremental cost per VTE and PE averted per life-year. To evaluate the robustness of our results, we performed a probabilistic sensitivity analyses.

Results: The ICER associated with SCD alone compared with no prophylaxis were $84,550 per QALY gained, $2,827 per VTE averted, and $19,553 per PE averted. Meanwhile, combination therapy (SCD + LMWH) cost $1,134,579 less than no prophylaxis and resulted in 7 additional QALY, as well as 100 VTE averted and 14 less PE. Varying transition probabilities, costs, and utilities across the expected distribution of each parameter resulted in 56% and 53% of ICER estimates for SCD alone and SCD + LMWH, respectively, falling below the commonly accepted willingness to pay (WTP) threshold of $50,000/QALY gained. Compared with no prophylaxis, SCD and SCD + LMWH were associated with cost savings and higher number of VTEs averted in 26% and 55% of ICER estimates, respectively. Furthermore, SCD and SCD + LMWH were also associated with cost savings and higher number of PE averted in 26% and 57% of ICER estimates, respectively.

Conclusions: Combination perioperative prophylaxis with SCD + LMWH is associated with cost savings and appears to be the most dominant economic strategy to prevent VTE. Therefore, it should be considered in women undergoing laparoscopic surgery for gynecologic malignancies.

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275 - Poster

Evaluating racial molecular complexity in gynecologic cancers

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Objectives: Understanding the molecular pathways that drive gynecologic cancer cells is common. However, using this knowledge for targeting actionable mutations incorporates molecular and population sciences. We aim to evaluate the complexity that race could play in this role.

Methods: Pretreatment tumor samples from surgery or image-guided core biopsies were obtained and sent to a third party commercial molecular profiling company. A total of 148 biomarkers were tested using various methods of immunohistochemistry, chromogenic or fluorescent in situ hybridization, reverse transcriptase–polymerase chain reaction, Illumina microarray, or next generation sequencing. “Positive” results demonstrate mutations, overexpression, or positivity of methods used for actionable biomarkers. Patients were grouped by self-designated race and molecular profiling results were compared using appropriate statistics with odds ratio (95% CI) to determine correlation to race.

Results: Molecular profiling was performed on 175 patients from 2012 to 2015. Racial breakdown was as follows: 141 (79%) patients were white and 34 (24%) were black. The majority of samples were ovarian cancer (n = 127, 71%) and advanced stage III/IV disease (n = 139, 78%). A total of 1,979 positive results were found in the entire cohort, with 1,497 in whites and 436 in black patients. Compared with white patients, blacks demonstrated increased number of positive results per patient (10.6 vs12.8, $P = .04$). Biomarkers that demonstrated positive results in frequencies greater than a third of the patients were higher in black patients (12 biomarkers, 8.2%) compared with whites (7 biomarkers, 4.7%) ($P = .03$). Odds ratios for biomarkers more commonly found in black patients were significant for HSP90AA1 (OR 0.067, 95% CI 0.007–0.54, $P = .028$), IGFBP (OR 4 0, 95% CI 0–0.49, $P = .04$), PD-1 (OR 0.218, 95% CI 0.05–0.93, $P = .04$), and PD-L1 (OR 0.12, 95% CI 0.03–0.5, $P = .005$).

Conclusions: Molecular profiling demonstrated that black patients had higher levels of complexity with greater number of positive results per patient and more biomarkers with high-frequency positive results. These data demonstrate the need for further molecular and population studies to tease out the effects of race and ethnicity on the malignant properties of gynecologic cancer cells.

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276 - Poster

Development and validation of chemoradio-prediction model using reverse-phase protein arrays in locally advanced cervical cancer

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Objectives: The efficacy of radiation largely depends on the radiosensitivity of the tumor. In recent years, we have learned a great deal about the effects of apoptosis, cyclo-oxygenases, angiogenesis, hypoxia, and temperature on radiation, making it possible to manipulate the radiation response of cervical cancer to achieve a better treatment outcome. However, a multipanel prediction model has not been developed yet.

Methods: To develop a prediction model, 22 proteins were selected for markers: (1) hypoxia-regulating pathways (CAIX, HIF1a, VEGF), nucleotide repair (ERCC1), EGFR pathway (EGFR, HER2, pHER2, HER3, pHER3, HER4), apoptotic proteins (BCL2, p53, pNFkB, surviving), angiogenesis (CD31), proliferation (Cox2, PCNA), and cell adhesion/collagenase (CD44, CD133, MMP9, E-cadherin, N-cadherin). The protein expression was measured using a reverse-phase protein array method. Two hundred locally advanced cervical cancers were grouped into training and independent validation sets. Their classification performance was estimated on the training set by using 2 different resampling methods and compared with the accuracy observed in the independent validation set. The study was approved by the local research ethics committee.

Results: With a median follow-up of 7 years, 60 of 200 patients experienced a recurrence. On the training set, 15 of 22 proteins were associated with survival. Survival prediction model (random survival forest) using the 15 proteins showed higher prediction than using clinical variables (concordance index of 0.77 vs 0.67, $P = .017$). RT resistance prediction model development and validation in another set will be presented.

Conclusions: Radio-prediction model using reverse-phase protein assays is a valuable method for prognostication in cervical cancer.

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277 - Poster

High-grade serous ovarian cancer primary tumor *BRCA1* mRNA expression is a candidate biomarker for patient selection for intraperitoneal chemotherapy

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Objectives: Among patients from Gynecologic Oncology Group 172 whose primary tumor had low BRCA1 staining (<10%) on immunohistochemistry, intraperitoneal (IP) chemotherapy use was associated with an improvement in the median 36-month overall survival (OS) compared with intravenous (IV)-only chemotherapy. To test this finding using another patient cohort that received IP chemotherapy, we tested associations of BRCA1 and BRCA2 tumor mRNA expression with survival outcomes using high-grade serous ovarian cancer (HGS OvCa) data from The Cancer Genome Atlas (TCGA).

Methods: Data from HGS OvCa patients treated with IP (n = 90) or IV-only (n = 398) adjuvant chemotherapy were downloaded from TCGA. Progression-free survival (PFS) and OS were compared between the IP and IV chemotherapy groups using permutation testing (10,000 permutations) stratified by BRCA1 or BRCA2 tumor mRNA expression level. Multivariate Cox proportional hazards regression also tested associations of BRCA1 or BRCA2 tumor mRNA expression levels as continuous variables with PFS and OS.

Results: BRCA1 and BRCA2 tumor mRNA expression was not significantly ($P > .05$ for all) associated as an independent predictor on multivariate regression with OS or PFS among patients treated with IP chemotherapy. Each 1 standard deviation increase in primary tumor BRCA2 expression was significantly associated with decreased OS among patients treated with IV-only chemotherapy (HR 1.23, 95% CI 1.06–1.43, $P = .006$). Patients whose tumors had lower (<20th percentile) BRCA1 expression did not show OS improvement from IP versus IV chemotherapy (mean, 40.3 vs 38.8 months, $P = .660$). Patients whose tumors had higher (>20th percentile) BRCA1 expression experienced mean 13.5-month increased PFS ($P < .0001$) and

16.3-month increased OS ($P < .0001$). Patients experienced significantly increased PFS and OS from IP chemotherapy without regard to BRCA2 expression stratification.

Conclusions: The 20th percentile of HGS OvCa patients in the TCGA with the lowest primary tumor BRCA1 mRNA expression did not experience increased OS after IP chemotherapy compared with those who received IV-only adjuvant chemotherapy. Primary tumor BRCA1 expression is a candidate biomarker for patient selection for IP chemotherapy.

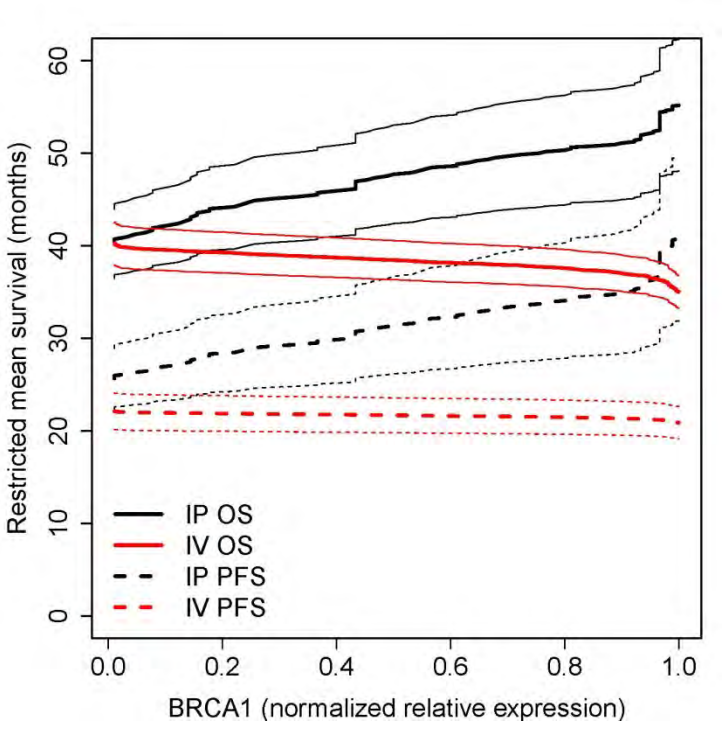

Fig. 1
Restricted mean survival as function of BRCA1 mRNA expression.

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278 - Poster
Histopathology discrepancy of preoperative endometrial sampling and final specimen: How does this influence selective lymph node dissection?
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Objectives: Preoperative histology is a major component in the perioperative selective lymph node (LN) dissection decision process. Discrepancy between preoperative endometrial sampling and final specimen histopathology is generally accepted. The goals of this project are to determine if discrepancy of histopathology is associated with alteration of adjuvant treatment or outcome.

Methods: We performed a retrospective cross-sectional analysis of all patients undergoing surgery for endometrial cancer at a single institution from 2010 to 2014. All patients underwent preoperative endometrial sampling. Histopathology discrepancy was evaluated for potential in variation of perioperative LN dissection. Criteria for not performing LN dissection was defined as preoperative endometrioid histology, grade 1 or 2 lesion, myometrial invasion of 50% or less, and primary tumor diameter of 2 cm or less.

Results: A total of 352 patients were identified, of whom 64 (18.2%; 95% CI 14.5%–22.6%) were noted to have discrepancy in histopathology. In 17 (4.8%) of 352 patients (95% CI 2.9%–7.7%), preoperative sampling was reviewed as a grade 1 or 2

endometrioid lesion and final specimen was upgraded to grade 3. Two (0.6%) of 352 patients (95% CI 0.1%–2.3%) met perioperative criteria for not performing LN dissection and final histopathology would have indicated LN dissection. In both these patients, preoperative sampling was grade 2 endometrioid, final pathology was grade 3 mixed endometrioid/serous. One patient had stage IIIC1 disease and was lost to follow-up. The other had stage IIIC2 disease at initial surgery and received chemotherapy/radiation without evidence of recurrence 56 months after completion. In 3 (0.9%) of 352 patients (95% CI 0.2%–2.7%), preoperative sampling was reviewed as a grade 3 lesion and final specimen was downgraded to grade 1 or 2 disease. In all patients, the primary tumor diameter was greater than 2 cm and therefore underwent LN dissection. One patient with stage IA disease was lost to follow-up. Two patients with stage I disease received radiation therapy and have no evidence of recurrence at 5 and 10 months, respectively.

Conclusions: Despite an 18% discrepancy of histopathology, discrepancy that would alter a perioperative decision for LN dissection only occurs in 0.6% of cases in this retrospective single institutional experience. Myometrial invasion and tumor size may be more influential than histology in LN selection criteria.

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279 - Poster

Poor functional status and post–acute care needs after ovarian cancer debulking surgery

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Objectives: To assess the incidence of and risk factors for poor functional status and need for post–acute care services after debulking surgery in ovarian cancer patients with an emphasis on discharge to a skilled nursing facility (SNF).

Methods: Using the 2006 to 2012 National Surgical Quality Improvement Program Database, all patients who underwent primary surgical debulking with a postoperative diagnosis of ovarian cancer and had documentation of discharge location were identified. Patients were excluded if their functional status at baseline was dependent or partially dependent and if they died before discharge. Discharge destination was dichotomized as home versus SNF. Descriptive data included demographics, comorbidities, perioperative outcomes, and complications. Complex surgery included concurrent gastrointestinal or genitourinary procedures. Multivariable logistic regression was used to evaluate the association of clinical and surgical factors on discharge destination.

Results: A total of 1,864 patients underwent ovarian debulking surgery. Of these, 53% were of age 60 years or older and 46% had 1 or more comorbidities; 6.1% (n = 114) were discharged to SNF. Age (51% vs 82% ≥60 years), body mass index (median 26.6 vs 27.8), comorbidities (45% vs 71% with ≥1), complex surgery, (9% vs 18%), operative time (mean 169 vs 202 minutes), and complications (8% vs 32%) differed between non-SNF and SNF discharges ($P < .05$ for all). In multivariable logistic regression analyses, increased age, comorbidities, complex surgery, and increased complications were independently associated with discharge to SNF. Those aged 70 years or older had 6.4 times the risk as those aged less than 50 years (95% CI 2.64–15.71, $P < .001$). The presence of 1 or more comorbidities (OR 1.4), more complex surgery (OR 2.2), and complications (OR 2.2) increased the risk of discharge to SNF. The rate of readmission did not differ between the 2 groups.

Conclusions: Six percent of ovarian cancer patients were discharged to SNF after surgery. Independent risk factors for discharge to SNF include older age, comorbidities, increased surgical complexity, and postoperative complications. Efforts to optimize baseline functional status and minimize surgical complications may improve discharge rates to SNF and postoperative functional status. Cost containment efforts must carefully weigh interventions geared at altering post–acute care needs, readmission, length of stay, and complication management with overall cancer survival.

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280 - Poster

Colon cancer as a second primary cancer after endometrial cancer based on shared etiology

M.C. Lim. *National Cancer Center, Goyang-si, South Korea*

Objectives: To investigate the incidence and survival outcomes of colon cancer (CC) as a second primary cancer (SPC) after the diagnosis of endometrial cancer (EC)

Methods: Standardized incidence ratios (SIRs) and survival outcome of colon cancer as a second primary cancer (CCSPC) among women with EC were analyzed from the Korea Central Cancer Registry between 1993 and 2011.

Results: Of 14,797 women with EC, 147 (0.99%) women developed CCSPC during a mean follow-up period of 5.48 years. The overall SIR for CCSPC was 2.56 (95% CI 2.16–3.00). The most frequent sites of CCSPC were the ascending colon (3.77), followed by transverse colon (3.45), descending colon (2.06), and rectum (1.99). The SIR for CCSPC was more than 3 at ascending colon (4.37) and transverse colon (4.91) in the patients diagnosed with EC less than 5 years before the diagnosis of CC. The SIR for CCSPC was 5.19 at the ascending colon and 3.82 at the transverse colon in EC patients less than 60 years old. The 5-year and 10-year overall survival rates were 84.8% and 80.4% in women with EC only, 83.6% and 66.6% for women with any SPC, and 89.2% and 76.3% for women with CCSPC, respectively.

Conclusions: The incidence rates of CCSPC increase in women with EC compared with the general population, especially at the ascending colon. The 10-year overall survival rates were decreased in EC patients with CCSPC compared with EC patients without CCSPC.

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281 - Poster

Impact of interval from definitive surgery to initiation of adjuvant chemotherapy (ISC) on survival in advanced epithelial ovarian cancer

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Objectives: We investigate the prognostic impact of the interval from surgery to initiation of adjuvant chemotherapy (ISC) in advanced epithelial ovarian cancer.

Methods: We enrolled patients with advanced epithelial ovarian cancer (FIGO stage III and IV) who were treated at the Samsung Medical Center from January 1, 2001, to December 31, 2010. We excluded patients who received neoadjuvant chemotherapy.

Results: A total of 507 patients (stage III: 448; stage IV: 59) were enrolled, and the median ISC was 9 days with a range of 4 to 84 days. We divided the patients into 3 groups: (1) no gross residual group (n = 109, 21.5%), (2) optimal group (n = 206, 40.6%), and (3) suboptimal group (n = 192, 37.9%); delayed ISC is associated with increased HRs of overall survival only in the optimal group. Subsequent analyses were performed in the optimal group, and we found that ISC as a continuous variable (HR 1.016, 95% CI 1.005–1.031, $P = .007$), history of consultation to the department of general surgery (HR 2.744, 95% CI 1.345–5.599, $P = .006$), and platinum resistance (HR 7.175, 95% CI 4.112–12.52, $P = .007$) were significantly associated with poor overall survival. On multivariate analysis, ISC continued to be a significant poor prognostic factor (HR 1.018, 95% CI 1.003–1.033, $P = .022$).

Conclusions: Based on the data collected, delayed adjuvant chemotherapy subsequent to surgery most likely would result in a negative impact on overall survival in advanced epithelial ovarian cancer patients who had optimal cytoreduction.

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282 - Poster

Self-reported quality of life among patients who have undergone outpatient intraperitoneal chemotherapy for ovarian cancer

K. Gotimer, C. Bondoc, E. Chalas and J.A. Villella. *Winthrop University Hospital, Mineola, NY, USA*

Objectives: To assess the impact of outpatient intraperitoneal (IP) chemotherapy on quality of life (QOL).

Methods: Cross-sectional study of patients with optimally cytoreduced stage III and IV ovarian cancer who received IP chemotherapy between 2006 and 2011 at a single institution. A self-administered, anonymous survey based on a QOL instrument, the FACT-O, assessed 4 domains: physical health (PH), mental health (MH), social health (SH), and patients' subjective sense of worth (WO) of IP chemotherapy.

Results: Seventy-one participants were mailed surveys, of whom 52 (73.2%) returned the survey, 4 were excluded (incomplete), and 48 (67.6%) were included in the final sample. Mean age was 62.4 ± 10.3 years. Mean time from completion of chemotherapy was 30.8 months (range, 3–58 years). In the PH domain, 50.0% of patients reported that fatigue severely affected their QOL. Other aspects were pain (39.6%), gastrointestinal problems (37.5%), “chemotherapy brain” (29.2%), and alopecia (25%). In the MH domain, 25% of patients reported that therapy put significant stress on their life, 20.8% experienced anxiety, and 14.6% depression. In the SH domain, 27.5% reported that IP chemotherapy interfered with work. The majority (83.3%) reported that the effectiveness of IP chemotherapy was “worth” the side effects, 95.8% did not regret it, and 87.5% would recommend it to a friend. Eleven patients had recurrent disease at the time of survey completion, of whom 90% indicated IP chemotherapy was worthwhile and would recommend it to a friend, and none regretted the decision to receive this therapy.

Conclusions: IP chemotherapy has been shown to improve overall and progression-free survival and yet is not universally prescribed. It is known to have more side effects than intravenous chemotherapy. Further understanding of impact on QOL may help guide practice and patient counseling, thus improving adherence. The present study suggests that while these side effects affect QOL, patients feel that the therapy is worthwhile and do not regret treatment.

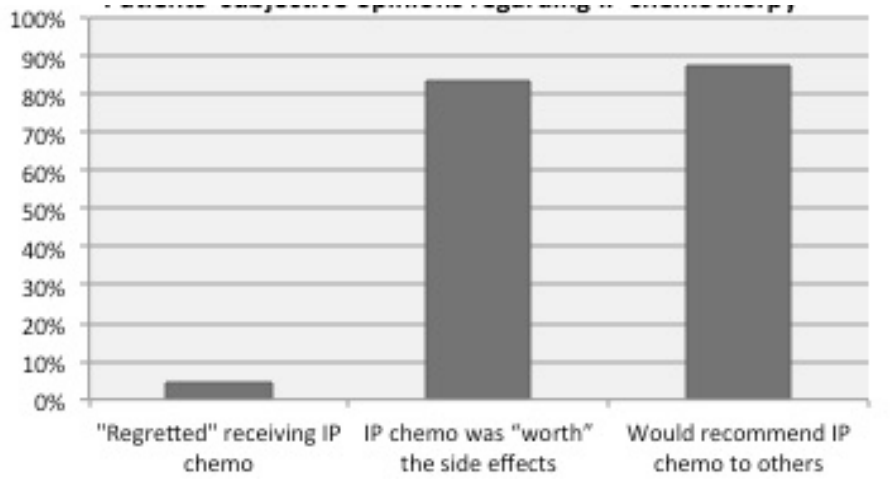

Fig. 1
Patients’ Subjective Opinions Regarding IP Chemotherapy.

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283 - Poster
The survival rate of abdominal radical trachelectomy versus abdominal radical hysterectomy for stage IB1 cervical cancer ≥2 cm
X. Wu, X. Li and J. Li. *Fudan University Shanghai Cancer Center, Shanghai, China*

Objectives: To compare the survival rates of abdominal radical trachelectomy (ART) with those of abdominal radical hysterectomy (ARH) for stage IB1 cervical cancer. Our objective was to know whether it was safe to perform ART for stage IB1 cervical cancers of 2 cm or larger.

Methods: Patients with stage IB1 cervical cancer who underwent ART and lymph node dissection between November 2006 and December 2014 had been compared to patients treated with ARH by the same surgeon at our institution in the same period. The control group consisted of patients with stage IB1 diseases who met the inclusion criteria of a fertility-sparing surgery.

Results: Of the 107 and 141 patients who underwent ART and ARH, respectively, 61 and 82 patients had a tumor of 2 cm or larger (*P* = NS). With a median follow-up of 30 and 49 months, 2 patients treated with ART and 3 patients treated with ARH had recurrences: the 5-year recurrence-free survival (RFS) rate was 97.8% and 97.0%, respectively (*P* = NS). Only 3 patients died in the ARH group. The 5-year overall survival (OS) was 100% for the ART group and 96.9% for the ARH group (*P* = NS). Considering tumors measuring 2 to 4 cm, the 5-year RFS and the 5-year OS were 96.5% and 100%, respectively, for the ART group, and 94.8% and 94.8% for the ARH group. The difference of 5-year RFS and 5-year OS between the 2 groups did not reach statistical significance.

Conclusions: ART appears to have equal or better survival rates to ARH and can be performed safely in stage IB1 cervical cancers 2 cm or larger in size.

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Appendectomy for mucinous ovarian tumors: Is it really necessary?

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Objectives: Recent literature suggests that the appendix is usually affected in cases of mucinous ovarian carcinomas and that primary appendiceal adenocarcinoma commonly spreads to the ovary. Therefore, the objective of our study is to investigate the frequency of appendiceal pathology in women undergoing surgery for mucinous ovarian tumors.

Methods: A retrospective analysis of medical records of patients who underwent appendectomy for a suspicious pelvic tumor which was finally diagnosed as mucinous adenocarcinoma, mucinous borderline rumor, or mucinous cystadenoma between 1994 and 2014.

Results: Ninety-six patients were included in the study. Of the 96 patients with mucinous ovarian tumors, 42 (43.8%) were benign, 35 (36.4%) had low malignancy potential, 16 (16.6%) were mucinous cystadenocarcinomas, and 3 (3.2%) patients were diagnosed as having metastatic appendiceal carcinoma involving the ovary. No evidence of metastasis to the appendix was found in the cases with ovarian borderline tumor. Of 96 appendectomies performed, only 1 (1%) metastatic mucinous appendiceal tumor of ovarian origin was discovered. At the time of surgery, in the cases of malignancies, no gross appendiceal abnormalities were identified.

Conclusions: Although only 3 ovarian tumors (3.2%) were metastatic from primary appendiceal adenocarcinoma, our view is that appendectomy during surgery for apparent early-stage mucinous ovarian cancer is warranted. Because there was no infiltration of the appendix in the case of mucinous ovarian borderline tumors, we believe that appendectomy could have been omitted during surgical staging. Also, our data suggest that the macroscopic appearance of the appendix during surgery does not always indicate the underlying pathology and should not be used as a criterion for the appendectomy.

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285 - Poster

Tumor-infiltrating lymphocytes in endometrial cancer with loss of expression in mismatch repair: A cohort study of patients with metachronous colorectal cancer

K.S. Grzankowski, J.B. Szender, K. Kanehira, S.B. Lele and K.O. Odunsi. *Roswell Park Cancer Institute, Buffalo, NY, USA*

Objectives: Although the association of endometrial cancer and Lynch syndrome is well documented, a clear consensus on which women should undergo tumor and germline testing is lacking. The debate is fueled by a paucity of resources and increased costs associated with universal testing of endometrial tumors.

Methods: We performed immunohistochemical analysis of 14 formalin-fixed and paraffin-embedded endometrial cancer specimens from patients with a history of both colorectal and endometrial cancers to assess expression of mismatch repair genes, MSH2, MSH6, MLH1, and PMS2, and the presence of associated tumor-infiltrating lymphocytes (TILs). Clinical outcome analyses were conducted.

Results: Loss of expression of 1 the 4 markers was seen in 50% of the patients. TILs were present in the entire population that demonstrated this loss of expression. No patients had TILs if normal expression was demonstrated with IHC. There was no difference in overall survival between the 2 groups. Women with TILs identified were diagnosed with their first cancer at an younger age (P = .004).

Conclusions: The presence of TILs correlates with loss of expression in 1 or more of the mismatch repair genes associated with Lynch syndrome. The presence of these cells should be noted during pathologic assessment of endometrial cancer and may potentially be used to triage to IHC or germline testing in patients at risk for Lynch syndrome.

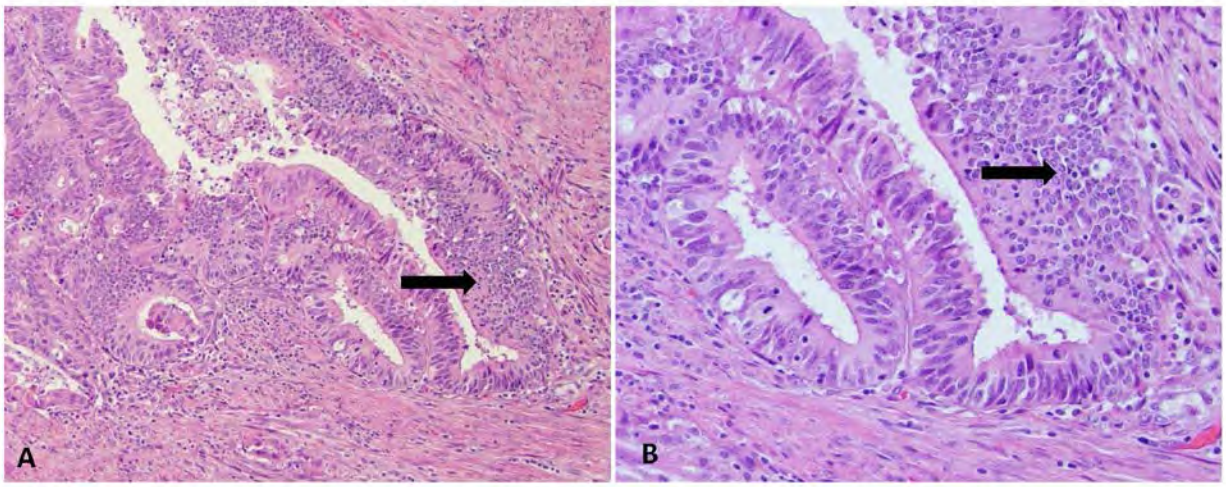

Fig. 1
Representative H&E images (A: 100x, B: 200x) showing presence of tumor infiltrating lymphocytes marked by arrow in endometrioid adenocarcinoma invading myometrium.

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286 - Poster
Decreased postoperative opioid consumption following implementation of enhanced recovery pathway after gynecologic surgery
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Objectives: To determine differences in morphine equivalents in the postoperative period with an enhanced recovery program (ERP) after gynecologic surgery.

Methods: We examined 153 consecutive patients who underwent laparotomy (144 cases were included) after the implementation of our ERP program and compared these to 74 (71 cases were included) historical controls. Patients receiving scheduled opioids before surgery at the time of anesthesia preoperative assessment were excluded. Pain management for the historical controls varied but included epidurals (24%) or patient-controlled analgesia (PCA) pumps (82%). Standardized postoperative orders were for scheduled oral pregabalin (4 doses only) and acetaminophen on postoperative day (POD) 0 and ibuprofen on POD1. Breakthrough pain was treated with oral oxycodone or intravenous hydromorphone. Morphine equivalents were calculated for the first 3 POD. The Wilcoxon rank sum and Fisher exact tests were used for comparison.

Results: The median morphine equivalents per day were reduced by 77% with implementation of an ERP program (median 28.4 mg [range, 1.5–253.5 mg] before ERP versus 6.6 mg [0–100 mg] after ERP, P < .0001). When evaluating daily differences, the greatest reduction in morphine equivalents was noted on POD0 (90% reduction: pre-ERP 49.6 mg [range 4-637.5 mg] vs. 5 mg [range 0-140 mg], P = <0.0001). All pre-ERP patients required opioid breakthrough pain medication compared with 81% in ERP (P < .0001). The median length of hospital stay postimplementation of our ERP was 3 days. Although not statistically significant, patients who received at least 1 dose of pregabalin, acetaminophen, and ibuprofen on POD1 required a lower median morphine equivalent daily dose than those patients receiving no doses of pregabalin, acetaminophen, and ibuprofen (median 21.3 mg [range 0–100 mg] versus 7.5 mg [0–159 mg], P = .0885).

Conclusions: Implementation of an ERP program reduces postoperative opioid administration in gynecologic surgery patients undergoing exploratory laparotomy. Continued accrual of patients may further support the importance of using nonopioid pain medications in an ERP.

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TCGA-based risk stratification of early-stage, high-grade endometrioid endometrial carcinoma

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Objectives: The Cancer Genome Atlas (TCGA) characterized endometrial carcinoma into 4 molecular groups. High-grade endometrioid endometrial cancers (HGEECs) represent a heterogeneous subtype of carcinomas, and adjuvant treatment of early-stage disease remains controversial. We hypothesize that early-stage HGEECs can be risk stratified based on molecular features defined with TCGA.

Methods: Patients with surgical stage I or II, FIGO grade 3, endometrioid endometrial carcinomas were identified from institutional databases. Clinicopathologic variables were collected from medical records, and recurrence-free patients were followed for a minimum of 2 years. Specialty pathologists reviewed all diagnoses and scored all cases for immunohistochemistry (IHC) staining of PMS2 and MSH6 as a surrogate for microsatellite instability (MSI). Next-generation sequencing was used to detect mutations in *TP53* and *POLE*. Appropriate 2-sided statistical tests were used.

Results: Of the 55 early-stage HGEEC patients, 15 had recurrences and 40 remained recurrence free. There were no statistically significant differences in age at diagnosis or other pathologic features between patients with and without recurrences. Hotspot mutations in the exonuclease domain of *POLE* were found in 5 (9%) of 55 patients (POLE group). IHC loss in PMS2 or MSH6 suggested MSI was present in 24 (44%) of 55 patients (MSI group). Of the remaining 26 cases without evidence of hypermutability (not POLE or MSI), 15 (58%) were wild type for *TP53* (TP53WT group) and 11 (42%) had mutations in *TP53* (TP53mut group). Of the patients with recurrence, 7 (47%) were in the TP53mut group, compared with 4 patients (10%) without a recurrence ($P = .005$). Median progression-free survival (PFS) and overall survival (OS) were significantly worse for the TP53mut group (PFS: 12.9 months [95% CI, 8.7–17.0] for TP53mut not reached for other subgroups, $P = .002$ [Figure]; OS: median survivals not reached, $P = .037$).

Conclusions: Our data suggest that *TP53* mutations, though frequent in uterine serous carcinomas, appear to be associated with recurrent disease and worse outcome in HGEEC. Focused molecular profiling of endometrial cancer may assist in stratification of early-stage patients and identify those for whom more aggressive adjuvant treatment may be beneficial.

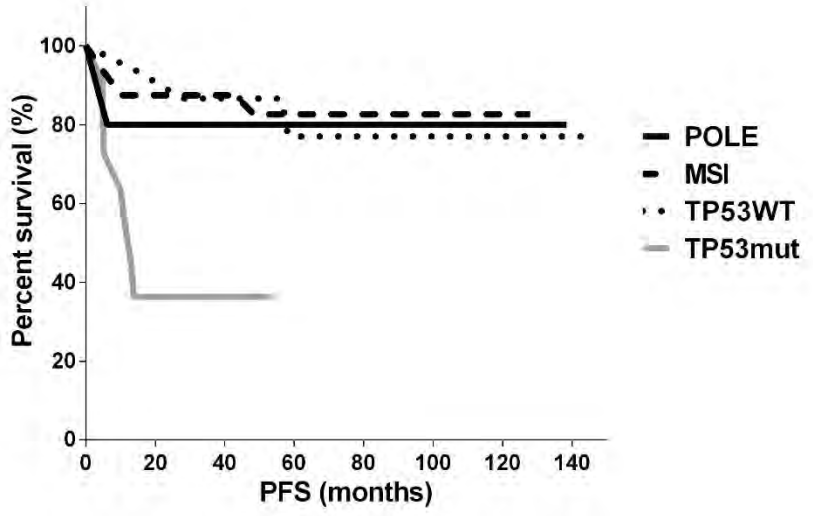

Fig. 1
Progression-Free Survival by Subgroup.

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Initiation of a formalized precision medicine program in gynecologic oncology

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Objectives: In an effort to better incorporate precision medicine into clinical practice, we initiated a pilot project to screen, discuss, and genetically characterize patients with metastatic or recurrent gynecologic malignancies for whom no curative standard of care exists.

Methods: In July 2014, we initiated a multidisciplinary Precision Medicine Board (PMB) whose purpose was to uniformly apply a molecular profiling technology to select and prioritize early-phase clinical trial enrollment for high-risk gynecologic malignancies. Additional objectives were to record outcomes and enable scientific discussions of mutations that may foster local translational research. FoundationOne (F1) was the preferred genomic platform; results were reviewed by a team composed of disease site specialists, phase I trialists, and basic and translational scientists affiliated with the Gynecologic Cancer Program. A detailed database for each patient was created and is followed prospectively for treatment use and resultant outcomes.

Results: To date, we have presented 62 cases with interpretable F1 testing on 60 tumor samples (31 ovarian, 18 uterine, 9 cervical, and 4 other female genital tract). Most patients were heavily pretreated with a median of 3 prior therapies. Significant genomic alterations were commonly found in all tumor types (median 3); 65% of all patients had alterations amenable to US Food and Drug Administration–approved therapies in other cancers or biologic rationale for ongoing clinical trial enrollment. *TP53* (45%), *PIK3CA* (27%), *CDKN2A/B* (16.7%), and *ARID1A* (16.7%) were the most frequently noted genes with mutations; analysis of mutations by tumor site was quite different from The Cancer Genome Atlas data (47% of our biopsies were recurrent). Molecular profiling resulted in identification of few actionable mutations (6%); we have matched 4 patients on therapies based on actionable mutations.

Conclusions: The predominant function of our PMB is to establish a forum to enhance clinical and translational research while providing clinical care for refractory malignancies. We have matched specific mutations to ongoing trials and are developing investigator-initiated studies based on trends within genomic profiling results. Longer-term follow-up will be required to determine the success of this strategy.

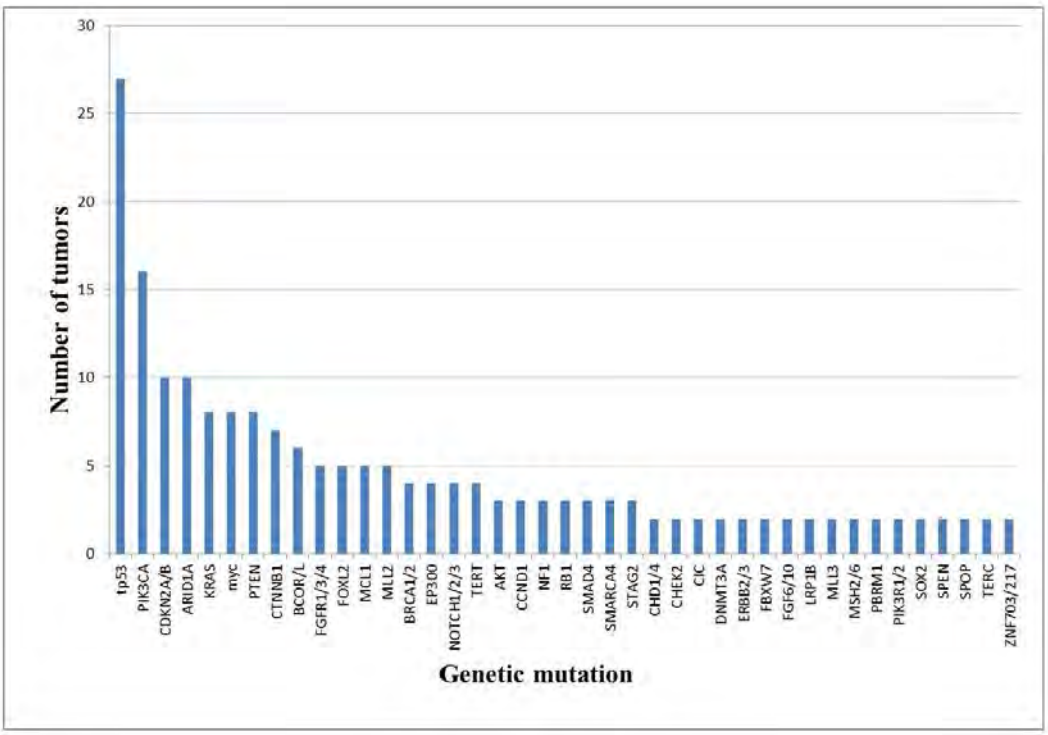

Fig. 1
Genetic mutation prevalence.

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Undifferentiated endometrial sarcoma: Does adjuvant treatment impact outcomes of stage I disease?

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Objectives: Undifferentiated endometrial sarcoma (UES) is an aggressive rare malignancy with no treatment consensus. Treatment of stage I disease is surgery with either observation or adjuvant chemo- and/or radiation therapy (RT). Our goal was to assess the outcomes of various treatment modalities, and to identify prognostic factors associated with survival.

Methods: Patients with undifferentiated endometrial sarcoma reported to the National Cancer Data Base from 1998 to 2012 who underwent at least a total hysterectomy were selected. To exclude for potentially palliative interventions, we included only patients with stage I disease for this analysis. Overall survival was estimated using the Kaplan-Meier method, univariate comparisons were made with log-rank tests, and multivariable analysis was performed using Cox proportional hazards modeling. All tests were 2-tailed with threshold significance level set at $P < .05$.

Results: A total of 2,202 undifferentiated endometrial sarcoma cancer patients were identified, and 552 patients met inclusion criteria. Increasing tumor size was significantly associated with a decrease in survival (5-year overall survival [OS] 61%, 54%, 37% for sizes <5 cm, 5–10 cm, >10 cm, respectively; $P < .001$). The 5-year OS for stage IA (61%) and IB (53%) was also significant ($P = .01$). Comparison of adjuvant therapy for stage IA showed no significant difference in treatment outcomes ($P = .554$). For stage IB, there was an increasing nonsignificant trend in survival when comparing no treatment, RT only, chemotherapy only, and chemotherapy + RT, respectively (5-year OS 38%, 50%, 53%, 62%, respectively; $P = .125$). No other factors were found to be associated with survival on univariate analyses including age, race, insurance, income, education, residential setting, year of diagnosis, facility type/location/distance, or Lymphovascular space invasion. On multivariable analysis, only tumor size (HR 2.5, 95% CI 1.641–3.818, $P = .001$) and stage (HR 0.549, 95% CI 0.39–0.772, P = .001) significantly predicted survival.

Conclusions: Increased tumor size in UES confined to the uterus is a poor prognostic factor. There was no difference in survival in stage IA patients receiving adjuvant therapy versus observation. When present, prognosis in stage IB disease is worse. However, the type of adjuvant therapy or combination is unclear. Optimal treatment of this disease remains elusive.

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Increasing HPV vaccination in the postpartum population using an EMR-based versus nursing protocol intervention

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Objectives: Vaccination rate against the human papillomavirus (HPV) is low in the United States. With the widespread implementation of electronic medical records (EMR), there is an opportunity to study the impact of EMR-driven interventions compared with other provider-based interventions to increase vaccination rates.

Methods: Two distinct interventions to improve HPV vaccination were introduced to a prospective cohort of postpartum patients at 2 affiliated county hospitals in November 2014: a nursing protocol at hospital A and an EMR postpartum order set at hospital B. All eligible patients ages 26 years and less were identified for the subsequent 6 months (n = 237). Descriptive statistical methods were used to assess baseline characteristics of the 2 groups. A multiple logistic regression model was used to compare postintervention vaccination rates.

Results: The 2 groups had similar baseline characteristics with regard to age but differed significantly in ethnicity, race, language, insurance status, and sites of prenatal care (hospital clinic based versus outside clinic based). At Hospital B, 66% of eligible patients accepted the HPV vaccine when offered whereas at Hospital A, only 32% of eligible patients accepted the vaccine when offered. Based on univariate association tests, ethnicity, language, and site of prenatal care were identified as covariates believed to affect the association between outcome and intervention methods. After adjusting for these variables, patients at Hospital B were 5 times more likely to get the vaccination than those at Hospital A (OR 5.865, CI 3.358–10.245, $P < .0001$).

Conclusions: EMR-based interventions are a highly successful method of increasing HPV vaccination in the hospital setting, more so than nurse-driven protocols. Neither intervention required additional financial resources for implementation. Ongoing research is needed to identify ways to reduce patient refusal rates and missed opportunities to increase HPV vaccination rates in the inpatient clinical setting.

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Use of near-infrared angiography during rectosigmoid resection and reanastomosis in women with gynecologic malignancies

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Objectives: To investigate the usefulness of near-infrared angiography (NIRA) for the assessment of anastomotic perfusion at the time of rectosigmoid resection and reanastomosis in women undergoing surgery for gynecologic cancer.

Methods: We retrospectively identified all patients who underwent rectosigmoid resection for a gynecologic malignancy between 2013 and 2015. NIRA was assessed using a fluorescence-based endoscopic imaging system. Various clinicopathologic data were abstracted and analyzed. Appropriate statistical tests were used.

Results: Of the 175 patients identified, NIRA was used in 32 (18%). No statistically significant differences were noted in age, body mass index (BMI), hypertension, diabetes, preoperative albumin levels, steroid use, or history of preoperative radiation or chemotherapy between the NIRA and non-NIRA patient groups. The primary indication for surgery was ovarian carcinoma in both groups (84% for both, $P = .9$). Seventeen (53%) of 32 NIRA patients underwent primary debulking surgery compared with 78 (54%) of 143 non-NIRA patients ($P = .9$). All cases of rectosigmoid resection underwent stapled primary anastomosis.

"High-risk" anastomoses, characterized by an anastomotic height of less than 10 cm from the dentate line, were found in 7 (22%) of 32 NIRA patients versus 39 (27%) of 143 non-NIRA patients (P = .1). Diverting ileostomy was performed in 2 (6%) of 32 compared with 34 (24%) of 143 patients, respectively (P = .029). Postoperative abscess was noted in 2 (6%) of 32 compared with 25 (17%) of 143 patients, respectively (P = .2). Incidence of rectal anastomotic leak was found in 1 (3%) of 32 compared with 8 (6%) of 143 patients, respectively (P = 1.0).

Conclusions: In the setting of rectosigmoid resection, NIRA appears to be a safe adjunct to primary reanastomosis and can help guide decision management for intestinal diversion in women undergoing complex gynecologic cancer surgery. Prospective trials with larger numbers of patients are needed to validate its usefulness.

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Clinical utility of routine postoperative laboratory studies in uncomplicated patients undergoing robotic hysterectomy for endometrial cancer

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Objectives: Routine postoperative (PO) laboratory testing is commonly performed on endometrial cancer patients undergoing robotic surgery but may only rarely detect clinically significant abnormalities requiring intervention in asymptomatic patients. We sought to evaluate the usefulness of routine PO laboratory testing in uncomplicated endometrial cancer patients after robotic hysterectomy.

Methods: A multi-institution retrospective chart review from January 2010 to February 2015 was conducted. Data were collected from electronic medical records and were analyzed using descriptive statistics.

Results: Of 403 patients identified, 23 were excluded for intra- or postoperative complications or comorbidities requiring PO laboratory monitoring, thus leaving 380 evaluable patients. Median age was 62 years, median body mass index was 32, and median length of stay was 1 day. The majority (66%) underwent lymphadenectomy. All patients had at least 1 PO complete blood count measurement. A total of 205 patients (54%) had abnormal PO hemoglobin values (median 11.6, range 7.3–15.1); however, only 1 (0.5%) required a blood transfusion for symptomatic anemia. Similarly, 204 patients (54%) had abnormal PO white blood cell counts (median 10.8, range 3.4–28.7), but only 2 (1%) required intervention, both for symptomatic urinary tract infections. There were no asymptomatic patients whose routine PO complete blood counts alone prompted intervention. On PO day 1, 345 patients (91%) underwent a basic metabolic panel measurement. In 39 patients (11%), potassium levels were corrected; all of these were asymptomatic and most (54%) had normal range levels. Similarly, 37% of patients with PO magnesium levels had corrective interventions; all were asymptomatic, and 64% had normal range magnesium levels. There were otherwise only 2 (0.6%) asymptomatic patients whose abnormal routine PO laboratory findings led to intervention: one with an elevated creatinine consistent with acute kidney injury prompting fluid boluses, and one with hyponatremia prompting intervention. The total charges for routine PO laboratory testing amounted to $260,882, or an average of $782 per patient.

Conclusions: In this study, the rate of detecting clinically significant PO laboratory abnormalities in asymptomatic patients was low. Routine PO laboratory studies in this patient population may not be necessary. Cost-effectiveness analyses of routine laboratory testing in this setting are warranted.

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A phase Ib study of pexidartinib (PLX3397) and weekly paclitaxel in patients with advanced solid tumors including an ovarian cancer subset

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Objectives: Colony-stimulating factor 1 signals through its transmembrane tyrosine kinase receptor (CSF1R) to control the number and phenotype of tumor-associated macrophages (TAMs) and other CSF1-target cells. TAMs enable tumor growth and metastasis. Pexidartinib, a potent small-molecule inhibitor of CSF1R, KIT, and mutated FLT3 receptor tyrosine kinases was studied with weekly paclitaxel in patients with advanced solid tumors to (1) establish the recommended phase 2 dose (RP2D) of pexidartinib plus weekly paclitaxel; (2) obtain safety data for future combination studies; and (3) look for efficacy signals in solid tumors including an ovarian cancer subset.

Methods: Eligible patients had advanced solid tumors for which taxane treatment was appropriate. Part 1 was a 3 + 3 dose escalation of oral pexidartinib twice daily and weekly intravenous (IV) paclitaxel at 80 mg/m^2. Part 2 was an expanded safety cohort treated with pexidartinib at the RP2D and weekly paclitaxel. After week 4, at least 3 doses of paclitaxel were required every 4 weeks. Response was determined using RECIST 1.1 criteria.

Results: In part 1 (n = 28), the maximum pexidartinib dose was 1,600 mg/day. There was no dose-limiting toxicity and 1,600 mg/day was selected for part 2 (n = 26) based on drug exposure. Frequent grade 3 adverse events were anemia (33%), fatigue (18%), hypophosphatemia (18%), lymphopenia (15%), neutropenia (15%), and hypertension (12%). In part 2, five patients with ovarian cancer and 1 with primary peritoneal cancer (all platinum refractory) were evaluable for efficacy. All had taxane-resistant disease. Mean age was 60 years (range, 44–74 years), number of lines of prior chemotherapy was 6 (range, 3–9), and duration of last prior taxane regimen was 5 months (range, 3–9 mos). Three patients had radiographic responses (Table 1).

Conclusions: The encouraging efficacy signal in this subset prompted an expansion study to evaluate RECIST response and blood/tissue biomarkers in up to 30 patients with platinum-refractory ovarian, primary peritoneal, or fallopian tube cancer. Based on drug exposure and tolerability, the cohort dose schedule is oral pexidartinib 1,200 mg/day (600 mg given orally twice a day) with IV paclitaxel 80 mg/m^2 per week.

Table 1
Clinical Summary of 3 Patients with Platinum Refractory Epithelial Gynecologic Malignancies who Responded to Paclitaxel and Pexidartinib.

Age (y)	Prior lines of chemo (#)	Duration last taxane (mos)	Response	CA-125 C1D1/Nadir*	Response duration (days)	PFS (d)
74	9	5	CR	82/23	190	240
44	7	4	PR	57/35	95	149
63	9	6	SD	ND/3059	113	168

*NL ≤ 30.2 U/mL

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Genital cancer in the primary immunodeficiency GATA2 deficiency
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Objectives: Seventy percent of healthy women will clear human papillomavirus (HPV) infection in 1 year, and more than 90% will clear the infection by 2 years. Patients with primary immunodeficiency caused by mutations in *GATA2*, a transcription factor key to the development and maintenance of hematopoiesis, are susceptible to infections because of progressive monocytopenia, and B-cell and natural killer (NK) cell lymphopenia. NK cell dysfunction and deficiency in GATA2 are thought to predispose individuals to severe, persistent, and oncogenic HPV infections. The aim of this study was to report the risk of HPV disease in patients with the primary immunodeficiency GATA2.

Methods: We retrospectively reviewed the medical records, laboratory, histopathology, and cytopathology records of all female patients with identified GATA2 deficiency followed at the National Institutes of Health.

Results: Of 35 women with GATA2 deficiency, 77% had HPV, 66% had genital warts, and 54% had extragenital warts. Median age at diagnosis of dysplasia (n = 18) was 27 years (range, 15–59 years). Median age at diagnosis of genital cancer (n = 7) was 34 years (range, 22–40 years). One patient died of cervical cancer. HPV infection persisted over time. No patient demonstrated long-term HPV treatment response without bone marrow transplantation.

Conclusions: GATA2 deficiency is commonly associated with persistent, severe, multifocal HPV disease in young women. More importantly, these patients are at high risk for developing HPV-related genital cancers. Currently, bone marrow transplantation is the only known curative treatment for HPV disease in GATA2 deficiency. Patients with GATA2 deficiency need earlier and more frequent surveillance for HPV disease. GATA2 deficiency is associated with a high rate of HPV genital disease and should be suspected in young women with severe HPV disease.

Table 1
Genital HPV disease in the primary immunodeficiency GATA2 deficency.

Genital malignancy related(HPV+ patients)	Cases (n=27)	% of HPV+ patients
HPV malignancy	7	26%
Cervical dysplasia	15	56%
persistent	5	19%
low grade	4	15%
high grade (Grades 2 and above)	8	30%
Vulvar dysplasia	12	44%
persistent	8	30%
low grade	4	15%
high grade (Grades 2 and above)	6	22%
Anal dysplasia	4	15%
Multifocal dysplasia (>2 sites)	11	41%
Vulvar carcinoma	3	11%
Cervical carcinoma	2	7%
Vaginal carcinoma	2	7%

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295 - Poster

Oncologic outcome of less radical surgery versus radical hysterectomy C1 in small early stage I cervical cancer

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Objectives: The aim of our study was to compare oncologic outcomes in women who underwent experimental less radical LAP2 protocol (sentinel lymph node mapping [SLNM] + laparoscopic lymphadenectomy + extrafascial vaginal hysterectomy) with those who underwent SLNM + radical hysterectomy (RH-C1) for small early stage IB1 cervical carcinoma.

Methods: Patients with early invasive cervical cancer (squamous or adenocarcinoma, tumor size <2 cm, stromal invasion <1/2 of stroma [<10 mm] + lymphovascular space invasion [LVSI]) who were in the experimental LAP2 protocol at our institution between December 2000 and September 2012 were compared with a control group treated with “standard radicality” SLNM + RH (C1) in the period between January 1999 and September 2012. All patient, surgical, pathological, and follow-up data were prospectively collected in the SLNM protocol and LAP2 protocol group. The association between the discrete variables was assessed using the χ^2 test with Yates correction, and the Kaplan-Meier method was used to calculate disease-free and overall survival.

Results: Positive lymph nodes were detected in 8 (6.4%) of 126 women who were part of the experimental LAP2 protocol. In the sentinel lymph node (SLN)–negative group, we observed 1 local vaginal recurrence (1/118 [0.85%]) and the patient is now in complete 12-month remission after chemoradiotherapy. All node-positive patients are currently in complete remission.

Of 126 women in the control group treated with RH, 11 (8.7%) had positive lymph nodes. In the SLN-negative group, we observed 1 patient with distant recurrence and 1 patient with central pelvic recurrence (2/115 [1.74%]), both of whom died. One patient with positive lymph nodes had pelvic and distant recurrence and died of the disease. There were no statistical differences between the 2 groups in relation to the following prognostic variables: histopathology, node positive rate, and LVSI. We did not find any statistical differences in relation to recurrence-free survival and disease-specific survival.

Conclusions: Less radical surgery after negative FS in SLN with laparoscopic pelvic lymphadenectomy and vaginal hysterectomy type A in selected patients can be a feasible and safe method and has a similar oncologic outcome with better quality of life in comparison to RH.

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296 - Poster

Utilization of an institutional algorithm for fertility preservation in young women with endometrial cancer

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Objectives: To describe the clinicopathologic characteristics of a cohort of women with endometrial cancer eligible for fertility-sparing treatment, and compare outcomes between women electing fertility preservation (FP) over definitive treatment with total hysterectomy (TH) at initial diagnosis.

Methods: Using our institutional algorithm, women were identified who met the criteria for uterine preservation at our institution between 2005 and 2015. Patients were divided into 2 groups: those who opted for FP and those who opted for definitive management with TH. Clinicopathologic data were abstracted and analyzed using appropriate statistical tests.

Results: Of 123 patients with endometrial cancer diagnosed at age less than 40 years, 51 (41%) patients were eligible for uterine preservation. Of these 51 patients, 23 (45%) chose FP and 28 (55%) chose TH. Median age was 33 years (range, 24–40 years) in the FP group compared with 37 years (range, 26–40 years) in the TH group ($P = .025$). There was no statistically significant difference in race or body mass index between cohorts. Nulliparity was noted in 20 (87%) of 23 FP patients and 23 (82%) of 28 TH patients ($P = .6$). Of the 23 patients who chose FP, 17 (74%) were initially treated with megestrol acetate, 5 (22%) had a levonorgestrel intrauterine device inserted, and 1 patient declined medical management. Regression of disease was noted in 16 (70%) patients. Definitive management with TH was ultimately chosen in 12 (52%) of 23 FP patients; median time from diagnosis to hysterectomy was 17.5 months (range, 4–46 months). Four live births resulted in this cohort. Of the 28 patients who chose TH, 25 (89%) demonstrated uterine-confined disease and 19 (68%) had no evidence of myoinvasion on final pathology. At a median follow-up of 34 months (range, 4–116 months), all 51 patients remained alive with no evidence of disease recurrence in any patient who underwent hysterectomy in either cohort. Of the 11 patients who never underwent hysterectomy, 7 (64%) experienced resolution of disease and 4 (36%) continue to be receive hormonal agents.

Conclusions: Less than half of eligible women chose FP when diagnosed with early-stage endometrial cancer. Management of endometrial carcinoma using a fertility-sparing strategy appears to be associated with favorable outcomes and remains a reasonable option for women carefully selected through our institutional algorithm.

Table 1
Selection Criteria for Uterine Preservation in Endometrial Cancer Cases.

Age ≤ 40
Well differentiated endometrioid adenocarcinoma; FIGO grade 1
Diagnosis based on D&C
Tumor does not invade the myometrium by MRI

Absence of suspicious nodes or metastatic disease by imaging
Absence of synchronous ovarian tumor by imaging
No evidence of Lunch syndrome (Perform IHC for MMR proteins)
Strong desire to preserve reproductive function –uterine preservation
No contraindications to medical treatment with progestins or pregnancy
Evaluation by REI team strongly recommended
Patient compliant with follow-up protocol
Patient understands that this is not a common standard treatment

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297 - Poster

Implementation of an inpatient nursing protocol to improve HPV vaccination administration in the postpartum population

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Objectives: Human papillomavirus (HPV) vaccination rates are low in the United States. Nursing protocols to identify patients who are candidates for vaccinations have been proven successful in increasing flu and pneumococcal vaccination rates and may help to increase the identification and use of the HPV vaccine. The inpatient postpartum setting provides a good opportunity to implement a nurse-based protocol to identify and vaccinate eligible patients for the HPV vaccine.

Methods: A nursing protocol was implemented starting November 2014 at a single institution. All eligible patients ages 26 years and younger were identified. A preintervention cohort of eligible patients from the preceding 6 months (n = 75) was used to identify the baseline vaccination rate and the postintervention cohort of patients (n = 49) to determine the postintervention vaccination rate for 6 months from November 2014 until April 2015. Descriptive statistical methods were used to assess baseline characteristics of the 2 groups. A multiple logistic regression model was used to compare vaccination rates before and after the intervention. Qualitative analysis was conducted to determine reasons for missed opportunities and refusals.

Results: The 2 groups had similar baseline characteristics. HPV vaccination rates rose from 75% (56 of the 75 eligible patients) to 90% (44 of the 49 eligible patients) after the nurse-based protocol was implemented. Based on univariate association tests, ethnicity and language were identified as covariates believed to affect the association between outcome and intervention. Receipt of prenatal care, either at the hospital-based or the community-based clinics was not a significant covariate. After adjusting for these significant effects, patients in the postintervention cohort were 3.4 times more likely to get vaccination (OR 3.418, 95% CI 1.129–10.34) compared with the preintervention cohort. The rates of vaccine refusal remained low at 5% suggesting the primary driver for increased vaccination was the reduction of missed opportunities from 20% to 4%.

Conclusions: The nursing protocol intervention in a hospital setting was successful in increasing HPV vaccine administration by reducing the number of missed opportunities with no additional financial costs. Further studies are needed to determine if a similar intervention would be successful in other clinical settings.

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298 - Poster

Role of lymph node dissection in women older than 65 years with early-stage high-grade endometrial cancer

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Objectives: In this study, we examine the impact of lymph node dissection on disease-specific mortality among elderly women (≥65 years) with high-grade, stage I endometrial cancer.

Methods: An analysis was performed of women included in the Surveillance, Epidemiology and End Results (SEER) Medicare Database, with surgicaly confirmed or presumed stage 1, high-grade endometrial cancers (adenocarcinoma, carcinosarcoma, clear cell carcinoma, and papillary serous carcinoma). All cases were diagnosed between 1992 and 2009. Disease-specific mortality was compared between women who did and did not undergo surgical staging with a lymph node dissection. Logistic regression models are used to determine the factors associated with lymph node dissection. Cox proportional hazard methods were used to assess survival.

Results: Of the 3,950 women who met criteria for inclusion in the analysis, 2,862 (72.5%) underwent surgical staging and 1,088 (27.5%) were presumed to be in stage 1. When compared with women of ages 66 to 70 years, women older than 80 years were less likely to undergo lymph node dissection (OR 0.53, CI 0.42–0.65). Using the period before 1997 as a reference, women with a later diagnosis were more likely to undergo a lymph node dissection; years 1998 to 2003 (OR 1.62, CI 1.34–1.94) and years 2004 to 2009 (OR 2.31, CI 1.91–2.79). Disease-specific mortality did not vary based on year of diagnosis. Compared with women who underwent a lymph node dissection, those who did not undergo a lymph node dissection did not have higher rates of disease-specific mortality, (HR 1.12, 95% CI = 0.94–1.33). Among patients who underwent surgical staging, 437 (15.3%) received chemotherapy and 1,376 (48.1%) had radiation, compared with 85 (7.8%) and 439 (40.3%), respectively, who were not surgically staged.

Conclusions: Elderly women with low-stage, high-grade endometrial cancer who are not staged surgically undergo similar adjuvant treatment regimens and have a comparable disease-specific mortality compared with those who undergo surgical staging.

Table 1
Multivariate Cox proportional hazards model for disease specific and overall mortality in the entire study population.

	Disease	All Cause
Age		
66-70	Ref.	Ref.
71-75	1.32 (1.06-1.64)	1.56 (1.36-1.80)
76-80	1.25 (1.00-1.58)	1.99 (1.73-2.30)
80+	1.92 (1.53-2.42)	3.31 (2.87-3.83)
Years		
1992-1997	Ref.	Ref.
1998-2003	1.10 (0.91-1.33)	0.99 (0.89-1.11)
2004-2009	0.83 (0.67-1.03)	0.88 (0.76-1.01)
Race		
White	Ref.	Ref.
Black	1.21 (0.92-1.60)	1.25 (1.05-1.49)
Other	0.95 (0.65-1.40)	1.00 (0.80-1.24)
Marital Status at Diagnosis		
Unmarried	Ref.	Ref.
Married	0.94 (0.80-1.11)	0.88 (0.80-0.97)
Unknown	0.88 (0.57-1.37)	0.87 (0.67-1.14)
SEER registry		
Central	Ref.	Ref.
East	0.97 (0.78-1.20)	1.01 (0.89-1.15)
West	1.02 (0.83-1.24)	1.05 (0.94-1.18)
Income		
1st Quartile	Ref.	Ref.
2nd Quartile	0.90 (0.72-1.12)	0.91 (0.80-1.03)
3rd Quartile	0.83 (0.66-1.04)	0.83 (0.73-0.96)
4th Quartile	0.97 (0.77-1.22)	0.94 (0.82-1.08)
Other	0.53 (0.25-1.14)	0.93 (0.66-1.31)
Urban/Rural		

Urban	Ref.	Ref.
Rural	0.79 (0.43-1.45)	1.18 (0.86-1.62)
Charlson Score		
0	Ref.	Ref.
1	0.97 (0.78-1.20)	1.29 (1.15-1.45)
2+	1.42 (1.13-1.80)	1.74 (1.52-1.99)
Histology		
Adeno/Muc High	Ref.	Ref.
CARCINOSARCOMA	2.67 (2.15-3.31)	1.82 (1.58-2.10)
CLEAR CELL	1.68 (1.22-2.31)	1.23 (1.01-1.50)
PAPILLARY	1.54 (1.27-1.86)	1.20 (1.07-1.35)
LN Examination Status		
Examined	Ref.	Ref.
None Examined	1.12 (0.94-1.33)	1.14 (1.03-1.26)
Radiation		
None	Ref.	Ref.
Radiation	1.49 (1.28-1.74)	1.10 (1.01-1.21)
Unknown	1.20 (0.56-2.58)	0.83 (0.53-1.30)
Chemo		
None	Ref.	Ref.
Yes	1.22 (0.97-1.54)	1.13 (0.97-1.33)

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Frequency of intimate partner violence history in gynecologic and breast cancers

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Objectives: Intimate partner violence (IPV) has been linked to cancer-related well-being. Frequency of IPV and sexual violence among women with cancer by specific cancer site has not been well characterized. Here the frequency of self-reported current and lifetime IPV was estimated among women diagnosed with cancer by primary site and the potential impact of IPV on delaying detection measured as stage at diagnosis.

Methods: Women, ages 18 to 79 years, with an incident, primary, biopsy-confirmed cancer were recruited from 2 state cancer registries (Kentucky and North Carolina) within 12 months of their diagnosis (2009–2015). In a phone interview, consenting women reported current and past IPV experiences, current partner interfering behavior (PIB), sociodemographics, and cancer-related well-being indicators. Cancer registries provided stage, site, date of diagnosis, and age. Multivariable logistic regression analyses were used to determine whether women experiencing lifetime or current IPV or PIB were more likely to present (1) at a later stage at diagnosis, or (2) with specific cancer sites: cervical/vulvar, endometrial, and ovarian cancer relative to breast cancer.

Results: A total of 2,320 women were included in the analysis. Of these, 1,981 had breast cancer, 158 had endometrial cancer, 84 had ovarian cancer, and 97 had cervical or vulvar cancer. Of women with cervical or vulvar cancer, 57.3% disclosed IPV or PIB, which was significantly higher than seen in the breast cancer group (37.2%, $P < .001$). When stratified by timing, the cervical cancer group had a higher frequency of past IPV (38.1% vs 26.7%) and current IPV or PIB (18.6% vs 10.2%) compared with those with breast cancer (26.7%, $P = .0003$). There were no significant differences in the frequency of lifetime IPV or current PIB between endometrial and ovarian cancer compared with breast cancer. Neither lifetime IPV nor current PIB were associated with being diagnosed at a later stage for all women or by cancer site.

Conclusions: Cervical and vulvar cancer are associated with an increased likelihood of lifetime IPV compared with other gynecologic cancer or breast cancer patients. IPV history is correlated with cancer-related well-being and may be an important determinant of quality of life.

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300 - Poster

Factors influencing clinical trial enrollment among ovarian cancer patients

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Objectives: At an institution with abundant clinical trial access and a strong culture of enrollment, we aimed to characterize patients who did not enroll in a clinical trial and identify potential barriers that may limit enrollment among patients with advanced ovarian cancer presenting for first-line chemotherapy.

Methods: We conducted a retrospective chart review of patients diagnosed with stage II-IV epithelial ovarian cancer (EOC) from December 2009 to April 2013, a period during which clinical trials (cooperative group, pharmaceutical, and investigator initiated) were open and available to all types of EOC patients, including optimally debulked, suboptimally debulked, or those undergoing neoadjuvant chemotherapy. Trial enrollment status, demographics, tumor characteristics, and treatment details were recorded. SAS version 9.3 was used for descriptive statistics and univariate analyses.

Results: A total of 144 patients met study criteria. Of these, 93 were enrolled in a trial, and 51 were not. Older patients were less likely to be on clinical trial (median age 68 vs 61 years, $P = .008$). Stage ($P = .68$), race ($P = 1.00$), and performance status ($P = .24$) were similar between the groups. Histology differed between the 2 groups with a higher percentage of low-grade serous ovarian cancer in the trial group (14% vs 2%). Distance did not affect trial enrollment, because nearly half of all patients in both groups lived more than 50 miles from the treatment center (41% vs 44%, $P = .36$). Trial patients received more primary chemotherapy (8.6 vs 0%, $P < .0001$), less neoadjuvant chemotherapy (4.3% vs 31.4%, $P < .0001$), and more intraperitoneal chemotherapy (27% vs 10%, $P = .016$), dose-dense taxol (28% vs 8%, $P = .005$), and maintenance therapy (67% vs 12%, $P < .0001$). Despite similar residual disease status (51% vs 49% with no gross residual, $P = .33$) and median number of total regimens received (2 in each group; $P = .37$), patients on trial had longer overall survival (71% vs 52% 3-year survival, $P = .026$). Progression-free survival approached significance (20 vs 9 months, $P = .065$).

Conclusions: In an institution where the culture is to offer clinical trials to all eligible patients, 35% of frontline EOC patients did not participate. The association between clinical trial nonparticipation and increasing age was reported by the AGO cooperative group. A limitation of this analysis is the lack of data regarding why older patients did not enroll: eligibility, physician bias or patient choice. These factors need to be identified so trial enrollment can better reflect the actual EOC patient demographics and not a select younger group.

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301 - Poster

Mismatch repair abnormalities are associated with aggressive tumor pathology in young women with endometrial cancer

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Objectives: To describe the clinicopathologic characteristics and outcomes of a cohort of reproductive-age women with mismatch repair (MMR) abnormalities treated at a comprehensive cancer center.

Methods: All women 45 years of age or younger with endometrial carcinoma who were treated at our institution between 2005 and 2015 were identified. Patients were included if they had immunohistochemical (IHC) staining for MMR proteins on their tumor tissue, with loss of staining indicative of microsatellite instability (MSI). Clinicopathologic data were abstracted and analyzed using appropriate statistical tests.

Results: Of the 200 patients identified, 131 had documented MMR IHC analysis. Ninety-six (73%) of 131 had retained MMR staining (NL) and 35 (27%) of 131 had an abnormality in 1 or more MMR proteins on IHC (ABNL). Of these 35 patients, 17 (49%) had Lynch syndrome on germline testing. Median age in the ABNL group was 40 years (range, 28–45 years) and in the NL group was 39 years (range, 24–45 years) ($P = .4$). Median body mass index was 25.1 (range, 18.4–63.6) in the ABNL group and 31.6 (range, 17.6–73.1) in the NL group ($P = .004$). There were no statistically significant differences in polycystic ovary syndrome or diabetes incidence between the groups. Definitive surgical management with hysterectomy was noted in 122 (93%) of 131 cases. Final pathology demonstrated stage III/IV disease in 7 (20%) of 35 ABNL patients versus 8 (9%) of 87 NL

patients (*P* = .09). FIGO grade 3 was seen in 10 (29%) of 35 patients versus 6 (7%) of 87 patients, respectively (*P* = .004). Endometrioid histology was noted in 31 (89%) of 35 versus 82 (94%) of 87 patients, respectively (*P* = .06). Twenty-four (69%) of 35 MSI patients had myoinvasive disease versus 36 (41%) of 87 patients with retained MMR proteins (*P* = .007). Lymphovascular space invasion (LVSI) was noted in 14 (40%) of 35 ABNL patients compared with 17 (20%) of 87 NL patients (*P* = .019). Median progression-free (PFS) and overall survival was not reached for either group, and there was no difference in PFS between groups (*P* = .6). No deaths were reported in the total cohort of 131 patients, with a median follow-up of 28.7 months (range, 0.7–108.2 months).

Conclusions: In a cohort of reproductive-age women with endometrial carcinoma, patients with documented MSI were noted to have higher-grade tumors, more frequent myoinvasive disease, and a greater incidence of LVSI. Survival outcomes were favorable regardless of the presence of MMR abnormality.

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302 - Poster

Effects of evolving treatment strategies on the incidence-based mortality of advanced ovarian cancer

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Objectives: The US mortality rate of advanced ovarian cancer (OC) has been falling for the past several years; it has been debated whether the decline is due to decreasing incidence or improved treatment. We aim to evaluate the trend in OC mortality over time in the context of an evolving standard of care.

Methods: A study of the incidence-based mortality (IBM) per 100,000 women from OC was conducted using the National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) 9 database. SEERstat was used to calculate annual age-adjusted rates, and trends in IBM, for OC diagnosed from 1995 to 2012. The IBM calculates the rate of cancer-related deaths in a given year from a cohort of patients diagnosed during a specific period before death. IBM, unlike survival or mortality calculations, isolates patients diagnosed and treated in a fixed period, thereby permitting assessment of the temporal association of a change in practice to disease-specific mortality. Joinpoint statistical software permits analysis of change points in continuous linear trends. Joinpoint was used to identify if and when significant changes in IBM trend occurred (*P* < .05 indicating significance).

Results: There was no significant change in the IBM during the years 1995 to 2000. From 2001 to 2012, the IBM fell from 4.6 to 2.9, an annual percentage change (APC) of –4.0% (95% CI –4.3 to –2.6). Joinpoint analysis identified a statistically significant change in trend in 2001 (95% CI 1999-2005).

Conclusions: Using IBM methodology, we noted a fall in cancer-specific mortality of OC beginning in 2001 independent of incidence. The 95% CI predates the NCI's 2006 NCI clinical alert endorsing intraperitoneal (IP) chemotherapy for patients with OC. However, the change is consistent with the effects of publication of Gynecologic Oncology Group (GOG) 104 in 1996 and resultant more frequent use of IP cisplatin. Published literature has documented such an evolution in practice from the years 2003 to 2008, consistent with our findings. It is impossible to prove causality with this methodology. Nonetheless, our results show improved survival for women with OC after increased prescription of IP chemotherapy. This suggests improved health outcomes among OC patients resulting from publication of clinical trial results and a lag between publication date and better survival in the range of 2 to 8 years.

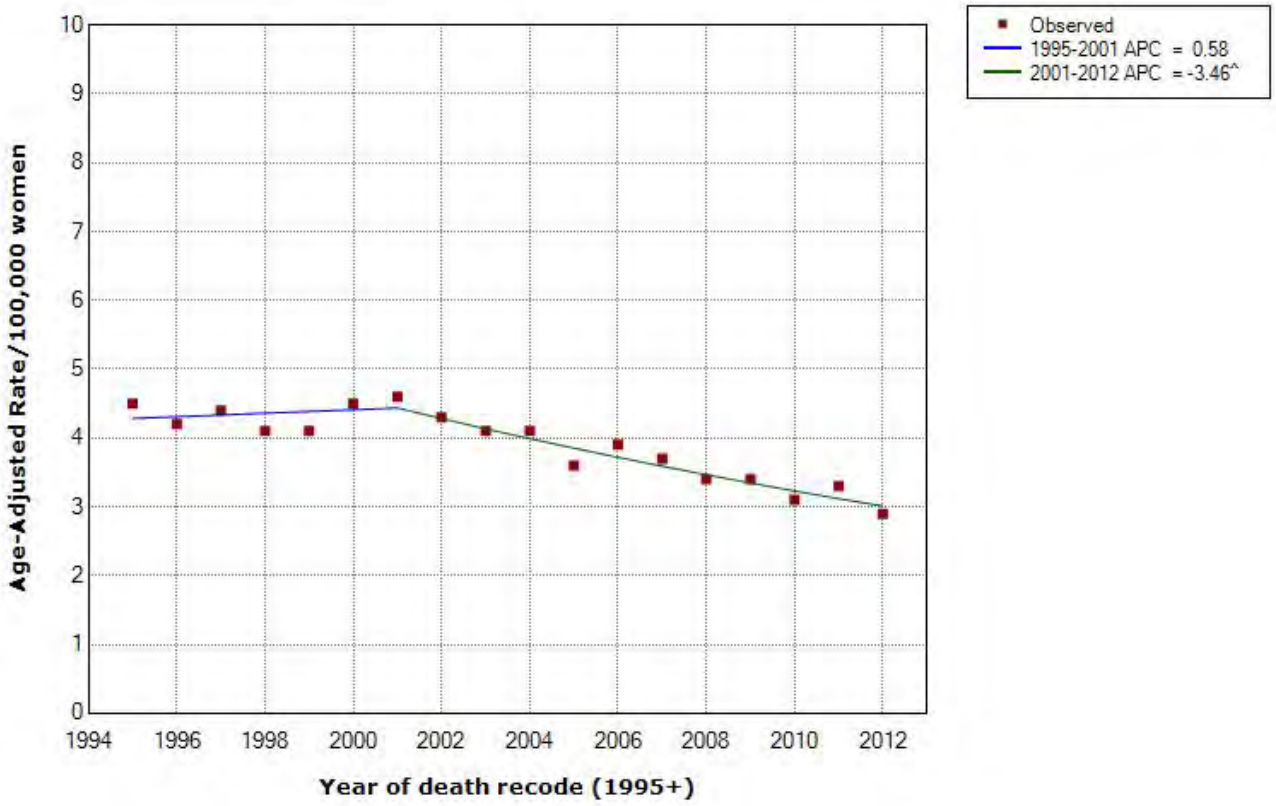

Fig. 1
Incidence-based Mortality (6yr) Advanced Ovarian Cancer: 1 Joinpoint.

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303 - Poster

Comparison of sentinel lymph node mapping with standard pelvic lymphadenectomy in patients with grade 1 and 2 endometrial cancer

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Objectives: (1) To evaluate sentinel lymph node (SLN) mapping and ultrastaging in the detection of lymph node (LN) metastasis in patients with endometrioid G1, G2 cancers, less than 50% depth of invasion (DOI), any lesion size, and no suspicious adenopathy, and (2) to compare SLN mapped patients with patients treated with pelvic lymphadenectomy and no SLN mapping.

Methods: We evaluated all early-stage endometrial cancer cases in a surgery database (September 2010 to September 2013) with G1, G2 endometrial cancers who underwent robotic hysterectomy with staging pelvic lymphadenectomy and no para-aortic lymphadenectomy. Group A (n = 59) underwent SLN mapping followed by pelvic lymphadenectomy and group B (n = 128) underwent only pelvic lymphadenectomy. SLNs were analyzed with H&E staining followed by ultrastaging and immunohistochemistry. Demographic and clinicopathologic data were compared in univariate analyses. Pathology was risk-stratified per Gynecologic Oncology Group (GOG) 249 criteria.

Results: The cohort mean age was 61.8 ± 10.0 years (n = 187). All final pathology was endometrioid G1 or G2 and 12 (7.2%) of 167 cases were upstaged to stage IB on final pathology. There were no significant differences in FIGO stages between groups. Mean LN counts for groups A and B were 18.8 ± 8.3 and 18.0 ± 9.3, respectively. Mean SLN count for group A was 3.7 ± 2.2 and the bilateral detection rate was 86.4% (13.6% unilateral). No significant difference between groups for mean DOI (17.5 ±

19.6% vs19.4 ± 21.7%). DOI for Groups A and B were: no invasion (28.8% vs 25%), less than 50% (64.4% vs 64%), and more than 50% (8.5% vs 10.9%). Lymphovascular space invasion in the 2 groups was 8.5% versus 11.7% (*P* = .62). LN metastasis was detected in 5 (8.5%) of 59 in group A versus 3 (2.3%) of 128 in group B (*P* = .11). In group A, all metastases were low-volume metastases (1 with micometastasis and 4 with isolated tumor cells). Group B included 2 micro- and 1 macrometastasis. No metastases were detected in the 49 patients with noninvasive carcinoma, 6 (5%) of 120 metastasis with less than 50% DOI, and 2 (10.5%) of 19 cases with more than 50% invasion on final pathology (*P* > .05).

Conclusions: There was a statistical trend toward more LN metastasis in patients with G1, G2 endometrial cancer and frozen section less than 50% DOI using an SLN algorithm compared with patients treated with standard pelvic lymphadenectomy. An expansion of the database analysis to 275 cases would achieve statistical significance.

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304 - Poster

RNAseq identifies a unique molecular profile for high-grade serous carcinoma originating from serous tubal intraepithelial carcinoma

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Objectives: Evidence suggests that high-grade serous "ovarian" carcinoma (HGSOC) can originate from precursor lesions, termed *serous tubal intraepithelial carcinoma* (STIC), located in the distal end of the fallopian tube. However, it is unclear whether tumors originating from STIC lesions differ in biology or outcome from HGSOC without identifiable STIC. Therefore, we investigated whether tumors associated with STIC lesions exhibit a different gene expression profile than HGSOCs without STIC lesions using next-generation RNA-Seq analysis.

Methods: Tumor samples were obtained from 21 HGSOC patients undergoing tumor debulking surgery. Fresh tumor specimens were collected from ovary, fallopian tube, and abdominal metastasis for each patient. Tissue sections from each site were assessed for histopathology to confirm high-grade serous histology and tumor content (>50% tumor cellularity required for analysis). The presence or absence of STIC lesions in permanent section material submitted to surgical pathology was documented for each case. RNA extracted from frozen sections was used for determining expression profiles by RNA-Seq using the Illumina Hiseq flowcell platform. Data analysis included principle component analysis (PCA), hierarchical clustering, and differential gene expression analysis.

Results: PCA and hierarchical clustering demonstrated high variability among tumors from different patients. Paired samples from the ovary and abdominal metastatic site for individual patients were highly similar (8/9 patients). Paired samples from fallopian tube tumors (n = 6) were similar in 4 patients and different in 2 patients. Expression profiles of tumors with and without identiable STIC lesions were compared. Differential gene expression analysis identified 161 genes, including several in growth receptor pathways, as differentially expressed (FDR <0.1, fold change > ±1.6) between tumors with STIC (7 patients) and without STIC (12 patients) (Fig 1).

Conclusions: Our data suggest that HGSOCs associated with STIC lesions possess a unique molecular profile that may provide insight into pathogenesis and help to identify novel targeted therapies.

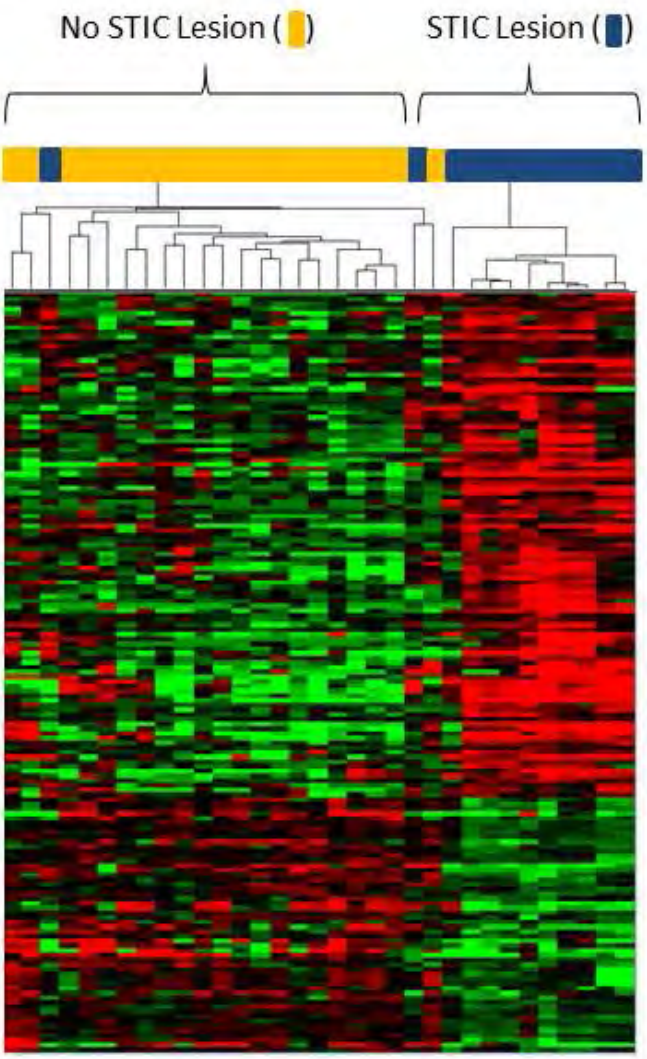

Fig. 1
Heatmap of differentially expressed genes between HGSOC with and without STIC.

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305 - Poster
Menopause-related quality of life following risk-reducing surgery and correlation with satisfaction with surgical decision
S.A. Thomas[a], O. Moskowitz[a], B. Horton[a] and S.C. Modesitt[b]. [a]*University of Virginia School of Medicine, Charlottesville, VA, USA,* [b]*University of Virginia Health System, Charlottesville, VA, USA*

Objectives: Women with a significant hereditary risk for developing breast or ovarian cancers may choose to undergo a risk-reducing salpingo-oophorectomy (RRSO). Women undergoing an RRSO experience early surgical menopause. The objectives of this study were to assess the quality of life (QOL) after RRSO, to determine satisfaction with the decision to undergo surgery and to assess for potential associated risk factors for regret or worse QOL after surgery.

Methods: Women with a history of RRSO in the past 10 years were identified from the High Risk Breast/Ovarian Cancer clinic at a single institution after obtaining institutional review board approval. Patient consent was obtained and they then completed the QOL questionnaire and a demographic/health status survey, and additional clinical data were abstracted from medical records. The menopausal QOL was assessed using a validated Likert-scale questionnaire (MENQOL) regarding menopausal symptoms with respective sexual, psychosocial, vasomotor, and physical domains. MENQOL scores assessed the

presence of symptoms and degree to which the participant is bothered by the symptoms, with higher values denoting a worse QOL. Descriptive measures with 95% confidence intervals were calculated.

Results: Fifty-two women enrolled in the study, with a mean age of 48.3 years at the time of the study and 44.4 years at the time of the RRSO. Forty-six participants were satisfied with their surgical decision and the mean QOL score for all the participants was 3.19 (95% CI 2.9–3.5). Participants who were satisfied with having the RRSO had better QOL scores compared with those who were dissatisfied (3.19 vs 5.88) and were significantly older at the time of surgery than women who were dissatisfied/unsure (46.8 vs 39.3; *P* = .042). When examined according to use of hormone replacement therapy versus alternative therapy, there was no significant difference in QOL scores for participants. Participants with a history of depression had worse QQL score (3.73 vs2.86; *P* = .034). Furthermore, on the psychosocial QOL domain, participants with a history of depression had significantly worse QOL (3.94 vs 2.71; *P* = .015).

Conclusions: The vast majority of women undergoing RRSO were satisfied with their choice; however, a history of depression was significantly associated with worse QOL scores. Women who were dissatisfied/unsure about their decision to undergo surgery were younger at surgery and had worse menopause-related QOL symptoms, regardless of the use of hormone replacement therapy.

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306 - Poster

Prospective validation of an intraoperative algorithm to determine the extent of surgical staging in early endometrial cancer

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Objectives: To prospectively validate an intraoperative surgical staging algorithm to stratify patients with endometrial cancer by risk of lymph node metastasis.

Methods: Patients with endometrial cancer clinically confined to the uterus were prospectively enrolled at a single, high-volume cancer center between January 2012 and June 2015. Patients were stratified intraoperatively into 2 groups based on risk of nodal involvement using cell type, tumor grade, myometrial invasion, and tumor size in accordance with an established protocol from the Mayo Clinic. Frozen section analysis was performed as indicated and intraoperative predictions were compared with final paraffin-based histopathologic findings. Low-risk patients received extrafascial hysterectomy with bilateral salpingo-oophorectomy; high-risk patients received complete surgical staging including bilateral pelvic and para-aortic lymphadenectomy. Statistical analysis was performed comparing intraoperative and postoperative risk assessment with cancer recurrence and nodal metastases.

Results: Of the 200 patients enrolled, 194 underwent surgery and 190 had complete data for analysis. The study population had a mean age of 69 years, body mass index of 35, and 98% were white. Of these, 89% (173/194) were endometrioid cancers, with 108 grade 1, 52 grade 2, and 34 grade 3 tumors. The mean follow-up time was 20 months (range, 3–45 months). The intraoperative algorithm identified 133 (70%) high-risk and 57 (30%) low-risk cancers. Three of 133 high-risk cancers were later downgraded to low risk based on final pathology. All 7 patients with lymph node metastases or recurrence were identified as high risk: 5 nodal metastases, 2 cancer recurrences, and 1 both. Of the 57 cancers identified as low risk, 12 were later upgraded to high risk on final pathology because of the depth of myometrial invasion (n = 6) or tumor grade (n = 6). No patient with low-risk cancer developed recurrence. The intraoperative algorithm demonstrated 100% sensitivity (8/8) and 31% specificity (57/182) as determined by positive lymph nodes and/or disease recurrence.

Conclusions: In this prospective investigation, intraoperative stratification of endometrial cancer is a useful strategy to identify patients at high risk for lymph node metastases or recurrence. The current algorithm has low specificity, and modifications are needed to better tailor the extent of surgery to match the disease risk.

Table 1
Results of intraoperative algorithm.

Intraoperative algorithm	Lymph node positive	Disease recurrence	Total patients
High Risk*	6	3	133
Low Risk	0	0	57

* Note: one patient had both +LN and + disease recurrence

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307 - Poster
Validation of the 'surprise question' in gynecologic oncology: comparing physicians, advanced practice providers, and nurses
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Objectives: The "surprise question": "Would you be surprised if this patient died in the next year?" has been validated in nongynecologic cancer as highly predictive of 12-month morality. It has been used as a major inclusion criterion in studies showing benefit to specialized palliative care (SPC). It has not been studied in the gynecologic oncology (GO) population or with nonphysician providers. Our objectives were to (1) evaluate the prognostic significance of the surprise question in GO patients, and (2) compare the performance of the surprise question among different provider groups.

Methods: The surprise question was asked of a group of 18 GO providers from a single academic institution (7 physicians, 7 advanced practice providers [APP], and 4 chemotherapy nurses [registered nurses, RNs]) regarding their patients currently receiving radiation or chemotherapy. Demographic and clinical data were abstracted from chart review and mortality data were collected 12 months later.

Results: The 263 patients included had a median age of 64 years and the majority were white (94%). The most common cancer was ovarian (50%); 58% had stage III/IV disease and 46% had recurrent disease. There were 54 deaths (1-year mortality rate of 20.5%). Risk of mortality was significantly higher for patients with a response of "No" to the surprise question from the physician (40% vs 10.6%, $P < .01$), APP (43.2% vs 7.6%, $P < .01$), and RN (50.8% vs 13.1%, $P < .01$). The unadjusted odds ratio for death within a year associated with a "No" answer to the surprise question by the physician, APP, and RN were 5.6 ($P < .001$), 9.21 ($P < .001$), and 6.86 ($P < .001$), respectively. The APP group had the highest sensitivity (79.5%), whereas the RN group had the best specificity (75.6%).

Conclusions: The surprise question is a simple, feasible, and effective tool to identify GO patients who have a greatly increased risk of 12-month mortality when administered by physicians, APPs, or chemotherapy nurses. This one question screen could be used to identify patients appropriate for early referral to specialized palliative care or patients in whom to consider initiating conversations about goals of care and advanced care planning.

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308 - Poster
Contribution of age to clinical trial enrollment and tolerance with ovarian cancer
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Objectives: Increasing age has been correlated with shorter survival in ovarian cancer (OC) patients, a finding attributed to diminished ability to tolerate standard therapy. Elderly patients, however, are less likely to be enrolled in trials, and thus data evaluating their tolerance of and response to front-line treatment in trials are limited. Our aim was to describe how elderly patients enrolled in OC clinical trials fare, with respect to toxicity and response, compared with younger women.

Methods: We performed a retrospective cohort study of all OC patients enrolled in front-line chemotherapy trials at our institution between 2000 and 2013. We dichotomized patients by age: less than 70 years and 70 years and older. Clinical and

pathologic factors were compared between groups, and progression-free and overall survival were calculated. To assess tolerance of chemotherapy, we compared number of delays and dose modifications as well as heme and non-heme toxicities. SAS 9.3 was used for statistical analyses.

Results: A total of 357 patients were enrolled in clinical trials for primary treatment of OC during the study period; 85 were of age 70 years or older. Both groups had similar ethnicity (P = .38), stage (P = .11), performance status (P = .097), CA-125 (median 330 vs 225, P = .26), and histology (P = .052). Elderly patients completed a comparable number of cycles during first-line chemotherapy (mean 5.7 vs 6.1, P = .08) and had similar rates of dose modifications (1.1 vs 1.1, P = .79) and delays (0.6 vs 1, P = .43). Heme toxicities were statistically not different but appeared higher among older patients with grade 4 ANC in 19% vs 31% (P = .12) and grade 4 thrombocytopenia in 4% vs 14% (P = .055). Grade 2 or higher neuropathy (67% vs 80%, P = .14) and other non0heme toxicities (≥grade 3: 12% vs 11%, P = 1.00) followed a similar trend. On multivariate analysis, age 70 years or more (HR 1.58, 95% CI 1.13–2.22, P = .008), stage III/IV (HR 6.35, 95% CI 2.59–15.54, P < .0001), and residual disease (HR 2.14, 95% CI 1.49–3.08, P < .0001) were independently predictive of overall survival.

Conclusions: Our data support the correlation between advancing age and decreased survival with OC. This finding has been attributed to undertreatment, inherently more aggressive disease, or toxicity-related treatment limitations. In this analysis of clinical trial patients, all received, at minimum, standard of care chemotherapy with no great differences in tolerance to therapy as both cohorts experienced similar rates of toxicities, delays, and dose modifications. Further research is needed to identify mechanisms to compensate for the disparity that age imposes on outcome.

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309 - Poster

Hospitals with high-volume ovarian cancer care are associated with more radical cytoreductive surgery and fewer complications

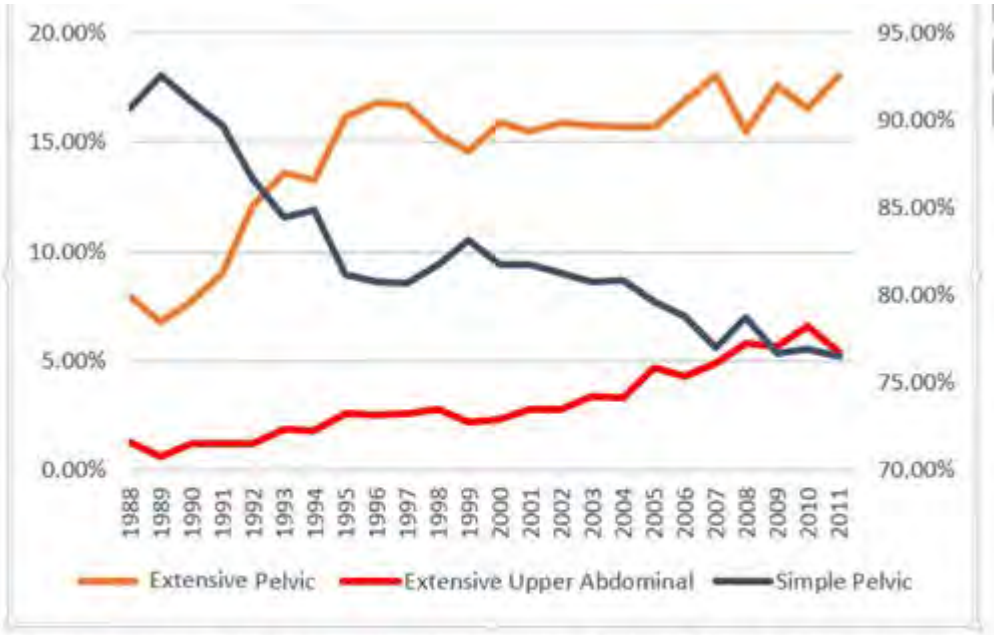
A.K. Sinno[a], X. Li[b], R.E. Thompson[b], E.J. Tanner III[a], R.L. Stone[a], S.M. Temkin[a], A. Nickles Fader[a], D.S. Chi[c] and K.C. Long[c]. *[a]Johns Hopkins Hospital, Baltimore, MD, USA, [b]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, [c]Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objectives: To describe the US national trends and factors associated with radicality of cytoreductive surgery (CRS) in women with advanced ovarian cancer (OC).

Methods: An analysis of the National Inpatient Sample database was performed. All unique admissions from 1988 to 2011 for patients with advanced OC undergoing laparotomy with "oophorectomy" plus "excision/destruction of peritoneal lesion" were identified. CRS radicality was defined as simple pelvic (SP), extensive pelvic (EP), and extensive upper abdominal (EUA; Figure). Hospitals were categorized into equal volume-based tertiles (low, medium, high) based on the number of OC surgeries performed annually. Annual trends in CRS radicality were analyzed. Patient- and hospital-specific factors were examined for their associations with CRS radicality and complications in a contemporary period between 2007 and 2011.

Results: In total, 56,414 admissions were analyzed. The rate of EP and EUA resections increased significantly over time (8% to 18.1%, P < .01; 1.3% to 5.4%, P < .001, respectively; Figure 1). On multivariate analysis, patients were more likely to undergo EUA if they were operated on in the Northeast United States (referent), at urban (OR 2.3, 95% CI 1.07–4.97), or large hospitals with more than 100 beds (OR 1.4, 95% CI 1.01–2.19), or if they had private insurance (OR 1.45, 95% CI 1.09–1.95). High-volume hospitals performed more EUA resections (OR 2.65, 95% CI 1.82–3.83) and had fewer complications compared with low- and medium-volume hospitals performing EUA (10.2%, 21.2%, and 21.7%, respectively; P = .01). Specifically, patients receiving care at high-volume hospitals experienced lower rates of hemorrhage, vascular or nerve injury, prolonged hospitalization for more than 7 days and non-routine discharge than at low- and medium-volume hospitals (P < .05).

Conclusions: The US rate of radical cytoreductive surgery for advanced OC increased significantly during the time frame evaluated. Patient and health care system–specific factors were associated with surgical radicality. At high-volume hospitals treating OC, patients received more radical surgery with fewer complications than when radical surgery was performed at low-and medium-volume hospitals. These results support further study of a centralized OC care model.



Simple pelvic: procedures not classified as extensive pelvic or extensive upper abdominal. Extensive Pelvic: procedures that include small bowel resection, rectosigmoid resection, colectomy, bladder resection. Extensive upper abdominal: procedures that include splenectomy, cholecystectomy, liver resection, diaphragm resection.

Fig. 1
Trends in Simple Pelvic (Right Axis), Extensive Pelvic and Extensive Upper Abdominal Resections (Left Axis), for Advanced Ovarian Cancer 1988-2011.

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310 - Poster
Minimal access surgery compared with laparotomy for secondary cytoreduction in patients with recurrent ovarian carcinomas
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Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: To assess outcomes in patients who undergo secondary surgical cytoreduction (SSCR) using minimal access approaches compared with those who undergo laparotomy.

Methods: All consecutive patients with recurrent ovarian carcinomas (ROCs) who underwent SSCR from January 5, 2009, to June 14, 2014, were identified. Planned laparoscopic (LSC) and robotically assisted (RBT) cases were grouped together as the minimal access surgery (MAS) cohort. Intent-to-treat analyses were undertaken; cases converted to LAP were analyzed within the MAS cohort. Selection for MAS or LAP was based on surgeon preference. To attempt to minimize selection bias when comparing MAS and LAP outcomes, preoperative imaging was reviewed for all LAP cases to identify potential MAS candidates. Appropriate statistical testing was used.

Results: A total of 170 cases were identified (131 LAP, 8 LSC, 31 RBT). Of these, 145 (85%) were serous carcinomas. Carcinomatosis was noted on preoperative imaging in 25 (15%) and ascites in 5 (3%). Six (15%) of the 39 MAS cases were converted to laparotomy. A complete gross resection (CGR) was achieved in 155 (91%) cases. With a median follow-up of 26.4 months (range, 0.3–74.6 months), the median progression-free survival (PFS) was 24.8 months (95% CI 18.3–31.3 months). Median overall survival (OS) was not reached. Of the LAP cases, 68 (52%) were felt to be potential MAS candidates after review of preoperative images. The following analyses only include these 68 LAP cases and the 39 MAS cases. Median age was the same. Median body mass index was 28.7 kg/m^2 (range, 21.2–43.4 kg/m^2) for MAS and 26.8 kg/m^2 (range, 17.2–49 kg/m^2) for LAP (P = .3). Median operative time was 186 minutes (range, 56–482 minutes) for MAS compared with 213 minutes (range, 64–539 minutes) for LAP (P = .2). CGR was achieved in 37 (95%) MAS and 63 (93%) LAP cases (P = 1.0). Median estimated

blood loss was 50 mL (range, 5–500 mL) for MAS and 150 mL (range, 0–1,500 mL) for LAP (*P* = .001). Median length of stay was 1 day (range, 0–23 days) for MAS and 5 days (range, 1–21 days) for LAP (*P* < .001). Eleven MAS cases (28%) were discharged home the same day. Complications occurred in 3 (8%) MAS cases versus 15 (22%) LAP cases (*P* = .06). The 2-year PFS was 56.1% (standard error [SE] 9%) and 63.5% (SE 6%) in MAS and LAP cases, respectively (*P* = 1.0). The 2-year OS was 92.2% (SE 5.4%) and 81.4% (SE 5.5%) in MAS and LAP cases, respectively (*P* = .7).

Conclusions: MAS for SSCR is feasible in properly selected cases. MAS is associated with favorable perioperative outcomes and seems to result in similar oncologic outcomes.

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311 - Poster

Evaluation of metachronous breast and endometrial cancers before and after routine adjuvant tamoxifen usage

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Objectives: The interval between diagnosis of breast (BC) and endometrial (EC) cancer is not well established in women with metachronous primary tumors. We sought to examine this interval and identify associations with treatment-related and clinicopathologic factors.

Methods: We identified 141 patients who developed both cancers from 1966 to 2013. Patients were divided into 2 groups: group 1-BC first; group 2-EC first. Subanalysis performed of group 1 patients (n = 59) was stratified around adjuvant tamoxifen usage: pre- and post-1990 breast cancer diagnosis.

Results: Groups 1 and 2 had 59 and 82 patients, respectively. The mean interval was comparable (76 vs 74 months; *P* = .861). Subanalysis divided group 1 into pre- (n = 27) and post-1990 (n = 32) and resulted in different mean intervals between diagnosis of metachronous cancers (106 vs 50 months, respectively [*P* = .042]). Median progression-free survival (PFS) and overall survival (OS) for EC were longer in the pre-1990 group (PFS: 51 vs 26 months [*P* = .169]; OS: 59 vs 27 months [*P* = .190]). Median PFS and OS for BC were also longer in this group (PFS: 147 vs 109 months [*P* = .005]; OS: 166 vs 114 months [*P* < .001]).

Conclusions: Our data indicate that the mean interval between the diagnosis of EC and BC was approximately 6 years. Disease-specific EC survival was worse for patients with a prior diagnosis of BC. Stratification around implementation of tamoxifen usage shows comparable grade and stage but different intervals and survival rates, suggesting resulting effects from adjuvant therapy for breast cancer. These results are useful in counseling women at risk.

Table 1a

Patient Characteristics.

		Group 1:BC first	Group 2:EC first
Overall, n (%)		59 (41.8)	82 (58.2)
Age at diagnosis of the first cancer	Mean	61 (Range 26-78)	63 (Range 32-87) (p=0.15)
Time interval between diagnosis:			(p=0.861)
	Mean	2269 days or 76 mo	2208 days or 74 mo
	Median	1742 days or 58 mo	1585 days or 53 mo
	Range	7-11852 days	1-8477 days

EC PFS		51	26 (p=0.169)
EC OS		59	27 (p=0.190)
BC PFS		147	109 (p=0.005)
BC OS	Median	166	114 (p<0.001)
Combined OS		**166**	**114 (p<0.001)**
Cause of Death	From Cancer	14* (51.9)	10** (26.1)
	Other Cause	12 (44.4)	7 (30.4)
	Alive	1 (3.7)	8*** (43.5)

*7 BC, 5 EC, 2 not differentiated; **4 BC, 5 EC, 1 not differentiated; *** 1 of 8 with recurrent disease at data collection

Table 1b

Sub Table 1b: Sub analysis of Group 1, BC first, based on date of FDA approval of Tamoxifen for primary prevention of BC and treatment of advanced BC in 1990.

Patient Characteristics		**BC Prior to 1990**	**BC After 1990**
Overall, n (%)		27 (45.8)	32 (54.2)
Mean Age at Diagnosis of first cancer		60	61
		Number or Patients (%)	
EC Grade	1	12 (44.4)	11 (34.4)
	2	6 (22.2)	8 (25.0)
	3	9 (33.3)	13 (40.6)
EC Stage	Local	18 (66.7)	20 (62.5)
	Regional	4 (14.8)	5 (15.6)
	Distant	5 (18.5)	7 (21.9)
Time interval between diagnosis:			**(p=0.042)**
	Mean	3185 days or 106 mo	1497 days or 50 mo
	Median	2222 days or 74 mo	1244 days or 41 mo
	Range	46-11852 days	7-4025 days
Survival time in months			
EC PFS		51	26 (p=0.169)
EC OS		59	27 (p=0.190)
BC PFS	Median	147	109 (p=0.005)
BC OS		166	114 (p<0.001)
Combined OS		**166**	**114 (p<0.001)**
Cause of Death	From Cancer	14* (51.9)	10** (26.1)
	Other Cause	12 (44.4)	7 (30.4)
	Alive	1 (3.7)	8*** (43.5)

*7 BC, 5 EC, 2 not differentiated; **4 BC, 5 EC, 1 not differentiated; *** 1 of 8 with recurrent disease at data collection

312 - Poster

'Ask me, do you want to know the big picture?' Gynecologic oncology patient and provider perspectives on discussing prognosis

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Objectives: Prognosis affects decision making by providers and patients, and accurate understanding of prognosis may help avoid futile end-of-life care. Gynecologic oncology (GO) patient and provider perspectives on discussing prognosis have not been described. We sought to analyze patient and provider preferences regarding timing, amount, and type of information included in discussions of prognosis.

Methods: Semi-structured qualitative interviews regarding palliative care were conducted with 19 GO providers (7 physicians, 7 advanced practice providers, 5 nurses) and 29 patients with advanced or recurrent gynecologic cancer from an academic medical center. Communication about prognosis was one interview domain. Two coders independently and iteratively analyzed transcripts using qualitative analysis.

Results: Median patient age was 61 years, the most common cancer was ovarian (59%), and 90% had recurrent disease. Providers were 74% women, with a median of 15 years in practice. Themes included patients wanting frank discussions about prognosis; interest in information about the future was not limited to life expectancy. Preferences regarding timing and content were highly individualized. All clinicians reported having prognosis conversations. Providers saw these conversations as part of their clinical role, though they found them difficult. Providers commonly equated prognosis purely with life expectancy. Providers recognized variation among patients in preferences regarding these conversations, but did not report directly asking patients about their preferences.

Conclusions: Patients with advanced gynecologic cancer want frank discussions about what the future might hold, often including but not limited to life expectancy. Providers see these discussions as being within their scope of practice but find them difficult. Opportunities exist for provider education regarding communication skills to assess patient preferences for when and what information to give. Given that all clinicians report having these conversations, education should be provided to physicians, nurses, and advanced practice providers.

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313 - Poster

Robotic surgery for endometrial cancer (EC): Identifying risk factors for surgical complications using the Clavien-Dindo classification system

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Objectives: Accurately reporting and grading surgical complications is essential to quality improvement in robotic pelvic surgery. The Clavien-Dindo (C-D) classification system is a validated and reproducible tool that ranks complications in terms of the therapeutic interventions necessary to correct the complication and their potential for residual disability. We sought to identify risk factors responsible for complications in EC patients undergoing robotic pelvic surgery using the C-D classification system.

Methods: We undertook a retrospective cohort study of 156 EC patients who underwent robotic hysterectomy and lymphadenectomy by 4 experienced gynecologic oncologists between April 2008 and May 2014 in a tertiary care facility. Complications as rated by the C-D classification system were analyzed using univariate and multivariate regression to identify predictors.

Results: The mean body mass index (BMI) was 35.7 kg/m^2 (range, 20–59 kg/m^2), mean age was 64.5 years (range, 26–92 years). Complications occurred intraoperatively in 14.1% (n = 22), postoperatively in 28.8% (n = 45), and according to C-D definitions in 30.1% (n = 49). On multivariate logistic regression analysis, elevated BMI, intraoperative blood loss, and omentectomy were significant predictors for intraoperative complications (Table 1). Conversions occurred in 12.8% (n = 20). On multivariate logistic regression analysis, predictors for conversion to laparotomy were omentectomy, adhesiolysis, FIGO stage, elevated BMI, and increased intraoperative blood loss. Conversion to laparotomy and increased parity were

independent predictors for postoperative complications. Predictors for C-D grade 3 or higher complications (defined as complications requiring active surgical, endoscopic, or radiologic intervention [grade 3] or intensive care unit care [grade 4]) were conversion to laparotomy, increased parity, and increased operative time.

Conclusions: Increased operative time, conversion to laparotomy, and increased parity were all independently associated with grade 3 or higher complications by the C-D classification system. Increased parity was unanticipated. To inform quality improvement strategies, further analysis of the mechanisms by which this factor contributes to surgical morbidity is currently under way.

Table 1
Multivariate logistic regression for predictors of intra-operative & postoperative complications, Clavien-Dindo classification ≥3 & conversions.

	Intra-operative complications		Postoperative complications		Clavien-Dindo Classification >3		Conversions	
	P value	**Odds Ratio (95%CI)**	**P value**	**Odds Ratio (95%CI)**	**P value**	**Odds Ratio (95%CI)**	**P value**	**Odds Ratio (95%CI)**
Omentectomy	0.022	17.19 (1.52 - 194.88)					0.032	17.02 (1.28 – 226.51)
Body mass index	0.006	1.12 (1.03 – 1.21)					0.026	1.1 (1.01 – 1.19)
Estimated blood loss	0.00001	1.01 (1.007 – 1.019)					0.00002	1.014 (1.008 – 1.02)
Diabetes type II			0.01	0.23 (0.07 – 0.69)				
Conversion			0.002	6.87 (2.08 – 22.73)	0.011	4.76 (1.44 – 15.73)		
Parity			0.014	1.48 (1.08 – 2.03)	0.023	1.48 (1.06 – 2.06)		
Preoperative Hemoglobin			0.028	0.71 (0.52 – 0.96)				
Operative time					0.021	1.009 (1.001 – 1.016)		
Adhesiolysis							0.027	5.8 (1.22 – 27.61)
FIGO stage							0.02	3.04 (1.19 – 7.79)

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314 - Poster
Treatment patterns and outcomes for bowel obstruction in elderly ovarian cancer patients: A population-based analysis
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Objectives: To assess treatment patterns and outcomes for elderly ovarian cancer patients who develop bowel obstruction (BO).

Methods: All patients with stage II–IV ovarian cancer, aged 66 years or older, who were admitted for BO 6 months or more after cancer diagnosis from 2002 to 2011 were identified from the Surveillance, Epidemiology and End Results Program (SEER) Medicare database. Patients were categorized based on their interventions: surgery, gastrostomy or jejunostomy (G/J) tube, or somatostatin. Those who had a G/J tube placed at the time of failed surgery were analyzed as part of the G/J tube group. Management strategies of BO and outcomes were compared using the χ^2 test and a Cox proportional hazards regression model.

Results: Of 9,016 women with ovarian cancer, 1,154 met inclusion criteria. A total of 131 patients (11%) were treated with a G/J tube, 464 (41%) underwent a surgical correction attempt (with 63 of them failing and getting a G/J tube), 131 (11%) were managed medically with somatostatin, and 428 (37%) received none of the above. There was no difference in age, race, comorbidity, stage, histology, or region of care between patients who had surgery and those had a G/J tube. Of those patients who underwent surgery, 34% subsequently received chemotherapy, compared with 11% of those who received a G/J tube (OR 4.2, 95% CI 2.5–6.9), with a median time to chemotherapy of 70 and 35 days, respectively ($P = .006$). Of those patients treated with a G/J tube, 49% were admitted to hospice within 30 days of their intervention, compared with 17% treated surgically (OR 5, 95% CI 3.4–7.3). Median time to hospice was 14 days for patients in the G/J tube group and 109 days for the surgery group ($P < .0001$). Median survival was longer for patients who had surgery compared with those who had G/J tube placement (5.8 months [95% CI 4.6–7.2 months] vs 1.4 months [95% CI 1.2–1.7]; HR 0.31, 95% CI 0.24–0.36, $P < .0001$). This difference remained significant after adjusting for key covariates on multivariate analysis (HR 0.29, 95% CI 0.24–0.36, $P < .0001$). Patients who failed surgery and had a G/J tube placed had similar survival compared with those initially managed with a tube (2.5 and 1.2 months, respectively).

Conclusions: Surgery may benefit a small subset of carefully selected elderly women with ovarian cancer who develop BO. Efforts to identify those who derive no benefit may reduce the rate of unnecessary laparotomy. Given the limited survival outcomes of this population, patient preferences should be evaluated in future studies assessing the management of BO.

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315 - Poster

The role of preoperative radiation therapy in endometrial cancer

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Objectives: To describe the trend of preoperative radiation therapy usage over time in the management of endometrial cancer, and to investigate its association with 5-year survival.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried to perform a retrospective analysis of women with all stages of endometrial cancer between 1973 and 2012. Use of preoperative radiation therapy is stratified by year. Overall 5-year survival was determined using the Kaplan-Meier method with calculated 95% confidence intervals.

Results: Of 54,135 patients with endometrial cancer, 20.6% received preoperative radiation therapy between 1973 and 2012. The overall 5-year survival was 76.1% (95% CI 75.3%–76.9%) in the cohort receiving preoperative radiation therapy compared with 74.2% (95% CI 73.7–74.6) in the control cohort not receiving preoperative radiation therapy. Only 0.58% of patients with endometrial cancer received preoperative radiation therapy after the year 2000. Of these patients, 53.8% had regional disease (rather than localized or distant) and were more likely to be African American (OR 1.9, $P < .05$). In this more contemporary cohort, 41.1% of patients younger than 60 years and 58.8% of those older than 60 years received preoperative radiation. The overall 5-year survival for patients receiving preoperative radiation was 56.3% compared with 77.6% in the control cohort after the year 2000.

Conclusions: The use of preoperative radiation therapy has diminished over the years. Currently, patients with endometrial cancer who have regional disease, are older than 60 years, or are African American are more likely to get preoperative radiation. Overall, however, there was no clinical significance in 5-year survival between endometrial cancer patients who received preoperative radiation compared with those who did not. When only looking at a more contemporary cohort after the year 2000, a negative association begins to emerge between preoperative radiation and 5-year survival.

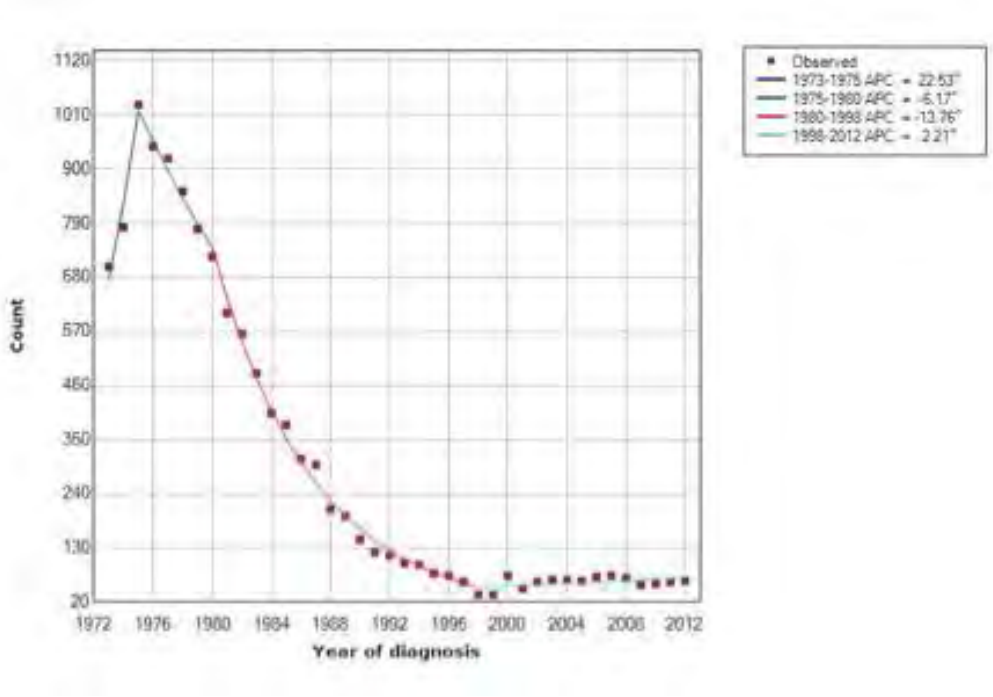

Fig. 1
Trend of Pre-operative Radiation Therapy in Endometrial Cancer.

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316 - Poster
Sentinel lymph node biopsy for patients with low-risk endometrial adenocarcinoma: A cost-effectiveness analysis
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Objectives: Although patients with grade 1 and 2 endometrial cancer have a low risk of metastatic disease, many patients undergo a complete pelvic and para-aortic lymphadenectomy (LND). LND has been associated with increased operating time, additional cost, and lower extremity lymphedema. The objective of this study was to determine the most cost-effective strategy of lymph node assessment for patients with low-risk endometrial adenocarcinoma.

Methods: A cost-effectiveness model compared 3 methods of surgical staging for patients with grade 1 or 2 endometrial adenocarcinoma: (1) routine pelvic and para-aortic LND for all patients, (2) selective LND based on depth of myometrial invasion (>50%) and intraoperative tumor size (>2 cm) (Mayo criteria), or (3) sentinel lymph node biopsy (SLNB). If a sentinel lymph node was not identified, an LND was performed. All patients had a robotic-assisted hysterectomy. Risk of lymphedema, probability of positive lymph nodes, and 5-year overall survival (OS) were estimated using published data. The costs of surgery, pathology, lymphedema treatment, and adjuvant therapy were calculated using 2015 Current Procedural Terminology (CPT) codes and Medicare reimbursement rates. Incremental cost-effectiveness ratios (ICERs) were calculated as the cost per additional 5-year survivor.

Results: For 40,000 patients with grade 1 or 2 endometrial adenocarcinoma, selective LND was the least expensive strategy at a cost of $185.5 million compared with $190.8 million for routine LND. SLNB was the most expensive at $205.5 million. Five-year OS was similar for selective LND and routine LND (90.1% vs 90.2%). Compared with selective LND, routine LND resulted in 14 additional 5-year survivors with an ICER of $713,708 per survivor. Five-year OS for SLNB was 90.7%. SLNB resulted in 215 additional 5-year survivors compared with routine LND with an ICER of $68,348 per survivor. SLNB had the lowest incidence of lymphedema at 8.6% compared with 15.3% for selective LND and 21.2% for routine LND.

Conclusions: SLNB is the most expensive and most effective strategy for lymph node assessment in patients with low-risk endometrial adenocarcinoma. SLNB is preferred with an ICER of $68,348 per additional 5-year survivor and the lowest incidence of lymphedema. Although routine LND is a reasonable alternative, it has the highest risk of lymphedema.

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317 - Poster

HPV vaccination practices among American Indian/Alaska Native providers

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Objectives: Cervical cancer is a preventable disease that disproportionately affects medically underserved communities. Attempts at prevention via human papillomavirus (HPV) vaccination are limited by poor rates of initiation and completion. Little is known about the knowledge-base and attitudes of medical providers for patients from the American Indian/Alaska Native (AI/AN) community. The present study elucidates the knowledge and attitudes of these medical providers regarding the HPV vaccination series.

Methods: A 4-part, 30-question survey was distributed in-person and online to healthcare-provider members of the Association of American Indian Physicians (AAIP). Information regarding demographics, practice patterns, general vaccination practices, knowledge regarding, and personal practice with the HPV vaccination series were queried and analyzed.

Results: There were 60 survey responses with a response rate of 26%. Most were of AI/AN ethnicity (78%) and a plurality practiced family medicine (46%). Respondents affirmed a willingness to provide both general vaccinations (>90%) and the HPV series to both females (98%) and males (88%). Providers affirmed the safety and efficacy of the HPV series (90%). However, providers report the belief that less than half of eligible males initiate and complete the vaccination series, while more than half of eligible females initiate and complete the series. Physician-perceived barriers to vaccination uptake included lack of parental awareness, parental misconceptions regarding the appropriate timing of vaccination, and concerns regarding cost and efficacy. Physicians reported that improved vaccination rates could be achieved by improved follow-up, dedicated staff, and culture-specific AI/AN educational materials.

Conclusions: Similar to non-AI/AN groups, physician comfort level with vaccination increased with the age of the patient and was most likely to recommend vaccination at an annual examination or based on patient or parent inquiry. Physicians felt that culturally specific educational materials may help increase vaccination uptake, suggesting the need for targeted, culturally specific outreach and education.

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318 - Poster

Early warning score: An indicator of adverse outcomes in postoperative patients on a gynecologic oncology service

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Objectives: In 2014, our hospital implemented an early warning score (EWS) system, which calculates an aggregate score based on vital signs and level of alertness. EWS of 8 or higher is associated with a mortality rate of 10% or greater in acute medical admissions. Postoperative pain or pain management may elevate EWS and decrease its specificity, therefore we evaluated EWS in postlaparotomy patients on a gynecologic oncology service.

Methods: This retrospective cohort included gynecologic oncology patients who had a laparotomy between September 2014 and July 2015. Patients were categorized by highest EWS over admission: EWS less than 5, EWS of 5 to 7, and EWS of 8 or higher. The primary outcome was a composite of death, transfer to the intensive care unit (ICU), rapid response team (RRT) activation, major cardiac event, pulmonary embolus (PE), sepsis, and reoperation. Planned ICU admissions were not included in the composite. Secondary outcomes were length of stay (LOS), 30-day readmission, and transfusion. Groups were compared using the χ^2 test for trend, analysis of variance, and Kruskal-Wallis tests, as appropriate. A receiver operating characteristic (ROC) curve was created to estimate the association of EWS with the composite outcome. Sensitivity and specificity of EWS for the composite outcome was determined.

Results: A total of 411 patients were included: 217 (52.8%) with EWS less than 5, 150 (36.5%) with EWS of 5 to 7, and 44 (10.7%) with EWS of 8 or higher. Twenty-five patients (6.1%) had the composite outcome, including 2 deaths, 12 ICU admissions, 9 RRT activations, 2 cardiac events, 4 PEs, 14 sepsis diagnoses, and 3 reoperations. Increasing age, cancer diagnosis and stage, and bowel surgery were associated with higher EWS. The composite outcome occurred in 34.1% of patients with EWS of 8 or higher versus 6.7% with EWS of 5 to 7 and 0% with EWS less than 5 ($P < .01$). EWS of 8 or higher was associated with longer mean LOS (8.1 vs 4.6 vs 3.5 days, $P < .01$), readmission (25.0% vs 12.7% vs 6.9%, $P < .01$), and transfusion (29.6% vs 14.8% vs 5.5%, $P < .01$). For the primary outcome, the area under the ROC curve was 0.91 (95% CI 0.87–0.96, Figure 1). EWS of 8 had 60.0% sensitivity and 92.5% specificity for the primary outcome.

Conclusions: In gynecologic oncology patients, EWS of 8 or higher after laparotomy is associated with a significant increase in postoperative adverse outcomes, longer LOS, and more readmissions and transfusions. Future studies should evaluate the ability of EWS to predict and prevent these outcomes.

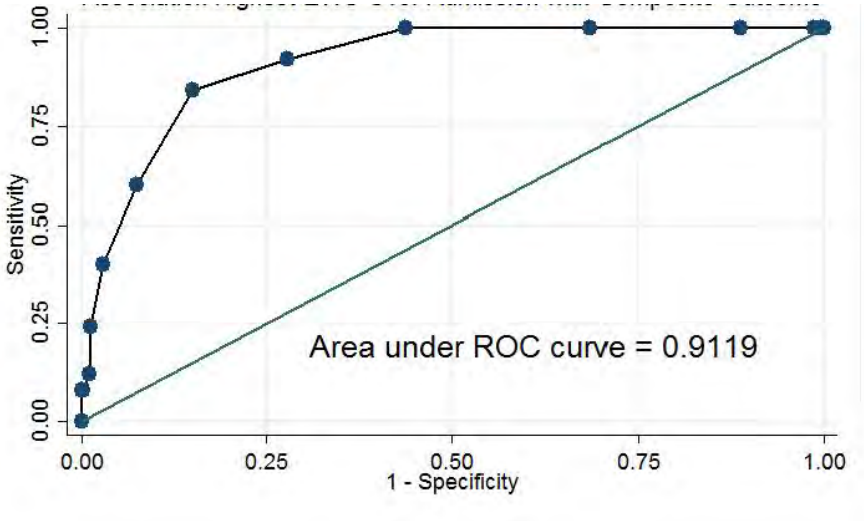

Fig. 1
Receiver Operator Characteristics Curve: Association Highest EWS Over Admission with Composite Outcome.

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319 - Poster
Supportive care plans: Linking patient-reported outcomes to evidence-based supportive care across the cancer continuum
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Objectives: The negative impact of deleterious symptoms on patient outcomes is well-documented. The goal of this study was to explore feasibility and usability of a novel supportive care planning technology (Carevive® CPS) linking patient-reported symptom outcomes (PROs) with management.

Methods: This prospective, multicenter pilot study at a large community cancer center enrolled gynecologic cancer patients (n = 49) and their providers (n = 3). Patients completed and received electronically generated supportive care plans during office visits. Study outcomes included usability and satisfaction (1–5 scales) and care plan referrals generated individually from PROs.

Results: Of the total 49 patients who enrolled, 67% (n = 33) completed posttest measures. All 3 providers also completed posttest measures. Patients and providers reported high overall satisfaction (mean 3.9 and 4.5, respectively). Provider satisfaction was highest with platform ability to identify/assess patient symptoms as well as address patient concerns/distress derived from patient-reported outcomes (mean 4.7 each). Both patients and providers reported high

system usability (mean 4.0 and 4.3). Care plan data for 90% of patients (n = 44) were also analyzed (19 with ovarian cancer, 12 with cervical cancer, and 13 with uterine cancer). Each patient received an average of 3 care plans (range 1–7) and 6.6 unique recommendations (range 2–11), over an average of 9 weeks (range 1–32) (Figure 1). The average number of unique recommendations made *per care plan* was 4.0 (range 1–9). The most common recommendations were for anxiety/depression (89% of patients, 59% reporting moderate-severe levels at its worst), moderate to severe fatigue (80% of patients), and pain (64% of patients, 46% reporting moderate-severe levels at its worst). Additional symptoms are included in Figure 2.

Conclusions: The CPS, developed to improve care processes and patient outcomes through delivery of personalized electronic care plans derived from PROs, aligned with quality care standards and current evidence. Usability and satisfaction are high, and use of the platform results in high referral rates for patients with gynecologic cancers.

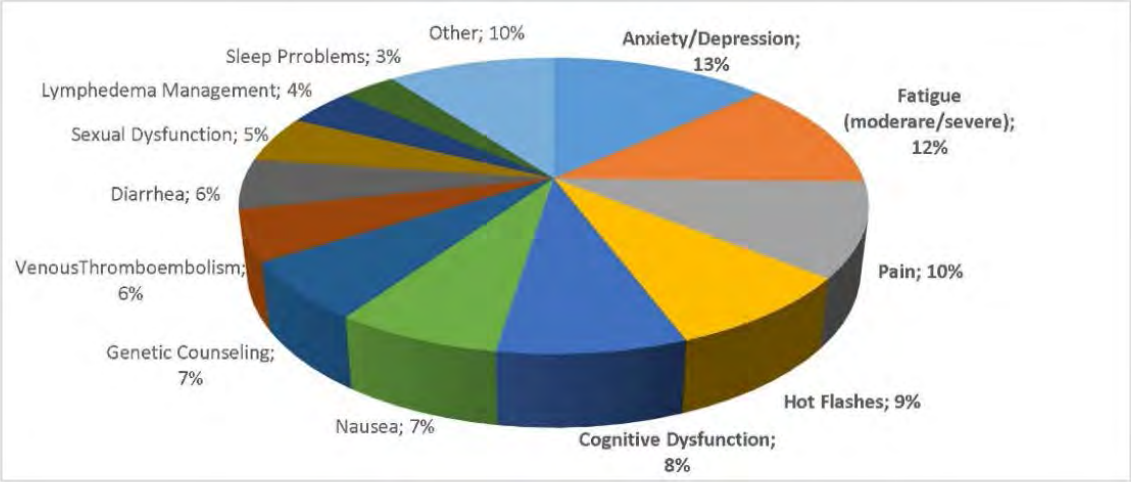

Fig. 1
Unique-Issue Specific Recommendations (n = 292) per Patient (n = 44), across All Delivered Care Plans.

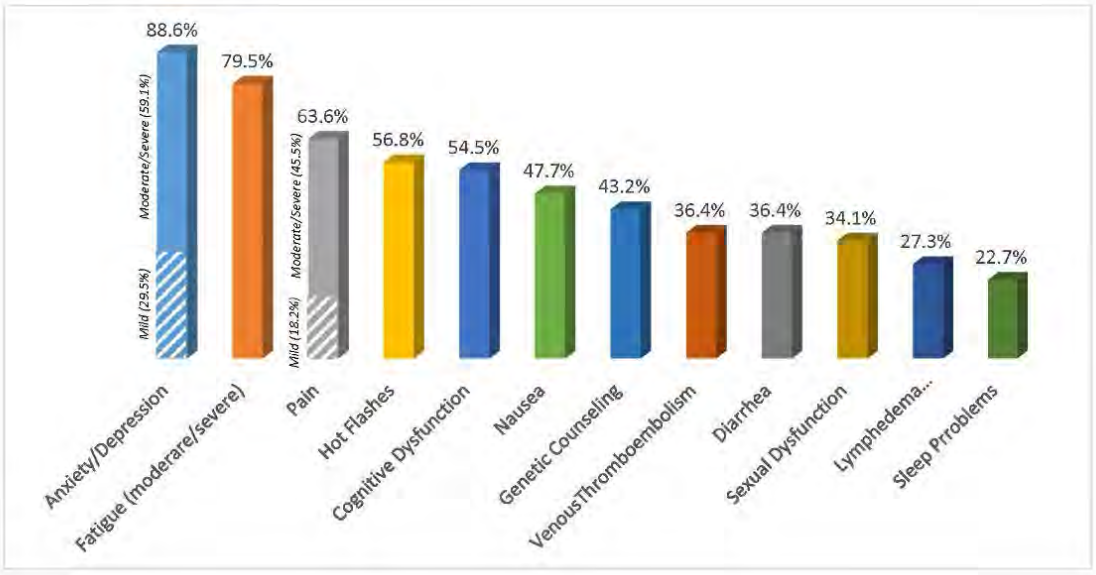

Fig. 2
Percentage of Patients (n = 44) who Received a Recommendation at Least Once.

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Extensive integrated molecular characterization of squamous cell carcinoma and adenocarcinoma of the cervix from within The Cancer Genome Atlas (TCGA): The Cancer Genome Atlas (TCGA) Cervical Analysis Working Group

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Objectives: To identify functionally altered signaling pathways that drive tumorigenesis of invasive cervical cancer through integrated analysis of genomic, transcriptomic, proteomic, and clinical data.

Methods: Blood and primary frozen tumor tissue were obtained from untreated women with invasive cervical cancer. Integrated analysis was done from mRNA, whole exome DNA, and miRNA sequencing data, and with DNA methylation and copy number data. A comprehensive core sample set consisted of 178 matched samples with some platform data on an additional 67 cases. Protein data were available in 155 cases.

Results: Integrated analysis showed novel molecular features and defined significant cervical cancer subgroups. Key distinguishing features of squamous cell carcinomas include activation of p53, p63, p73, AP-1, MYC, HIF1A, FGFR3, and MAPK signaling, which is similar to features characterizing squamous-like cancers in general. Alterations in RTK, PI3K, and MAPK pathway were observed across both squamous cell carcinomas and adenocarcinomas. Adenocarcinomas harbor more *ERBB2*, *ERBB3*, and *KRAS* alterations compared with squamous carcinomas. A unique set of endometrial-like cervical cancers was identified that was predominantly human papillomavirus (HPV)–negative and had high frequencies of *KRAS*, *ARID1A*, and *PTEN* aberrations. Molecular diversity was observed in squamous cell carcinomas where a subset of cases exhibited an epithelial-mesenchymal transition signature derived from mRNA and protein data with poor overall survival. Several findings underline the importance of the immune system in HPV-related cancers, including mutations in *HLA*, amplifications in immune targets (PD-L1, PD-L2) and an immune-related mRNA signature significantly associated with survival. Novel findings such as amplifications in the *BCAR4*lincRNA, associated with estrogen therapy resistance, were also identified. Extensive HPV characterization by Mass Array, and by DNA and RNA sequencing shows the presence of HPV in 95% of cases. Viral-cellular fusion transcripts were observed in 83% of HPV-positive cancers. HPV integration was observed in all HPV18-infected cases and 76% of HPV16-infected cases, with integration sites found in areas that had structural aberrations and associated with increased expression of target genes.

Conclusions: These findings provide insight into novel molecular subtypes for targeted therapies for cervical cancer.

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321 - Poster

Comparative effectiveness of first-line adjuvant chemotherapy for the management of ovarian carcinosarcoma

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Objectives: Ovarian carcinosarcomas are rare, aggressive tumors with a poor prognosis. The optimal first-line chemotherapy for these patients remains unknown. We sought to determine the progression-free survival (PFS) and overall survival (OS) for patients with ovarian carcinosarcomas treated with different first-line chemotherapies after primary surgical debulking.

Methods: This single-institution, retrospective cohort study investigated patients with ovarian or primary peritoneal carcinosarcoma from September 1996 to December 2014. Demographic information and first-line chemotherapy regimen was abstracted from patient charts. PFS and OS were determined. A 1-sample Student *t* test was used to compare PFS and OS between groups. $P < .05$ was deemed statistically significant.

Results: Thirty patients met inclusion criteria: 13 (43%) received carboplatin/paclitaxel as first adjuvant therapy, 8 (27%) ifosfamide/paclitaxel, 6 (20%) a different regimen, and 3 (10%) no chemotherapy. Patients treated with carboplatin/paclitaxel as first-line chemotherapy had a statistically significant longer median PFS than those who received ifosfamide/paclitaxel (9.4 vs 7.8 months, $P = .047$; Table 1). OS did not differ between the 2 groups (18.3 vs 19.6 months, $P = .176$). When comparing all platinum-containing regimens to non–platinum-containing regimens, platinum-containing

regimens led to a longer median PFS (13.6 vs 7.8 months, *P* = .037). OS was similar for platinum and nonplatinum regimens (20.9 vs 19.6 months, P = .334).

Conclusions: For patients with ovarian or primary peritoneal carcinosarcomas, median PFS is longer when carboplatin/paclitaxel is the first-line chemotherapy regimen compared with ifosfamide/paclitaxel. Also, patients treated with platinum-containing regimens have a longer median PFS than those receiving non–platinum-containing regimens. OS was similar for all treatment groups, potentially because of subsequent treatment crossover. Given the rarity and aggressive nature of this tumor type, further study into optimal adjuvant chemotherapy in these patients is needed.

Table 1
PFS and OS in months for first-line chemotherapy regimens for ovarian carcinosarcoma in months. *Carboplatin/paclitaxel demonstrated a statistically significant prolongation of PFS compared to ifosfamide/paclitaxel (p=0.047).

Chemotherapy	N	Median PFS (mo)	Median OS (mo)
No chemotherapy	3	1.4	1.4
Ifosfamide/Paclitaxel	8	7.8	19.6
Carboplatin/Paclitaxel	13	9.4*	18.3
Ifosphamide/Cisplatin	4	17.0	37.0
Carboplatin/Cytoxan	1	13.6	13.6
Adriamycin/Cisplatin	1	192.5	192.5

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322 - Poster
A report on the frequency of depression and anxiety in women with cancer by site
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Objectives: Symptoms of depression and anxiety are relatively common among women diagnosed with cancer. In this research we explored whether rates of being diagnosed with depressive or anxiety disorders differed by cancer site. Younger women diagnosed with cancers of poorer prognosis were hypothesized to be more likely to report being diagnosed with anxiety or depressive disorder after a cancer diagnosis.

Methods: Women of ages 18 to 79 years, with an incident, primary, biopsy-confirmed cancer were recruited from 2 state cancer registries (Kentucky and North Carolina) within 12 months of their diagnosis (2009–2015). In a telephone interview, consenting women self-reported history of depression, anxiety, sociodemographics, and well-being indicators. Cancer registries provided stage, site, date of diagnosis, and age. Logistic regression analyses estimated risk of being diagnosed with depression or anxiety after cancer by cancer site. As the most commonly diagnosed cancer with the best prognosis, breast cancer served as the referent group. Multivariate modeling included age, stage, and comorbid conditions.

Results: A total of 3,334 women completed interviews. Among the referent group, 18% reported having being diagnosed with depression and 15% with an anxiety disorder. Rates of depression were significantly higher among head/neck/lung cancers (32.4%, *P* < .0001) and bladder/kidney cancers (28.2%, *P* = .02). Similarly, rates of an anxiety diagnosis were significantly greater among head/neck/lung cancer (25.2%, *P* = .0002) and noncolorectal gastrointestinal cancer (28.5%, *P* = .04). No differences in either depression or anxiety disorders were noted in gynecologic cancer sites relative to breast cancer.

Conclusions: As hypothesized, rates of depression and anxiety were higher among women diagnosed with cancers with poorer prognosis with the exception of ovarian cancer. Given the high incidence of depression and anxiety in women with cancer (18% and 15%), clinical screening and appropriate references for such symptomatology may optimize overall cancer-related well-being.

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323 - Poster

Neoadjuvant chemotherapy is superior to primary debulking surgery in patients with presumed unresectable epithelial ovarian cancer

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Objectives: We sought to: (1) identify prognostic factors in epithelial ovarian cancer (EOC) treated with neoadjuvant chemotherapy (NACT) and interval debulking surgery (IDS), and (2) compare overall (OS) and progression-free survival (PFS) between NACT for presumed unresectable disease versus suboptimal primary debulking surgery (PDS).

Methods: This was a retrospective study of consecutive patients undergoing IDS after NACT at our institution from 2007 to 2013. Clinical factors were abstracted from medical records and complete clinical response (CCR) was defined as no gross disease at IDS. Survival times were estimated with the Kaplan-Meier method and compared using the log-rank test. The subset of patients receiving NACT for the indication of presumed unresectable disease were matched 1:1 on age and stage with a contemporary cohort of patients receiving suboptimal PDS between 2003 and 2011. Survival times were compared using stratified Cox models to account for the varying duration of follow-up within each matched pair.

Results: Eighty-eight patients were treated with NACT/IDS, and median PFS and OS were 1.3 and 2.6 years, respectively. The following factors were associated with improved survival after NACT: normalization of CA-125 before IDS (median OS 3.0 vs 1.9 years, $P = .02$); age less than 65 (3.3 vs 1.9 years, $P = .005$); CCR at IDS (5.6 vs 2.5 years, $P = .15$), and no gross residual disease after IDS (2.9 vs 2.2 years, $P = .06$). We saw no association between survival and number of post-IDS chemotherapy cycles, 3 vs more than 3 cycles, including among those with persistently elevated CA-125 at IDS (median OS 2.2 vs 2.7 years, $P = 0.63$). In our matched comparison of unresectable cases treated with NACT versus suboptimal PDS, we observed a significant OS advantage for NACT (HR 0.46, 95% CI 0.23–0.92), with no significant difference in PFS.

Conclusions: We saw no survival benefit with increasing duration of adjuvant chemotherapy after IDS, but selection bias likely minimizes the benefit in partial responders. Young age, clinical response, and residual disease are all likely predictors of OS. For primary EOC in which resection to residual disease less than 1 cm is unlikely, NACT is associated with longer survival than PDS. Analysis of morbidity and costs are ongoing. As these patients are likely best served by NACT, more reliable predictors of resectability are needed to better identify such cases.

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324 - Poster

Poor prognosis after conservative surgery in stage I mucinous epithelial ovarian cancer

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Objectives: To evaluate the oncologic safety of conservative surgery in premenopausal women with stage I mucinous epithelial ovarian cancer (mEOC).

Methods: We enrolled 97 patients who were (1) premenopausal at the time of surgery, and (2) diagnosed with FIGO stage I mEOC. The conservative surgical procedure was defined as a unilateral salpingo-oophorectomy with/without a contralateral ovarian wedge resection.

Results: The median age of the patients was 33 years (range 13–50 years) at the time of surgery. Sixty-three patients (64.9%) were stage Ia, and 34 (35.1%) were Ic. Fifty-three patients (54.6%) underwent conservative surgery, and adjuvant chemotherapy was administered to 61 patients (62.9%). During a median follow-up of 73.7 months (range, 7.1–243.5

months), 13 patients (13.4%) had a recurrence, and 8 patients (8.2%) died. Among the patients who underwent conservative surgery, 10 experienced recurrences, and the majority had a intraperitoneal recurrence (n = 8). By multivariate analysis, a significantly poorer prognosis was noted in patients who underwent conservative surgery (HR 6.26, 95% CI 1.53–25.53, *P* = .011) and also in patients with a high preoperative CA-125 (HR 1.98, 95% CI 1.26–3.11, *P* = .003). The 5-year disease-free survival rate was significantly lower in patients who underwent conservative surgery than in those who did not (77.7% vs 94.2%, *P* = .047).

Conclusions: Stage I mEOC patients who undergo conservative surgery seem to have a poorer prognosis. A further multicenter study with a larger cohort is required to evaluate the oncologic safety of conservative surgery in such cases.

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325 - Poster

Patient, treatment, and discharge factors associated with hospital readmission within 30 days after surgery for vulvar cancer

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Objectives: Hospital readmissions are common, costly, and increasingly viewed as adverse events. In gynecologic oncology, data on readmissions are limited. The goal of this study was to examine the patient, treatment, and discharge factors associated with unplanned readmission after surgery for vulvar cancer.

Methods: We identified all patients who underwent a simple or radical vulvectomy at our institution between January 2001 and June 2014. Patients were included if they had squamous cell carcinoma in situ or any stage of invasive cancer. A retrospective chart review was performed and clinical variables extracted. Using linear and logistic regression, these clinical variables were correlated with risk of readmission.

Results: A total of 363 patients were included in the analysis. Median age was 59 years and average body mass index was 29. Most patients had stage I disease (50.7%) and squamous cell histologies (71.3%). Radical vulvectomy was required in 39.1% of patients, and 23.4% of patients underwent nodal dissection. A large proportion of our cohort was discharged to rehabilitation facilities (7.7%) or with a visiting nurse (20.1%). Seventeen patients (4.6%) were readmitted within 30 days. Readmission length of stay ranged from 2 to 37 days and 35% of these patients required surgery. On univariate analyses, the number of comorbidities, radical vulvectomy, length of stay, nodal dissection, and discharge to rehabilitation were all predictors of hospital readmission. On multivariate logistic regression, the number of comorbidities remained significant (*P* = .005). Of those who were readmitted to the hospital within 30 days, 29.4% had been in rehabilitation whereas only 6.6% of the no readmission group had been discharged to rehabiliation (*P* = .003).

Conclusions: Readmission after surgery for vulvar cancer affected 4.6% of our population but led to reoperation and longer length of stay. Multivariate analyses suggested perioperative comorbidities, radicality, nodal dissection, and discharge to rehabilitation placed the patient at the greatest risk for readmission. Age, prior XRT, plastic surgery involvement, antibiotics, and discharge with visiting nurses did not affect the likelihood of readmission.

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326 - Poster

Centralized colposcopy clinic serving a high-risk population: Delays in cancer screening persist

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Objectives: Risk factors for cervical cancer in the United States include lower socioeconomic status, lack of access to care, and minority status. In 2008, our institution developed a centralized referral center for impoverished urban women diagnosed with a cytologic abnormality. Our goal was to determine the success rate of this center in decreasing delays in treatment and access to adequate care in a predominately African American (AA) population.

Methods: The records of all patients presenting to a centralized colposcopy clinic between 2009 and 2013 for abnormal cytology were reviewed. Demographic information obtained from charts included age, race, smoking history, insurance status, Pap smear result, pathologic reports, and treatments. The Student's *t* and Fisher exact tests were used where appropriate.

Results: A total of 318 patients were identified. Mean age was 31.5 years (11.3). Cytology was predominately atypical cells of undetermined significance (ASCUS; 41.5%) followed by low-grade squamous intraepithelial lesions (LSIL; 39.3%). This group was primarily AA (72.3%), had publicly funded insurance (84.0%), and was in the lower quintiles for income (73.3%). Higher-income patients (P = .01), those of AA race (P = .04), and those younger than 30 years (P = .02) were more likely to present for colposcopy within 3 months from an abnormal Pap smear. No association with insurance status was noted (P = .59). The median time from abnormal cytology to colposcopy was 79 days (range, 7–1,163 days). Forty-eight patients (15%) required excisional procedures, with a median time from diagnosis of 357 days (range, 14 to 978 days). Six patients (12.5%) in the excisional cohort failed to have undergone the procedure. Follow-up care was required for 254 patients (79.9%), of which 96 (37.8%) failed to follow-up.

Conclusions: Although centralized colposcopy should improve access to better quality of care, significant delays in diagnosis and treatment still exist. Better models, including on-site excisional procedures, should be explored in vulnerable, high-risk populations.

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327 - Poster
***BRCA* mutation variants in ovarian cancer patients: Does the mutation class matter?**
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Objectives: To identify if *BRCA* variant mutation class is predictive of clinicopathologic characteristics or survival.

Methods: We inspected all patients at a single institute who underwent genetic testing for a personal history of ovarian cancer from 2000 to 2015. Of nearly 600 patients with a diagnosis of ovarian cancer, those women identified with a *BRCA1* or *BRCA2* variant mutation were studied. We compared progression-free survival (PFS), overall survival (OS), surgical debulking status, histology, and platinum status of these patients.

Results: We identified 36 patients who tested positive for germline mutations in *BRCA1* or *BRCA2*. Analysis was performed comparing groups with *BRCA1* versus *BRCA2* variants. Median age at ovarian cancer diagnosis was 51 versus 57 years (P = .1736), respectively. The *BRCA1* group had a median PFS of 57 months and OS of 74 months. Alternatively the *BRCA2* group had a median PFS of 28 months and OS of 49 months (P = .1028 for PFS and P = .3144 for OS). The rate of optimal debulking, histology, platinum sensitivity, and rates of secondary cancer were comparable in both groups (P = 1). Most patients were diagnosed at stage IIIC, and the trend showed lower stage at diagnosis in the *BRCA1* variant–positive patients (P = .077). The class of mutation—substitution, deletion, or frameshift—was comparable in each group (P = .3403). A subanalysis stratified by class of mutation—substitution (n = 11), deletion (n = 13), or frameshift (n = 12) —revealed similar findings. Median age ranged from 52 to 55 years (P = .8785). Median PFS ranged from 21 to 57 months (P = .5710 favoring substitution) and median OS ranged from 66 to 69 months (P = .3321 favoring frameshift). Class of mutation did not alter the ability to perform optimal debulking in a patient (P = .9999). Women with a substitution mutation had the highest incidence of platinum-resistant disease, but this finding was not significant (P = .4735).

Conclusions: As *BRCA* mutation clusters are starting to be defined, it may be more valuable to identify the location of the variant than the actual class of mutation. With appropriate validation, these data may be implicated in risk assessment for BRCA variants of unknown significance.

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A prospective study of intraoperative uterine assessment in low-grade endometrial cancer
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Objectives: (1) To prospectively evaluate intraoperative factors influencing a surgeon's decision to perform full pelvic lymphadenectomy (FPL) after sentinel lymph node (SLN) biopsy in preoperative low-grade endometrial cancers. (2) To prospectively evaluate the ability of intraoperative (IO) assessment to predict the final pathologic size of an endometrial malignancy.

Methods: From March to August 2015, patients with low-grade endometrial cancer who underwent minimally invasive surgery with SLN injection were included in a prospective study. Institutional management of low-grade endometrial cancer during the study period was SLN mapping and biopsy followed by total laparoscopic hysterectomy/bilateral salpingo-oophorectomy with frozen section evaluation of the uterus; additional lymph node sampling was based on Mayo criteria and surgeon preference. After hysterectomy, the uterus was bivalved and the largest diameter of tumor was recorded by the surgical team. After the frozen section report, including a tumor size assessment by pathology, the surgeon completed an intraoperative questionnaire on factors influencing the decision to perform or withhold FPL.

Results: All patients underwent injection for SLN mapping. Of 26 patients, 19 (73%) underwent bilateral mapping, 5 (19%) unilateral, and 2 (8%) had no mapping. Four patients (15%) underwent FPL, with the following reasons listed: tumor size greater than 2 cm (n = 3), depth of invasion (n = 2), failure of SLN mapping (n = 2), grade (n = 1), and age greater than 70 years (n = 1). Twenty-one patients did not undergo FPL; the reasons cited were low grade (81%), invasion less than 1/2 (81%), tumor size (76%), SLN mapping (71%), age (14%), body mass index (10%), poor visualization (5%), patient preference (5%), and comorbidities (5%). Using Mayo criteria, the final pathologic tumor size would have stratified a few patients to different management (n = 5 [19%], based on intraoperative surgeon assessment, and n = 4 [15%], based on intraoperative pathologist assessment).

Conclusions: Intraoperative assessment of tumor size by the surgeon or pathologist incorrectly classifies risk of lymph node metastasis using the Mayo criteria in 1 of 5 cases. A prospective assessment of intraoperative factors that affect the decision to perform FPL in apparent early-stage EC demonstrates significant variability at one institution. These data highlight the need to develop a consensus algorithm that integrates SLN mapping into clinical decisions to proceed to FPL in endometrial cancer.

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Endometrial cancer surveillance adherence: Before and after June 2011 SGO position statement
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Objectives: In June 2011, the Society of Gynecologic Oncology (SGO) endorsed the conclusion that physical examination and symptoms should be the primary surveillance methods in patients with endometrial cancer. We sought to evaluate adherence to these guidelines at an urban academic public hospital by evaluating the use of computed tomography (CT) scans, vaginal cuff cytology (Pap smears), and serum CA-125 measurements ordered for endometrial cancer surveillance before and after publication of these guidelines.

Methods: We conducted a retrospective review of all patients undergoing surveillance for endometrial cancer at a single institution between June 2009 and June 2013. We assessed the number of patients without symptoms or abnormal physical examination findings who underwent surveillance CT scans, Pap smears, and/or CA-125 measurements during 2 years before and after SGO guideline publication.

Results: Ninety-two patients (48 and 44 patients before and after June 2011, respectively) with endometrial cancer were followed in the gynecologic oncology clinic during the study period. The mean patient age was 58 years. Fifty-four patients had endometrioid histology and 38 had high-risk endometrial cancer subtypes. No significant differences were seen in age, ethnicity, body mass index, or disease grade or stage when comparing those under surveillance before and after the SGO guidelines. X^2 analysis showed a significant decline in patients under surveillance using CT scans after the SGO guidelines (n = 13 [27%] vs n = 4 [9%], $P = .03$). We similarly found a significant decline in those under surveillance using CA-125 (n = 14 [29%] vs n = 5 [11%], $P = .035$) and Pap smears (n = 34 [71%] vs n = 8 [18%], $P < .001$). No significant difference was noted in disease status at the last follow-up between the 2 groups. Using Medicare-allowable charges for surveillance interventions, we found a decrease in the cost of surveillance by more than $10,000 ($14,102 in the 2 years before guidelines, $3,055 in the 2 years after the guidelines).

Conclusions: In a single urban academic public hospital after only 2 years, clinical adherence to the 2011 SGO endometrial cancer surveillance guidelines has resulted in a significant decline in the use of CT scans, CA-125, and Pap smears. This reduction does not appear to affect patient outcomes and led to an appreciable decrease in surveillance costs. This may have far-reaching significance for cost and resource allocation in endometrial cancer surveillance.

Table 1
Results.

		Pre-June 2011 n= 48	Post-June 2011 n=44	*P* value 95%(CI)	*P* value X^2(value, df)
		f=	*f*=		
Patients surveilled by CT Scans[a]		13(27.1%)	4(9.3%)		.030(4.72, 1)
Patients surveilled by CA125[a]		14(29.2%)	5(11.4%)		.035(4.44, 1)
Patients surveilled by Pap[a]		34(70.8%)	8(18.2%)		< .001(25.65, 1)
Number of Pap Smears Performed (mean)[b]		M=2.54(SD=2.34)	M=0.23(SD=0.52)	< .001(1.03-1.74)	
Disease Status at Last Follow Up[c]		*f*=	*f*=		
	Alive with Disease	3(6.3%)	3(6.8%)		
	Dead of Disease	3(6.3%)	0(0%)		
	Dead of Other Causes	3(6.3%)	1(2.3%)		
	No Evidence of Disease	26(52.2%)	25(56.8%)		
	Lost to Follow Up[d]	13(27.1%)	15(34.1%)		
					.407(3.99, 4)

a-A 2x2 chi square test performed
b-A Univariate analysis of variance was performed
c-A 2x5 chi square test performed on disease by pre- and post-June 2011
d-A one sample binomial test assessin the proportion of lost to followup (LTF) yielded no difference between the pre- and post-samples (*P* = 0.850)

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330 - Poster
Improved outcomes following the use of dose-dense paclitaxel-based neoadjuvant chemotherapy in advanced epithelial ovarian carcinoma
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Objectives: Prior trials have demonstrated improved survival when dose-dense paclitaxel (DDP) is given in combination with carboplatin every 3 weeks as adjuvant therapy after primary debulking in epithelial ovarian carcinoma (EOC). The use of a DDP-based regimen has not been well studied in the neoadjuvant chemotherapy (NACT) setting. The purpose of this study is to compare outcomes of advanced EOC patients receiving NACT with DDP to those receiving taxane every 3 weeks before interval debulking surgery (IDS).

Methods: This was a retrospective review of all patients who received NACT for advanced EOC between June 2012 and July 2015 at our institution. Patient demographics, chemotherapy-related toxicity, and IDS outcomes were compared between the patients who received DDP and those who received taxane. All patients received carboplatin every 3 weeks. The Fisher exact test was used to determine statistical significance.

Results: Seventy-five EOC patients were treated with NACT. Of these, 27 (36%) were treated with DDP and 48 (64%) were treated with standard taxane. Patient demographics of the 2 groups were similar. Median number of NACT cycles was similar between the cohorts (2.9 DDP vs 4.1 taxane). Five DDP patients (19%) were unable to complete chemotherapy and were switched to standard taxane. Toxicity, predominantly hematologic and gastrointestinal (GI), was greater in the DDP group. However, there were no episodes of febrile neutropenia in either group, and the percentage of patients requiring blood transfusion was similar—26% DDP vs 15% taxane (*P* = .24). GI symptoms were manageable. After IDS, 11 patients (41%) in the DDP group had no residual disease compared with 11 patients (23%) in the taxane group (*P* = .12). Three patients (11%) in the DDP group had a pathologic complete response compared with 1 (2%) in the taxane group (*P* = .13).

Conclusions: Although associated with an increase in toxicity, DDP appears in this preliminary study to facilitate higher rates of no residual disease and pathologic complete response than taxane at the time of IDS. These results warrant further investigation of DDP for patients with advanced EOC undergoing NACT and assessment of its impact on long-term outcomes.

Table 1
Demographics and Outcomes.

Characteristic	Dose Dense (N=27) Number (%)	Standard (N=48) Number (%)
Median age (range)	65 (46-81)	71 (52-92)
Histology		
Papillary serous	24 (89)	41 (85)
Mixed	2 (7)	4 (8)
Unknown	1 (4)	3 (6)
Stage		
IIIB	0	1 (2)
IIIC	19 (70)	37 (77)
IV	8 (30)	10 (21)
Neoadjuvant regimen		
Taxol/Carboplatin	22 (81)	17 (35)
Taxol/Carboplatin + Avastin	5 (19)	1 (2)
Taxotere/Carboplatin	0	23 (48)
Carboplatin	0	7 (15)
Cycles received (dose dense)	3.48 (2.89)	4.13
Grade 3/4 Toxicity		
None	3 (11)	28 (58)
Anemia	11 (41)	13 (27)
Requiring transfusion	*7 (26)*	*7 (15)*
Neutropenia	18 (67)	5 (10)
Thrombocytopenia	4 (15)	3 (6)
Neurological	0	3 (6)
Gastrointestinal	7 (26)	8 (17)
Metabolic	1 (4)	7 (15)
Thrombosis	2 (7)	2 (4)
Infection	0	2 (4)
Other	0	1 (2)
Response after neoadjuvant therapy		
Complete pathologic response	3 (11)	1 (2)
Partial	22 (81)	37 (77)
Progressive	1 (4)	6 (13)
Unknown	1 (4)	4 (8)

Debulking status		
No-residual disease	11 (41)	11 (23)
Optimal	10 (37)	21 (44)
Suboptimal	4 (15)	7 (15)
Not debulked	2 (7)	9 (19)

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Low intraperitoneal port placement rate in ovarian cancer patients: A population-based national assessment

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Objectives: We sought to determine the rate of intraperitoneal (IP) port placement in ovarian cancer patients in a population-based database maintained by the American College of Surgeons. Placement of IP ports can be used as an estimate of IP chemotherapy utilization.

Methods: We identified ovarian cancer patients and whether they received an IP port using ICD-9 and CPT codes in the National Surgical Quality Improvement Program database (NSQIP) from 2006 to 2012. Demographics, comorbidities, operative outcomes, and postoperative complications were abstracted. The *T* test, X^2 test, and univariable and multivariable regression models were used.

Results: A total of 2,733 ovarian cancer patients with no prior chemotherapy in the NSQIP were included. Only 144 patients (5.2%) had an IP port placed. Patients with higher body mass index were less likely to have an IP port placed (*P* = .018). Readmission rate was higher in the IP port group (13 vs 6.8%, *P* = .012). There was a trend toward a higher rate of postoperative abscess in the IP port group, though not statistically significant (4.7 vs 2.2%, *P* = .101). Assuming 60% of ovarian cancer patients present with stage II and III disease and the average national optimal debulking rate is 50%, 832 patients would have been candidates for IP chemotherapy in this cohort making the port placement rate 17% (144/832).

Conclusions: The National Comprehensive Cancer Network guidelines and National Cancer Institute recommend IP chemotherapy in optimally debulked stage II and III patients. Our results confirm a low rate of IP port placement and therefore IP chemotherapy for ovarian cancer in the United States. Further investigation is necessary to understand reasons for failure to adopt IP-based chemotherapy.

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Improved clinical sensitivity detection of circulating tumor cell assays using a dual selection strategy in women with epithelial ovarian cancer

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Objectives: Little is known about the role of circulating tumor cells (CTCs) in epithelial ovarian cancer (EOC). Methods available for selecting and enumerating CTCs traditionally analyze cells based on expression of epithelial cell adhesion molecule (EpCAM) only. Fibroblast activation protein α (FAPα), a marker of activated stromal fibroblasts in tumors, is highly expressed in EOC. The goal of this study was to evaluate the sensitivity of adding FAPα as a selection marker for the isolation of CTCs in EOC, and to compare FAPα and EpCAM expressing CTCs in various subgroups of women with EOC.

Methods: To isolate CTCs, we used 2 microfluidic chips in series, one with antibodies specific to cells bearing FAPα ($CTC^{FAP\alpha}$), the other to EpCAM (CTC^{EpCAM}). For analysis, EOC patients were divided into 3 groups: patients with advanced-stage (III/IV) disease undergoing interval debulking after neoadjuvant platinum-based chemotherapy (A-EOC-chemo), patients with advanced-stage disease undergoing primary debulking without prior chemotherapy (A-EOC-no chemo), and patients with early-stage (stage I) disease. Blood specimens from 11 normal donors were also analyzed.

Results: Sixteen patients with EOC were enrolled in this study, 8 A-EOC-no chemo, 5 A-EOC-chemo, and 3 stage I (Figure 1). Median CTC^{EpCAM} and $CTC^{FAP\alpha}$ count was 121 and 31 for stage I, 214 and 58 for A-EOC-no chemo, 48 and 28 for A-EOC-chemo, and 0.1 and 0.3 for normal donors, respectively. EpCAM and FAPα antigens were not co-expressed in single CTCs. Using our dual selection strategy, the sensitivity of CTC detection was 100% for all cohorts, including stage I patients. A 3-fold decrease in median CTC^{EpCAM} count was observed for A-EOC-chemo patients compared with A-EOC-no-chemo patients ($P < .007$), but no differences were seen in median $CTC^{FAP\alpha}$ counts between these 2 groups.

Conclusions: We found that FAPα is not co-expressed with EpCAM in CTCs, resulting in high clinical yields of CTCs and dramatically improving clinical sensitivity. In addition, CTC^{FAP} is more resistant to conventional chemotherapy with paclitaxel/carboplatin than CTC^{EpCAM}. Thus, CTC^{FAP} may be a potential biomarker of chemoresistance in EOC, offering opportunities for unique clinical indications for CTCs that were not available using only CTC^{EpCAM} as a biomarker.

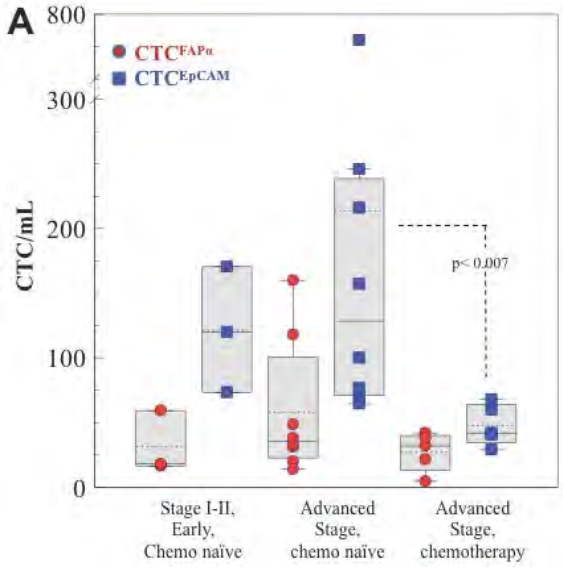

Fig. 1
Box Plot Data for CTCFAPα and CTCEpCAM Isolated from Blood of EOC Patients: Early Stage, Chemo Naïve, Advanced Stage, Chemo Naïve (A-EOC-no-chemo) and Advanced Stage, Following Chemotherapy Treatment (A-EOC-chemo). The solid lines in the box plots represent the median and the dotted line is the mean for the data shown.

Table 1
Average and median $CTC^{FAP\alpha}$ and CTC^{EpCAM} collected from EOC patients and normal donors.

Ovarian Cancer Stage and Treatment	$CTC^{FAP\alpha}$/mL avg (median)	CTC^{EpCAM}/mL avg (median)
Normal Donors (n=11)	0.3 (0.0)	0.1 (0.0)
Stage I (early), chemo naïve (n=3)	31.3 (18.0)	121.3 (120.0)
Advanced Stage, chemo naïve (n=8)	57.8 (35.5)	213.7 (128.5)
Advanced Stage, chemotherapy (n=5)	27.6 (32.0)	47.9 (42.0)

333 - Poster

Who is referred to the gynecologic oncology clinic with an adnexal mass?

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Objectives: There are many strategies for determining which patients with an adnexal mass warrant referral to a gynecologic oncologist. The purpose of this study is to characterize the evaluation of patients with adnexal masses before referral to the gynecologic oncology clinic.

Methods: Review of the clinic schedule identified all patients referred to an academic gynecologic oncology outpatient clinic. Chart review identified demographic information, menopausal status, body mass index (BMI), imaging and laboratory results, presence of comorbid conditions, and pathology results after biopsy or surgical excision.

Results: Of 788 women referred to the gynecologic oncology clinic in 2013, 281 (36%) were evaluated for an adnexal mass. Tumor markers were drawn before referral in 171 women (60%), with CA-125 measured in 167 (59%), CEA in 46 (16%), HE4 in 3 (1%), and the multivariate index assay (MIA) in 3 (1%). Society of Gynecologic Oncology (SGO)/American College of Obstetricians and Gynecologists (ACOG) referral criteria were met by 127 women (45%). Surgical excision was undertaken in 194 patients (69%), revealing cancer in 52 women (19%) and borderline tumors in 16 (6%). Postmenopausal women were more likely to meet referral criteria than premenopausal women (58% vs 27%, $P < .0001$). Women with severe obesity (BMI >35) were significantly less likely to meet referral criteria (32% vs 49%, $P = .01$). There were no significant differences in whether women met SGO referral criteria with diabetes, heart disease, private insurance, an indication for anticoagulation, or nonwhite race. Patients meeting referral criteria were more likely to have cancer (38% vs 3%, $P < .0001$), but not borderline tumors (6% vs 6%, $P = 1$).

Conclusions: The incidence of malignancy among patients referred to the gynecologic oncology clinic was 19% in this series. This incidence of malignancy is similar to that seen in a group of women scheduled for surgery by generalist gynecologists in a recent multicenter, prospective study. The incidence is significantly lower than that seen in published reports from other gynecologic oncology divisions as recently as 5 years ago. Most patients referred did not meet SGO/ACOG referral criteria and severely obese patients were less likely to meet criteria. Utilization of the HE4 and MIA tests was rare. These data may reflect a shift in practice patterns toward a “refer all” strategy for management of adnexal masses.

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Pediatric and adolescent pelvic masses: What is the role of the gynecologic oncologist?

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Objectives: Referral guidelines of the American College of Obstetricians and Gynecologists are available for premenopausal women with pelvic masses but are nonspecific for young women, adolescents, and children. A multidisciplinary team may be involved in the care of these young women, but the role of the gynecologic oncologist (Gyn/Onc) remains vague. The goal of this study was to compare clinical presentation and surgical outcome of women younger than 21 years with a pelvic mass, at a single institution with access to all pediatric and gynecologic subspecialty services, and determine utilization of the Gyn/Onc.

Methods: We reviewed the medical records of all women younger than 21 years undergoing primary surgery for a pelvic mass at a single institution from 2010 to 2015. The 2-tailed test with $\alpha = 0.05$ was used for statistical significance.

Results: A total of 138 patients were evaluated and 77 met study criteria: 57 (74%) with benign and 20 (26%) with malignant disease. Mean age was 13.5 years (0–21 years). The most common presentation was pain, seen in 58 (75%) of 77 cases. Mean size of the adnexal mass was 9.8 cm in the benign group and 15.5 cm in the malignant group ($P = .005$, 95% CI 1.81–9.58). Tumor size greater than 10 cm was found in 75% of malignancies, and all tumors 5 cm or less were benign (14%). Tumor markers were not used in 29% of the cohort; however, in cancer cases with tumor markers, 70% were elevated. A Gyn/Onc was consulted in 10 cases (13%), with 6 consults (60%) requested by pediatric gynecologists; however, only 2 (25%) of 8 were preoperative consults in malignant cases. Laparoscopy was completed in 35 (45%) of 77 patients, with most cases being

benign (30/57 vs 5/20). Most common benign tumors were mature teratomas (40 [70%] of 57). In the malignant category, 11 cases (55%) were stage I; borderline ovarian tumors (7/20) were the most common, followed by immature teratomas (4/20) and mixed germ cell tumors (4/20).

Conclusions: Young women with malignancies more often present with pain and large mass size (>5 cm) compared with women with benign disease. Gyn/Oncs are inconsistently involved in the management of young women and minimally invasive procedures are less commonly used. In addition, tumor markers such as α-fetoprotein, lactate dehydrogenase, and human chorionic gonadotropin in this younger population should be more consistently used to better delineate preoperative involvement of the Gyn/Onc.

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335 - Poster
Dissection of supraclavicular area metastatic nodes in patients with ovarian cancer in an interdisciplinary team approach
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Objectives: To describe the development of and experience in dissection of metastatic nodes in the supraclavicular (SC) area in patients with ovarian cancer using an interdisciplinary team approach.

Methods: From March 2012 to February 2014, 12 women underwent extended cytoreductive surgery including supraclavicular lymph node dissection (SCLND) by head and neck surgeons. The surgical extent of SCLND included compartmental level III and IV area and sometimes extended to level V area according to the clinical circumstances.

Results: Optimal cytoreduction was achieved in all patients. Median operative time was 495 minutes (range, 175–635 minutes). All preoperatively identified positive lymph nodes in the SC area were completely resected with the cooperation of head and neck surgeons. In 12 patients, 9 resections occurred on the left side, 2 on the right side, and 1 on both sides. Median number of retrieved and positive lymph nodes in the SC area was 12 (range, 6–21) and 3 (range, 0–21), respectively. There was no major complication requiring prolonged hospitalization. Chlye leakage developed in 1 patient, which was resolved by conservative management including a fat-free diet and compressive dressing. One patient experienced recurrence in surgical neck fields during follow-up (median, 14 months; range, 1–35 months).

Conclusions: In patients with ovarian cancer, SCLND performed in an interdisciplinary team approach is feasible with acceptable morbidities. Long-term follow-up is needed to know the impact on survival.

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336 - Poster
Risk factors for *Clostridium difficile* infection in patients undergoing treatment for gynecologic cancer
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Objectives: *Clostridium difficile*–associated diarrhea (CDAD) is a common and potentially dangerous complication of treatment for gynecologic cancers and is an important metric for quality of hospital care. We sought to evaluate risk factors associated with CDAD specific to gynecologic oncology patients.

Methods: In this retrospective review, all inpatient admissions to the gynecologic oncology unit of a tertiary referral center over a 4-year period were abstracted. Demographic, surgical, and medical comorbidities as well as medication use was obtained. Both surgical and medical admissions were included. Diagnosis of CDAD was only made when a positive result was confirmed with polymerase chain reaction (PCR). Standard statistical tests were used.

Results: A total of 728 women were included in the analysis. Cancer diagnoses included cervical (11.0%), uterine/endometrial (32.1%), ovarian/fallopian tube/primary peritoneal (53.3%), and vulvar/vaginal (3.5%). Fifteen patients had positive PCR-proven CDAD (2.01%). In bivariate analysis, radiation treatment, surgical admission, nasogastric tube use, corticosteroid/total

parenteral nutrition use, H2 blockers/proton-pump inhibitors, age, and primary disease location were not associated with CDAD. Cephalosporin use was associated with decreased risk of CDAD (55% vs 20% in those receiving cephalosporin; OR 0.21, 95% CI 0.06–0.74). Notably, platinum-based chemotherapy use (19% vs 47% in those who received a platinum agent; OR 3.61, 95% CI 1.29–10.13) and early stage (29% vs 60% with stage I-II disease; OR 3.59, 95% CI 1.26–10.21) were associated with increased risk of CDAD. In logistic regression analysis, platinum agents (aOR 5.7, 95% CI 1.91–17.10), early-stage disease (aOR 5.7, 95% CI 1.22–11.05), and cephalosporins (aOR 0.20, 95% CI 0.05–0.75) were found to be independent predictors of CDAD.

Conclusions: The use of platinum-based chemotherapies, as well as early-stage disease, appears to be significant risk factors for the development of CDAD in gynecologic oncology patients. Attention to these risk factors is warranted to prevent the dangerous sequelae of infection with this organism.

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Patterns of care and predictors of survival in patients with immature teratoma

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Objectives: Immature ovarian teratomas are rare, comprising 5% of all ovarian cancers. Most published reports come from small, single-institution experiences, which limit their generalizability. We performed a population-based analysis to determine the patterns of care and outcomes of women with immature teratoma.

Methods: The National Cancer Data Base (NCDB) was used to identify women diagnosed with immature teratoma from 1998 to 2012. We explored demographic and clinical characteristics, treatment trends, predictors of survival, and prognosis.

Results: A total of 1,045 patients with immature teratoma were identified. Most (77.1%) were diagnosed between ages 20 and 40 years, and presented at an early stage (Table, column 2). Unilateral salpingo-oophorectomy was the most common surgical modality, performed in 52% of cases. Nearly 60% of patients received adjuvant chemotherapy. The percentage of patients receiving chemotherapy increased with stage (Table, column 3). The relative risk (RR) of chemotherapy increased with stage (RR 1.50, 95% CI 1.29–1.73 for stage II; RR 1.40, 95% CI 1.27–1.56 for stage III; and RR 1.39, 95% CI 1.12–1.73 for stage IV), as well as grade (RR 3.55, 95% CI 2.63–4.80 for grade II; and RR 4.06, 95% CI 3.04–5.43 for grade III) and treatment at an academic compared with community-based center (RR 1.37, 95% CI 1.06–1.77). Older patients were less likely to receive chemotherapy (RR 0.61, 95% CI 0.40–0.92 for women >50 years). Age greater than 50 years (HR 22.22, 95% CI 6.23–79.26), lack of health insurance (HR 2.79, 95% CI 1.11–7.02), advanced stage (HR 7.69, 95% CI 3.31–17.84 for stage III and HR 28.36, 95% CI 8.93–90.0 for stage IV), and grade III disease (HR 8.18, 95% CI 1.73–38.59) were associated with worse outcomes. Race, year of diagnosis, location of care, and income did not correlate with survival. Overall, 5-year survival rates were excellent (Table, column 3).

Conclusions: Although immature teratomas have traditionally been thought to be most common in the first 2 decades of life, our findings suggest that the incidence is highest in the 20- to 40-year age group. Patients tend to present with early-stage disease. Most are managed with fertility-sparing surgery and chemotherapy and have an excellent prognosis. Later age at diagnosis, insurance disparities, advanced stage, and high-grade histology carry a worse prognosis.

Table 1

	% Diagnosis	% Receiving Chemo	5-Year Survival Rates
Stage I	69.5%		98.3% (95% CI 96.8-99.1)
A		43.9%	
B		57.1%	
C		73%	
Stage II	6.5%		93.2% (95% CI 82.9-97.4)
A		57.1%	
B		80%	

C		88.2%	
Stage III	13.7%	84.6%	82.7% (95% CI 74.3-88.5)
Stage IV	2.4%	80%	72.0% (95% CI 50.1-85.6)
Unknown	7.9%	42%	94.3% (95% CI 85.4-97.8)

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338 - Poster

The treatment is over, but the symptoms remain in gynecologic oncology cancer patients

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Objectives: The symptom burden of gynecologic cancer survivors has been understudied; therefore, we sought to describe the types and severity of symptoms in this group of women and explore treatment-related predictors of high symptom burden.

Methods: We performed a cross-sectional study of women with a history of cervical, uterine, ovarian, or vulvar cancer undergoing disease surveillance in an outpatient gynecologic oncology practice. Patients who survived for 2 or more years were included. Patients completed a symptom assessment questionnaire as part of routine care. Univariate and bivariate statistics were used to evaluate patient characteristics and symptom burdens. Multivariable logistic regression was used to assess for risk factors for high symptom burden.

Results: A total of 241 women had no evidence of disease and were not receiving treatment 2 or more years after diagnosis, and 77 were seen 5 or more years after diagnosis. They had a history of cervical (24.6%), uterine (41.1%), ovarian (25.8%), and vulvar (7.7%) cancers. They underwent treatment with surgery (91.5%), chemotherapy (55.2%), radiation (40.7%), biologic agent (10.1%), and hormonal agents (2.4%). Patients did not have significantly different symptom rates in the 2- and 5-year survivor groups (Table 1). The most common symptoms reported included fatigue, insomnia, pain, memory, and neuropathy. Seventy-five percent of patients reported 1 or more symptom, with 24% of patients reporting 3 or more symptoms of moderate to severe intensity. Prior chemotherapy was an independent risk factor for high symptom burden at 2 years, and prior radiation therapy was an independent risk factor for high symptom burden at 5 years.

Conclusions: Gynecologic cancer survivors have prolonged symptomology after treatment. Radiation treatment is associated with long-term symptoms whereas chemotherapy is associated with short-term symptoms.

Table 1

Symptoms Burden Among Survivors.

	2 Year Survivors N = 243 N (%)		**5 Year Survivors N = 83** N (%)	
	Any Severity	***Moderate/Severe***	***Any Severity***	***Moderate/Severe***
Pain	97 (40.4)	43 (17.9)	33 (42.8)	14 (18.2)
Fatigue	145 (60.2)	66 (27.4)	40 (51.9)	23 (29.9)
Nausea	28 (11.5)	8 (3.3)	13 (16.9)	3 (3.9)
Distress	66 (27.3)	36 (14.9)	22 (28.6)	14 (18.4)
Shortness of breath	65 (26.7)	22 (13.2)	20 (26.0)	3 (4.0)
Memory impairment	97 (40.2)	25 (10.4)	33 (45.2)	10 (13.0)
Anorexia	42 (17.4)	15 (6.2)	14 (18.2)	10 (13.0)
Depression	54 (22.4)	31 (12.9)	16 (20.8)	11 (14.3)
Vomiting	16 (6.6)	6 (2.5)	8 (10.4)	2 (2.6)
Neuropathy	86 (35.4)	41 (16.9)	33 (45.2)	18 (23.4)
Sexual dysfunction	31 (13.1)	21 (8.9)	12 (15.6)	9 (11.7)
Insomnia	105 (43.0)	47 (19.3)	34 (44.2)	18 (23.4)

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Lymphadenectomy in uterine cancer surgeries: A national perspective

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Objectives: The practice of lymphadenectomy (LND) in uterine cancer staging has evolved over time and its indications remain controversial. This study seeks to determine the extent of practice of LND in a national sample, and its related surgical outcomes and complications.

Methods: We identified patients with uterine cancer using postoperative ICD-9 codes in the National Surgical Quality Improvement Program database (NSQIP) from 2006 to 2012. Surgical procedures (hysterectomy and lymphadenectomy), demographics, comorbidities, peri- and postoperative outcomes, and postoperative complications were abstracted. Wilcoxon test, χ^2 test, and univariate and multivariate logistic regression models were used.

Results: LND was performed in 36% (4,687/13,093) of uterine cancer surgeries. The rate was similar regardless of approach (i.e., minimally invasive vs open). Patients undergoing LND were older (61 vs 59, $P < .001$) but had fewer comorbidities, particularly cardiovascular and pulmonary disease. Body mass index (BMI) was similar between the 2 groups at 29.7-8 kg/m^2. Surgeries that involved LND required 60 additional minutes (median 126 vs 186 minutes; interquartile range 80–185 vs 135–248 minutes; $P < .001$). Peri- and postoperative complications (myocardial infarction, stroke, sepsis, shock, return to the operating room) were similar between the 2 groups, except for deep vein thrombosis (DVT), which was more prevalent in the LND group (1.04% vs 0.77%, $P = .032$). The 30-day readmission rate was higher in the LND group (6.18% vs 4.3%, $P < .001$), however, 30-day overall mortality was better (0.42% vs 0.87%, $P = .003$).

Conclusions: In this national sample of patients who underwent surgery for uterine cancer, those who had LND tended to be older, but had fewer overall comorbidities. Although they had a higher incidence of DVT and postoperative readmissions, their postoperative mortality was lower. Future considerations for LND must account for surgical risk not necessarily related to BMI but to comorbidity profile, and whether it is feasible to reduce DVT and readmission in patients who undergo LND.

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Active Chemotherapy Treatment Adversely Affects Sexual Function in Gynecologic Oncology Patients

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Objectives: Sexual dysfunction is common after treatment of gynecologic malignancies. Age, cancer type, and surgery performed have been evaluated as contributory factors. The goal of the current study is to investigate the role of adjuvant therapy, including chemotherapy and radiation, in clinical sexual dysfunction among cancer patients.

Methods: A cross-sectional survey of outpatients in a gynecologic oncology clinic was completed at a single institution in May and June 2015. Participants completed validated questionnaires including the symptom-specific Female Sexual Function Index (FSFI) and global Short Form-12 (SF-12) health survey. Researchers performed chart review for demographic and clinical data. Multiple linear regression with stepwise forward selection was used to evaluate potential predictors of FSFI score, including SF-12 score, age, menopausal status, cancer type and stage, chemotherapy and radiotherapy histories, and next step in treatment plan.

Results: A total of 295 patients consented to participate. Of 167 patients who completed the FSFI, 137 (82%) had sexual dysfunction defined by a score of less than 26.55, with mean FSFI score of 15.9 ± 9.9. There was a moderately large positive correlation between FSFI and the SF-12 physical ($R = 0.43$) and mental ($R = 0.38$) scores ($P < .0001$ for both). Univariate analysis demonstrated a significant trend with time from chemotherapy and reports of sexual dysfunction. Mean FSFI was 9.0 ± 7.7 in patients currently undergoing chemotherapy, compared with recent (FSFI 16.8 ± 8.7), remote (FSFI 17.8 ± 10.3), and never (FSFI 18.4 ± 10.3) chemotherapy groups ($P < .0001$ with the analysis of variance [ANOVA]). Univariate analysis

demonstrated no difference in radiation groups (P = .96 with ANOVA). In multiple regression analysis, SF-12 subscores (P < .0001) and current chemotherapy (P < .0001) were statistically significant predictors of FSFI.

Conclusions: Self-reported sexual dysfunction is extremely common in the gynecologic oncology outpatient population. Sexual dysfunction as assessed by the FSFI correlates with general well-being as assessed by SF-12. Active chemotherapy was a significant predictor of sexual dysfunction, but radiation therapy was not. Chemotherapy education should include discussion of sexual dysfunction, as significant restoration of FSFI score was observed after cessation of chemotherapy.

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Upregulated Wnt signaling is associated with increased survival of patients with high-grade serous ovarian cancer

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Objectives: To evaluate Wnt signaling as a determinant of survival or chemoresistence, we analyzed associations of Wnt pathway genes and survival outcomes among high-grade serous ovarian cancer (HGS OvCa) patients treated with intraperitoneal (IP) or intravenous (IV)-only chemotherapy.

Methods: Data were obtained on HGS OvCa patients treated with IP (n = 90) or IV-only (n = 398) adjuvant chemotherapy from The Cancer Genome Atlas (TCGA). Multivariate Cox proportional hazards regression tested associations of 26 Wnt pathway genes with progression-free survival (PFS) and overall survival (OS). Gene expression as a continuous variable was demonstrated using restricted mean survival analysis. PFS or OS were compared between IP and IV chemotherapy groups using permutation testing stratified by tumor mRNA expression level.

Results: APC, APC2, WNT5A, and frizzled genes FZD2, 3, 4, 5 and 10 were each significantly (P < .05) associated with OS and/or PFS among patients treated with IV chemotherapy. FZD3 expression was also associated with OS and PFS among patients who received IP chemotherapy. Each one standard deviation increase of tumor FZD3 expression was associated with increased survival: IP group, OS: HR 0.25 (0.11–0.72), P = .009, PFS: HR 0.58 (0.37–0.92), P = .020; IV group, OS: HR 0.85 (0.72–0.99), P = .039, PFS: HR 0.83 (0.73–0.95), P = .006. Patients with low tumor FZD3 expression (bottom 20th percentile) who received IP chemotherapy experienced decreased mean OS compared with those treated with IV-only chemotherapy (21.7 vs 33.3 months, P < .0001). Upper 20th percentile versus bottom 20% percentile FZD3 expression was associated with 37.2-month mean OS advantage among patients treated with IP chemotherapy (58.9 vs 21.7 months, P < .0001). Consistent with Wnt signaling pathway interactions, increased APC2 expression had an inverse relation with survival compared with FZD gene expression: IV group, OS: HR 1.22 (1.05–1.42), P = .009, PFS: HR 1.28 (1.12–1.45), P = .0002.

Conclusions: Human-derived gene expression and clinical data suggest that upregulated Wnt signaling is associated with increased survival of HGS OvCa patients. Primary tumor expression Wnt pathway genes such as FZD3 are candidate biomarkers for selecting patients for IP chemotherapy.

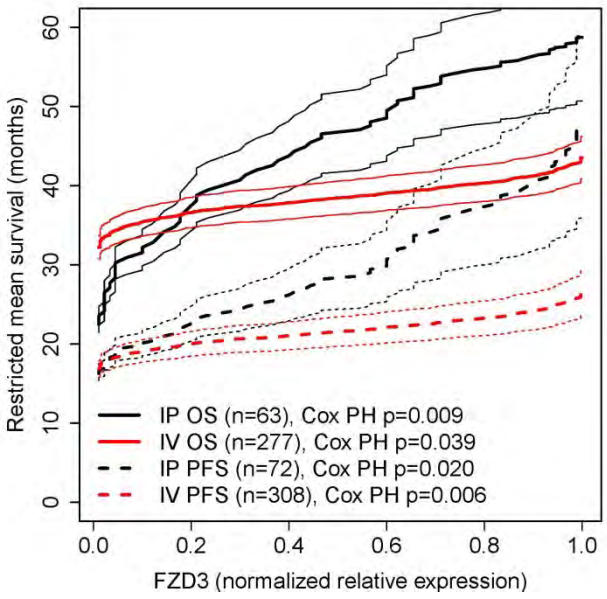

Fig. 1
Restricted Mean Survival as a Function of FZD3 Gene Expression.

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Adjuvant hysterectomy for cervical cancer: Indications, complications, and outcomes
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Objectives: To describe clinical features, morbidity, and survival among patients who underwent adjuvant hysterectomy after radiation for cervical cancer.

Methods: We conducted a retrospective study of patients treated for cervical cancer at 2 academic urban hospitals between 1999 and 2013. Adjuvant hysterectomy was defined as hysterectomy performed within 90 days of completion of radiotherapy administered with curative intent. Demographic, clinical, and treatment variables were abstracted. Survival analysis was conducted using the Kaplan-Meier method and long-rank test.

Results: We identified 1,119 women who received treatment for cervical cancer, of whom 485 underwent extrafacial or radical hysterectomy as a component of primary treatment. Of all hysterectomies, 25 (5.1%) were performed in the adjuvant setting. All subjects who had adjuvant hysterectomy underwent external beam radiation and brachytherapy, and 92% received sensitizing chemotherapy. Subjects had the following stage distribution: IB1 (4%), IB2 (40%), IIA (16%), IIB (40%), and IIIB (4%). Incomplete response to radiation therapy (48%) and reduction of brachytherapy dose (36%) were the most common indications for adjuvant hysterectomy. Residual disease was found in 80% of adjuvant hysterectomy specimens. Only 16% of adjuvant hysterectomies were completed using minimally invasive technique, and pelvic lymphadenectomy was performed in 20% of cases. Four cases (16%) resulted in perioperative complications including 2 cases with hemorrhage requiring transfusion, 1 of which also resulted in a ureteral injury, 1 case of pulmonary embolus, and 1 pelvic abscess treated with drainage. Two patients developed vesicovaginal fistulae, and 1 of these patients also subsequently developed a rectovaginal fistula. Median follow-up time was 57.6 months and the 5-year survival was 58% (95% CI 33%–77%). Women who underwent adjuvant hysterectomy tended to have inferior survival compared with subjects of the same stage who underwent primary surgery or radiation alone, but these differences did not reach statistical significance (P = .1 for stage 1B2, P = .18 and 2B, see Figure).

Conclusions: Adjuvant hysterectomy is a reasonable approach for women with locally confined cervical cancer incompletely treated with radiotherapy.

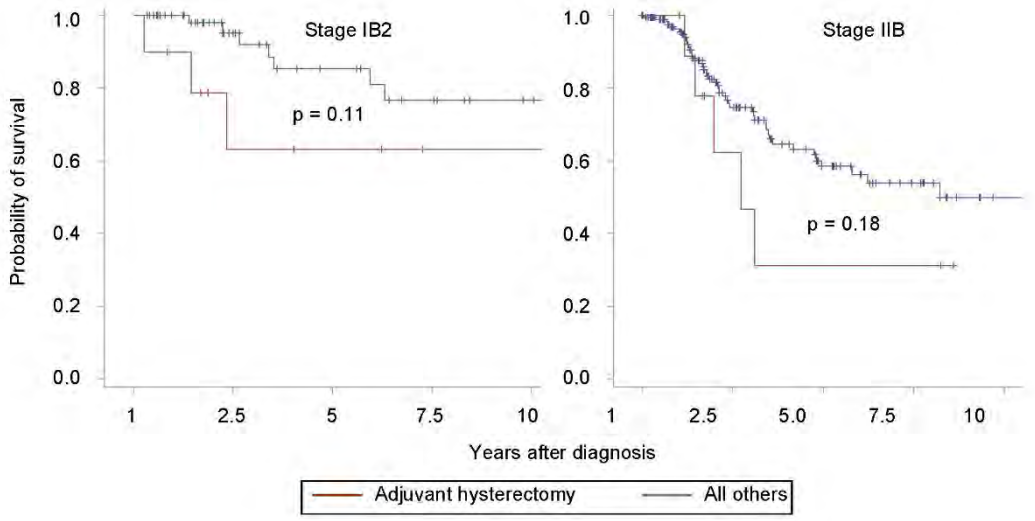

Fig. 1
Kaplan-Meier curves for subjects treated with adjuvant hysterectomy and subjects receiving any other treatment modality, stage 1B2 and IIB.

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Characteristics of primary peritoneal serous carcinoma in a U.S. population enriched for Jewish ancestry
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Objectives: To compare the clinical characteristics of *BRCA*-associated and sporadic primary peritoneal serous carcinoma (PPSC) cases and to describe the prevalence of PPSC in a tertiary care center with a large Jewish population.

Methods: An institutional review board–approved retrospective chart review identified consecutive patients who received a diagnosis of PPSC between January 1995 and December 2012. All patients met Gynecologic Oncology Group (GOG) criteria for PPSC by pathology re-review: ovaries normal in size, involvement of extraovarian sites greater than involvement of ovarian surfaces, and absent or minimal invasive disease in ovarian stroma. Demographic, clinical, and histologic information was abstracted from medical records.

Results: A total of 623 women with pelvic serous carcinomas were identified; 117 (19%) met criteria for a diagnosis of PPSC. Women who self-identified as Jewish were more likely to have PPSC than non-Jews, 25% versus 15% ($P = 0.004$). Seventy-three (62%) patients with PPSC underwent *BRCA* genetic testing, of whom 25 (34%) had deleterious mutations: 17 *BRCA1*, 6 *BRCA2*, and 2 with both *BRCA1* and *BRCA2*. BRCA1 mutation–associated cases were significantly younger than those with *BRCA2* and sporadic cases, 49 versus 60 versus 68 years, respectively ($P < .0001$). There were no differences in the preoperative CA-125 values, stage, optimal cytoreduction rates, or use of adjuvant chemotherapy between *BRCA*-associated cases and sporadic cases. Patients with *BRCA*-associated PPSC were more likely to have a personal history of breast cancer than sporadic PPSC patients, 24% versus 6% ($P = .05$). *BRCA*-associated PPSC had a trend toward improved survival compared with sporadic cases, with a median survival of 74 versus 48 months respectively ($P = .12$). *BRCA2* mutation carriers had superior survival compared with *BRCA1*mutation carriers, 99 versus 74 months (Figure 1).

Conclusions: PPSC is more prevalent among Jewish women with pelvic serous carcinomas than non-Jewish women (25% vs 15%). The higher frequency of PPSC among Jewish women compared with non-Jewish women cannot be attributed entirely to *BRCA* mutations in this cohort. *BRCA1*-associated PPSC patients are diagnosed at a younger age than *BRCA2*-associated or sporadic cases. Like other *BRCA*-associated pelvic carcinomas, *BRCA*-associated PPSC is associated with improved survival, which may be largely because of improved survival of *BRCA2* mutation carriers.

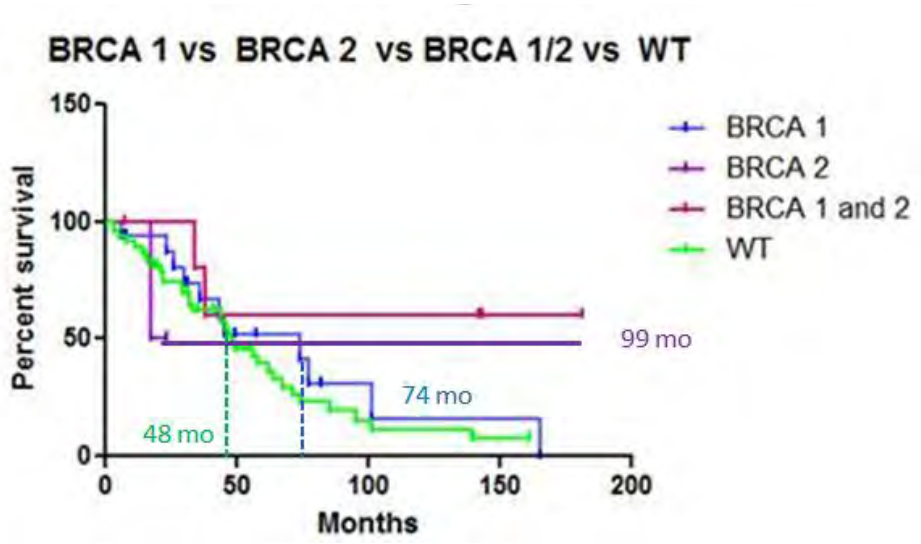

Fig. 1
Overall survival by BRCA mutation status.

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Missed opportunity visits in HPV vaccination in underserved adolescents

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Objectives: To characterize the missed opportunity visits (MOV) for human papillomavirus (HPV) vaccination at an underserved adolescent clinic.

Methods: A retrospective chart review was conducted of all female and male patients, aged 9 to 26 years, who were seen at the Corner Health Center (CHC) from July 1, 2012, to December 1, 2013. Information on demographics, visit type, provider type, and vaccination status was collected. A mandatory statewide vaccination registry was used to verify the patients' vaccination status. MOV was defined as a clinic visit of an age-eligible previously unvaccinated patient who remained unvaccinated after the visit.

Results: We identified 1,055 unique patients who attended 3,174 total clinic visits at the CHC. The median age was 19 years (range, 9–24 years). Seventy-one percent of patients were female, 52% were African American, and 40% were self-pay. Only 36% of vaccine-eligible patients received the HPV vaccine and only 17% were vaccinated at CHC. Based on our definition of MOV, 77% of visits were MOV and 81% of unvaccinated patients had at least 1 MOV. Of patients with at least 1 MOV, 67% were female and 52% were African American. MOV occurred at a rate of 84% for self-pay patients. All visit types had a similar rate of MOV (range, 35%–43%). Provider types had similar frequency of MOV (range, 72%–100%). A multivariable logistic regression indicated that the odds of being a patient with an MOV decreased with every year increase in age (OR 0.77, P = .018). Males had higher odds of being a patient with an MOV (OR 1.66, P < .01)

Conclusions: MOVs in HPV vaccination in underserved adolescents are common, and interventions targeting all provider types and visit types are needed. Interventions should include special consideration of male and younger patients, particularly given the fact that federal vaccination coverage ends at age 18 years. Mandatory state vaccination registries are essential in accurately monitoring vaccination status.

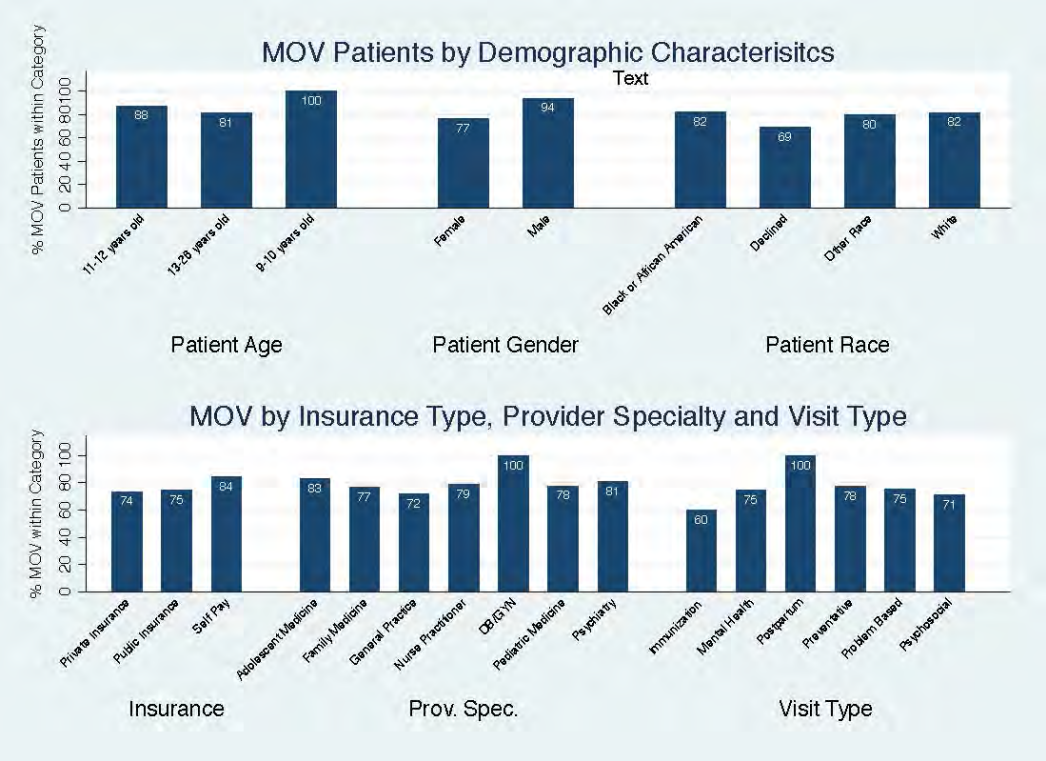

Fig. 1
Missed Opportunity Visits (MOV) Patients by Demographic Characteristics.

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Bevacizumab-induced hypertension in gynecological cancer: Does it resolve after completion of therapy?

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Objectives: Hypertension (HTN) induced by bevacizumab is a side effect that is often thought to resolve after treatment. However, there are currently no reports on rates of resolution. We assess the incidence and timing of the resolution of bevacizumab-induced HTN and its effect on prognosis.

Methods: We performed a retrospective cohort study of all patients who were treated with bevacizumab for gynecological malignancy at a single institution from 2012 through 2014. HTN was retrospectively diagnosed and staged based on CTCAE v4.0 criteria. Resolution of HTN was defined as 2 or more values of a return to baseline blood pressure and/or discontinuation/decrease of blood pressure medications. Standard statistical methods were used.

Results: We identified 104 patients; 35 were excluded because they were still receiving bevacizumab at the time of analysis. Median follow-up time was 17.5 months (range, 2–50 months). Of 69 patients, 34 (49.3%) had grade 2 or higher HTN induced by bevacizumab, 26 (37.7%) had grade 2 HTN, and 8 (11.6%) had grade 3 or 4 HTN. Of the 34 patients with HTN, 16 had pre-existing controlled HTN that increased with bevacizumab. Median number of bevacizumab cycles in those with HTN was 11 (range, 3–57), compared with 8 (range, 1–49) in those without (P = .09). Most patients (94%) received 15 mg/kg every 3 weeks. Onset of HTN occurred at a median of 67 days (range, 14–791 days). HTN resolved after the last dose of bevacizumab in 28 (82.4%) of 34patients, with a median time of 87 days (range, 3–236 days). Body mass index, history of HTN, blood pressure medications, prior bevacizumab treatment, number of bevacizumab cycles, and CA-125 and albumin levels at initiation of treatment were not independent risk factors associated with developing HTN on multivariate analysis. Median progression-free survival (PFS) for those with HTN was 12.5 months (range, 1.9–45.8 months) versus 11.0 months (range, 2.1–44.7 months) for those without (P = .24). Ten patients were either taking a β-blocker before the initiation of bevacizumab or started taking one during this study. Median PFS in these patients was 11.5 months (range, 4.0–21.9 months).

Conclusions: Eighty-two percent of bevacizumab-induced HTN resolved in a median of 87 days, which is within the expected range of 100 days, based on the pharmacokinetics of the drug clearance. HTN was not a biomarker of improved prognosis in our cohort. The use of β-blocker therapy in bevacizumab-induced HTN was not associated with improved PFS.

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Serous tubal intraepithelial carcinoma lesions are common in primary peritoneal serous carcinomas

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Objectives: To determine the incidence of serous tubal intraepithelial carcinoma (STIC) lesions in patients diagnosed with primary peritoneal serous carcinoma (PPSC) and the associated clinical outcomes.

Methods: An institutional review board–approved retrospective chart review identified consecutive PPSC patients diagnosed between January 2002 and December 2014 who underwent cytoreductive surgery at a single institution. All patients had results of at least bilateral salpingo-oophorectomy (BSO) and pathology available for review. All patients met Gynecologic Oncology Group (GOG) criteria for PPSC: ovaries normal in size, involvement of extraovarian sites more than involvement of ovarian surfaces, and absent or minimal invasive disease in ovarian stroma. Pathology re-review of the adnexae was performed by a gynecologic pathologist. Demographic, clinical, and histologic information was abstracted from medical records.

Results: Forty-four consecutive patients who met the criteria were identified. Thirty (68%) patients underwent comprehensive sectioning of the fallopian tubes. Thirteen (43%) STIC lesions were found within the fallopian tubes that underwent comprehensive sectioning versus 0 STIC lesions in those who had only representative tubal sectioning available (*P* = .0001). All STIC lesions involved the tubal fimbriae. Seven patients received neoadjuvant chemotherapy before undergoing interval debulking surgery (IDS); 2 of these patients were found to have persistent STIC lesions on final pathology at the time of IDS. Twenty-eight (64%) underwent *BRCA* mutation testing, and one-third were found to carry a deleterious *BRCA* mutation. Median age, frequency of Jewish ethnicity, *BRCA*status, average serum CA-125 at diagnosis, and clinical outcomes were comparable between the groups with and without STIC lesions.

Conclusions: STIC lesions are identified in almost half of cases of PPSC, and comprehensive tubal sectioning yields higher detection rate than representative sectioning. The fallopian tube fimbria is a likely site of origin of PPSC, and the fimbriae may be a site of persistent disease after neoadjuvant chemotherapy. *BRCA* mutation testing was underutilized in this cohort with PPSC.

Table 1

Characteristics of 44 consecutive patients with PPSC diagnosis.

	n = 44	%
Median age (years)	64 (range 39-87)	-
Jewish	25	57
BRCA mutation tested BRCA mutation confirmed	28 9	64 32
Neoadjuvant chemotherapy	7	16
Comprehensive tubal sectioning STIC lesion	30 13	68 43
Dead of disease	22	50
History of breast cancer	9	20
Median follow-up (months)	45 (range 5-106)	-

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Opinions and attitudes of gynecologic oncologists about the interaction with palliative care specialists

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Objectives: Gynecologic oncologists and palliative care (PC) specialists often jointly care for patients with advanced gynecologic malignancies. We sought to understand the attitudes and patterns of care of gynecologic oncologists with regard to their involvement with PC specialists in patient care.

Methods: A 27-item survey was sent to all Society of Gynecologic Oncology (SGO) members by electronic mail. The data were collected and analyzed using commercially available, web-based software. Descriptive statistics were used.

Results: Of the 144 SGO members who responded, the majority were female (55.5%), white (80.7%), aged 30 to 40 years (41%), and worked as attending physicians (75%) in academic hospitals (60%). Most respondents (91.6%) had a PC team available for consultation at their institutions. About half of the respondents felt that PC services were appropriately used versus underutilized at their institution (47.3% vs 51.2%). Thirty percent % of respondents felt that PCs should be involved with a patient at the time of first recurrence, whereas 41% felt PC specialists should be involved when a patient's prognosis is less than 6 months. Seventy-five percent of respondents agreed that PC specialists should be involved in a patient's care for symptom management at any stage of disease. Respondents were most likely to consult PC specialists for pain control and to discuss transition to hospice care (63.5% and 49.5% rated very likely, respectively). Overall, respondents felt most strongly that communicating prognosis is the responsibility of the primary team (83.5%), whereas the responsibilities associated with pain and symptom control, resuscitation status, and goals of care discussions were split between "primary team only" and "both teams." The largest identified barrier (73.3%) for consulting PC specialists was a concern that patients and families will perceive the primary team as abandoning their care. Overall, 96.5% of respondents answered that PC specialists are useful team members who improve patient care.

Conclusions: Even though the vast majority of respondents perceive PC specialists as useful, our findings suggest they are generally underutilized. Given the evidence demonstrating improved clinical outcomes with early PC, interventions to increase its utilization should be explored, particularly because pain and symptom control are important at all points of the disease process.

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Is there really an HPV genotype difference in African American versus Caucasian women? Insights from the ATHENA trial

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Objectives: In the United States, African American women (AAW) are more likely to die of cervical cancer than non-Hispanic white women. In addition, the incidence of cervical cancer is higher in AAW, which cannot be fully explained by a lack of screening. Recently, investigators reported a different human papillomavirus (HPV) genotype distribution in AAW (Hoyo et al). It has been argued that this difference might contribute to their higher incidence and mortality. The objective of this study was to assess whether disease is driven by different genotypes in AAW from the ATHENA trial.

Methods: At enrollment, all women were 21 years or older (46,887 eligible), and underwent cytologic examination with PreservCyt and HPV testing with both the Cobas HPV test, which separately detects HPV16, HPV18, and a pool of 12 other hrHPV genotypes, and LINEAR ARRAY genotyping. Those with higher than atypical squamous cells of undetermined significance (ASCUS) cytology or positive HPV results and a random subset cytology –/ HPV– were referred for colposcopy. Cervical biopsy results were adjudicated by expert pathologists. All patient information and test results were masked throughout.

Results: More than 6,400 women were evaluated in this analysis. The absolute risk of cervical intraepithelial neoplasia (CIN)3+ and CIN2+ in AAW in the overall population was statistically higher for women who were HPV16/18 positive versus those who were positive for the other 12 hrHPV types: 10.76 (95% CI 6.83–16.56) versus 2.91 (95% CI 1.74–4.83) and 13.92

(95% CI 9.38–20.18) versus 6.65 (95% CI 4.75, 9.24) for CIN3+ and CIN2+, respectively. Similarly, high-grade disease was driven by HPV16/18 in AAW with normal cytology and abnormal cytology (≥ASCUS). Likewise, looking at age deciles (from 21–59 years), the absolute risk of CIN3+ is always higher with HPV16/18 versus the 12 other hrHPV types for AAW irrespective of age (nonsignificant for >50 years because of the small number of cases)

Conclusions: The ATHENA trial, the largest cervical cancer screening study to date in the United States, indicates that most cases of high-risk cervical disease are caused by HPV16/18. This is in spite of reports indicating an HPV genotype distribution difference in AAW and non-Hispanic Caucasian women and its impact on disease prevention with currently available HPV vaccines. This is similar to what has been documented in non-Hispanic Caucasian women. Therefore, this calls into question the clinical relevance of creating race-specific HPV vaccines.

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Frailty as a predictor of adverse outcomes in patients undergoing surgery for gynecologic malignancies

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Objectives: We sought to determine if the modified frailty index (mFI) correlates with morbidity and mortality in patients undergoing gynecologic cancer surgery. Predicting outcomes is important in preoperative counseling and surgical planning. The concept of frailty is emerging as a potential tool for predicting worse surgical outcomes. It is defined as an increase in one's vulnerability for developing dependency or death because of a loss of physical or mental reserve, often in the absence of a defined comorbidity.

Methods: Patients who underwent gynecologic cancer surgery from 2006 to 2012 in the National Surgical Quality Improvement Program (NSQIP) database were analyzed. mFI was calculated using 11 preoperative variables. Associations between mFI and readmission, major complications, and 30-day mortality were assessed. A multiviariable logistic regression model was used to predict adverse outcomes, after adjusting for age, race, and body mass index.

Results: A total of 13,093 patients who had surgery for a gynecologic malignancy were identified (6,728 [51.4%] with uterine, 2,765 [21.1%] with ovarian, 2,373 [18.1%] with cervical, and 1,227 [9.4%] with other gynecologic cancers). For all gynecologic malignancies, there were 654 (5.0%) readmissions, 890 (6.8%) patients with 1 or more major complications, and 93 (0.008%) deaths within 30 days. When including all women who underwent gynecologic cancer surgery, increasing mFI was significantly associated with increased risk for major complications (OR 1.19, 95% CI 1.09–1.30, $P < .001$) and 30-day mortality (OR 1.49, 95% CI 1.18–1.87, $P = .001$), but not for readmission. For example, 30-day mortality increased from 0.4% in patients with an mFI of 0, to 7.6% in those with an mFI of 0.3 or higher. When analyzing each malignancy individually, this trend was noted in both uterine and ovarian cancer patients, both younger and older than 65 years of age. For example, 30-day mortality increased from 0.4% in uterine cancer patients with an mFI of 0, to 5.7% in those with an mFI of 0.3 or higher, and from 0.8% to 12.5% in ovarian cancer patients. There was no trend found for cervical or other gynecologic cancer patients.

Conclusions: The mFI can be calculated with routinely collected clinical data and is predictive of adverse outcomes in patients undergoing gynecologic cancer surgery, namely uterine and ovarian cancer, and may aid in preoperative counseling.

Table 1
Preoperative Risk Factors Included in the mFI.

	Domain (mFI)	Coding (NSQIP)
1	Diabetes mellitus	Insulin dependent diabetes mellitus or non-insulin dependent diabetes mellitus
2	Functional status	Partially or totally dependent
3	Respiratory problems	Chronic obstructive pulmonary disease
4	Congestive hear failure	Congestive heart failure
5	Myocardial infarction	Prior myocardial infarction

6	Other cardiac problems	Previous percutaneous coronary intervention or coronary surgery or angina
7	Hypertension	Hypertension requiring medication
8	Peripheral vascular disease	Peripheral vascular disease or resting pain
9	Impaired sensorium	Impaired sensorium
10	Cerebrovascular disease	Transient ischemic attach or cerebrovascular accident
11	Cerebrovascular disease with neurological deficit	Cerebrovascular disease with deficit

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The impact of percentage of time on chemotherapy on survival in recurrent ovarian cancer

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Objectives: Most women with ovarian cancer achieve remission after first-line chemotherapy. However, the majority will experience recurrence, and many women will receive additional palliative chemotherapy yet eventually succumb to their disease. With the benefit of additional palliative chemotherapy debatable, balancing quality of life with chemotherapy toxicity is of paramount importance. This study aims to determine whether additional time receivng salvage chemotherapy leads to improved overall survival (OS) in those with recurrent ovarian cancer.

Methods: A single institutional cancer registry was queried to identify women treated for recurrent ovarian cancer from 2004 to 2014. A retrospective chart review was performed to abstract clinical data on a randomly selected sample of 100 women. Patients were divided into tertiles based on percentage of time receiving chemotherapy from recurrence to death with the first tertile having the smallest percentage of time on chemotherapy and the third tertile having the greatest percentage of time on chemotherapy. Kaplan-Meier and the log-rank tests were used to compare survival between groups.

Results: Among all recurrent ovarian cancer patients, a greater percentage of time on chemotherapy from recurrence to death was associated with poorer OS (first tertile 44 months vs third tertile 31 months, $P = .02$). In those that became platinum resistant, a greater percentage of time of chemotherapy was associated with poorer OS whereas in platinum-sensitive women a greater percentage of time on chemotherapy did not improve OS (platinum resistant: first tertile 47 months vs third tertile 31 months, $P = .003$; platinum sensitive: first tertile 42 months vs third tertile 53 months, $P = .31$). In platinum-resistant women, a greater percentage of time on chemotherapy from platinum resistance to death also did not improve OS (first tertile 39 months vs third tertile 34 months, $P = .23$).

Conclusions: In this cohort of recurrent ovarian cancer patients, a greater percentage of time on chemotherapy did not lead to improved survival, and in some cases, worsened survival. In a palliative setting, caution should be taken against overtreating women, because this may lead to poorer quality of life without apparent benefit. Introduction of palliative care measures at the time of recurrence and the use of hormonal or noncytoxic therapies should be considered.

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Next-generation genomic signature highlights sustained AKT and estrogen receptor signaling as key mediators of resistance following phosphatidylinositol 3-kinase (PI3K) inhibition in patient-derived xenograft models with and without PIK3CA gene mutations

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Objectives: The objective of this investigation was to use patient-derived xenograft (PDX) models with and without *PIK3CA* gene mutation to understand the driving genomic events associated with the development of resistance to PI3K inhibition.

Methods: With institutional approval, NOD/SCID mice bearing xenografts derived from 2 primary human endometrioid endometrial human tumors (ENCA1, ENCA2) underwent genotyping revealing ENCA1-harbored *PIK3CA* and *PTEN* mutations, while ENCA2 demonstrated no detected mutations using the SNAPSHOT platform. Two arm cohorts (n = 12/arm) with equivalent tumor volumes received either NVP BKM-120 (30 mg/kg) or vehicle, and xenograft tumor volumes were assessed. Xenografts were harvested before therapy and at the point of sensitivity, resistance, or prolonged sensitivity. RNA was extracted for quantification using Illumina HiSEQ 2000 to determine the genome level changes in the ENCA1 and ENCA2 tumors. In the supervised analysis, using absolute-fold change (FC>2) and *P* value (*P* <. 05), differentially expressed genes were identified at the points of resistance and prolonged sensitivity. Pattern, functional, and pathway analyses were used to explore the biological meaning of these gene signatures.

Results: Both ENCA1 and ENCA2 manifested initial response to NVP BKM-120, and the 2 models had divergent sensitivity signatures. Pathway and functional analyses revealed key nodes in the 53 gene signatures associated with prolonged sensitivity were sustained abrogation of AKT and the mitogen-activated protein kinase (MAPK) signaling. While ENCA1 maintained prolonged sensitivity, ENCA2 developed resurgent growth. A 238 gene set was observed to have significant counterregulation with the development of resistance and was exclusive to ENCA2. Gene and pathway analysis demonstrated that resistance to PI3K inhibition was associated with marked increases in estrogen signaling and ubiquitination.

Conclusions: These results highlight that genomic events conferring sensitivity are distinct, depending on the presence of *PIK3CA* mutation. While prolonged sensitivity to PI3K pathways inhibition appears to be dependent on sustained inhibition of AKT and MAPK signaling, resistance was associated with heightened estrogen and ubiquitin activity. These data provide rationale for pairing PI3K pathway inhibition with hormonal or ubiquitin blockade to improve durable antitumor response.

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Feasibility and learning curve of robotic laparoendoscopic single site surgery in gynecology

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Objectives: Single-site laparoscopy has proven to be a desirable option for patients undergoing gynecologic surgery, with some studies indicating improved cosmesis and less perioperative pain compared with standard approaches. This study describes the safety and feasibility of a novel robotic laparoendoscopic single-site surgery (R-LESS) platform as it is newly incorporated into a surgeon's practice.

Methods: A review was conducted of 82 women undergoing R-LESS at a single institution from September 2013 through August 2015. All surgeries were performed by a single gynecologic oncologist with extensive experience in robotic surgery. Operative times were collected prospectively for the first 51 cases. Clinical parameters including age, estimated blood loss, body mass index (BMI), prior abdominal surgeries, conversion to laparotomy, procedure type, uterine weight, length of hospital stay, and complications were retrospectively collected from medical charts.

Results: A total of 81 surgeries were completed successfully with a single incision. Twelve surgeries were performed for cancer (1 ovary, 8 uterus, and 3 cervix). Seven patients underwent pelvic lymph node biopsy. The median total operative time for adnexal surgeries was 97 minutes (range, 57–177 minutes) and 128 minutes (range, 60–275 minutes) for hysterectomies. Mean docking time halved from 7.8 minutes to 3.4 minutes in a comparison of the first 10 cases with the last 10 cases. Operative time and console time also steadily decreased with experience. Surgical times were longer with larger BMIs, but the console time decreased with experience regardless of BMI. The mean uterine weight was 161.3 g (range, 30–460 g). Complications included 2 umbilical hernias and 1 conversion to multiport.

Conclusions: R-LESS is a feasible surgical platform for gynecologic procedures. As our surgical team gained experience, operative times decreased even as surgical complexity (BMI, number of prior abdominal surgeries) increased. Further study is needed to investigate the cost, benefits, and long-term outcomes of R-LESS.

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Phase 1/2a study of double immune suppression blockade by combining a CSF1R inhibitor (pexidartinib/PLX3397) with an anti–PD-1 antibody (pembrolizumab) to treat advanced melanoma and other solid tumors

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Objectives: Tumor-associated macrophages (TAMs) support tumor growth and cause tumor resistance to chemotherapy and radiation therapy. Myeloid-derived suppressor cells (MDSCs) suppress antitumor immunity and cause resistance to PD-1 inhibition. TAMs and MDSCs are both regulated in part by colony-stimulating factor 1 (CSF1), which signals via its receptor (CSF1R). Pexidartinib is an oral, small-molecule inhibitor of CSF1R. The normal function of PD-1, expressed on the cell surface of activated T cells, is to suppress excessive immune responses, eg, autoimmune reactions. Tumors use PD-1 signaling to downregulate immune-mediated elimination. Pembrolizumab is a potent and highly selective humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. We present the study design for a phase 1/2a clinical trial assessing the safety, efficacy, pharmacokinetics, and pharmacodynamics of the combination of pexidartinib and pembrolizumab in advanced solid tumors (NCT02452424).

Methods: In part 1 of this open-label, uncontrolled study, patients with advanced solid tumors will be treated with pembrolizumab (200 mg intravenously every 3 weeks) and escalating daily oral doses of pexidartinib to establish a recommended phase 2 dose (RP2D) combination regimen, and the safety and tolerability of the combination. In part 2, the combination RP2D will be studied in an expanded panel of solid tumor cohorts, including ovarian and triple-negative breast cancer, in up to 475 patients to assess safety and preliminary efficacy. Overall response rate and progression-free survival will be evaluated using RECISTv1.1 criteria. Exploratory objectives include identification of novel biomarkers of clinical activity and drug mechanisms of action. A truncated sequential probability ratio test will be used in each tumor cohort to allow early decision making for futility or success.

Results: Not available.

Conclusions: The results of this trial in progress should inform further development of the pexidartinib/pembrolizumab combination for solid tumors that respond to treatment in this study.

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Timing of referral to the New England Trophoblastic Disease Center: Does referral with molar pregnancy versus postmolar gestational trophoblastic neoplasia affect outcomes?

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Objectives: Every woman who receives care for gestational trophoblastic disease at the New England Trophoblastic Disease Center (NETDC) is referred by her primary physician. The aim of this study was to assess if referral with molar pregnancy is associated with different outcomes compared with referral with postmolar gestational trophoblastic neoplasia (GTN).

Methods: The records of the NETDC were queried for all patients with molar pregnancy or postmolar GTN from 1993 to 2013. Retrospective chart review was performed to extract relevant clinical and demographic data. Parametric and nonparametric tests were used to compare variables.

Results: From 1993 to 2013, 436 women with molar disease were evaluated at the NETDC. Of these, 68% were referred with molar pregnancy, and 32% were referred with postmolar GTN. The women referred with postmolar GTN were more likely to have had a complete mole as their antecedent pregnancy (72.7% vs 59.7%, $P < .01$) and to have been diagnosed at an earlier gestational age (10.0 vs 11.1 weeks, $P < .005$). Comparing women with postmolar GTN who were referred with a molar pregnancy with those who were referred with postmolar GTN, the women were at equivalent stages (stage III and IV 25.0% vs 21.5%, $P = .66$) and World Health Organization (WHO) score (WHO ≥ 7 0% vs 4.5%, $P = .60$). In addition, there was no

difference in time to persistence (67 vs 54 days, *P* = .53), time to remission (71 vs 69 days, *P* = .88), or number of lines of chemotherapy administered (*P* = .25).

Conclusions: In this trophoblastic disease specialty center, referral at the time of diagnosis of postmolar GTN versus molar pregnancy did not appear to affect the stage or WHO score at diagnosis, the need for multiple chemotherapy lines, or time to remission.

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Pathologic response at interval debulking surgery following neoadjuvant chemotherapy predicts improved survival in women with ovarian cancer

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Objectives: To determine if a pathologic response at the time of interval debulking surgery (IDS) predicts survival in patients undergoing neoadjuvant chemotherapy (NACT) for epithelial ovarian cancer (EOC).

Methods: We retrospectively evaluated 55 consecutive EOC patients treated with NACT followed by IDS. Pathologic response was classified as complete with no residual disease (cPR), microscopic (microPR), or macroscopic (macroPR) at the time of IDS. The surgeon's assessment of cytoreduction after IDS was categorized as resection to no gross residual (R0), optimal (<1 cm), or suboptimal (>1 cm). Kaplan-Meier analysis was performed to compare progression-free (PFS) and overall survival (OS) between pathologic response groups and cytoreductive status (R0 vs any residual disease).

Results: Patients were treated with NACT for stage IV disease (n = 29, 53%), radiologically bulky disease deemed not amenable to optimal cytoreduction (n = 29, 53%), venous thromboembolism (n = 4, 7%), and poor performance status (n = 3, 5%). No differences were observed between groups including age, grade, stage, and histology. Median number of NACT cycles was 3 (range, 1–6). cPR was observed in 6 (11%), microPR in 11 (20%), and macroPR in 38 (69%) patients. cPR was associated with improved median PFS compared with patients with any residual disease (micro PR/macro PR) (undefined vs 10 months, *P* = .01). There was no difference in median OS between women with cPR and those with any residual disease (undefined vs 37 months, *P* = .42). A difference in PFS was not observed between microPR and macroPR disease (11 vs 10 months, *P* = .10). After IDS, 36 (65%) patients had R0, 17 (31%) had optimal, and 4 (7%) had suboptimal cytoreduction. There were no survival differences between patients with R0 resection and those with any residual disease at IDS (PFS 11 vs 10 months, *P* = .75; OS 32 vs 31 months, *P* = .82). Univariate analysis revealed stage IV disease was the only predictor of worse PFS (*P* = .02). Stage, grade, and normalization of CA-125 before IDS did not affect survival.

Conclusions: cPR in women with advanced EOC undergoing NACT is uncommon, but appears to be associated with improved PFS. NACT led to R0 cytoreduction at IDS in the majority of women, but it had no impact on survival in this small cohort.

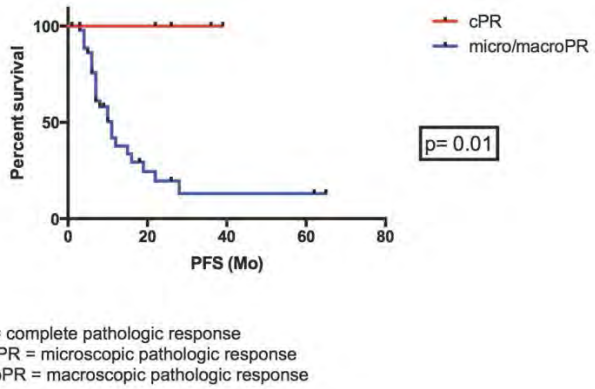

Fig. 1
Complete Pathologic Response at the Time of Interval Debulking Surgery Following Neoadjuvant Chemotherapy is Associated with Improvided Progression.

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Accumulation of cytosolic Cdk1 is associated with cell growth in epithelial ovarian cancer

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Objectives: Cyclin-dependent kinases (CDKs) are important cell cycle–regulating proteins that belong to a serine/threonine kinase family comprising a catalytic kinase subunit, together with cyclin protein partners. Cdk1 function in the nucleus is well known to be correlated with cancer, but cytosolic Cdk1 traits have not yet been identified. The aim of this study is to determine whether cytosolic Cdk1 function is associated with ovarian cancer growth.

Methods: Microarray results for cell lines of serous, mucinous, and Brenner types of ovarian cancers were reanalyzed and validated via ovarian cancer cell lines, Gene Expression Omnibus (GEO) datasets, and tissue microarray blocks. RO-3306, an inhibitor of Cdk1 and si-cdk1, was used to measure the growth rate of ovarian cancer cell lines via fluorescence-activated cell sorting analysis. In addition, combination treatment with RO-3306 and cisplatin was administered to an in vitro and in vivo xenograft mouse model.

Results: Tissue microarray blocks of epithelial ovarian cancer showed increased level of cytoplasmic Cdk1 ($P < .001$), but not in the nucleus ($P = .192$), regardless of histologic cell type. On survival analysis, Cdk1 overexpression conferred a significantly worse 5-year overall survival ($P = .047$). Also, the expression of Cdk1 was increased in ovarian cancer cell lines and GEO datasets. When the expression and activity of Cdk1 were inhibited by si-Cdk1 or RO-3306, the growth of ovarian cancer was diminished. Moreover, combined treatment with RO-3306 and cisplatin in ovarian cancer significantly elevated anticancer effects compared with single-agent treatment.

Conclusions: Cytosolic Cdk1 expression was elevated in ovarian cancer and predicts a poor overall survival rate. The inhibition of Cdk1 expression and activity reduced ovarian cancer growth.

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Everolimus and letrozole prolongs progression-free survival in relapsed estrogen receptor–positive ovarian cancer: Preliminary results of a phase 2 clinical trial

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Objectives: Single-agent aromatase inhibitor (AI) therapy is associated with limited clinical activity in ovarian cancer. Bowman et al reported that letrozole therapy in relapsed ovarian cancer was associated with no progression in 20% of patients at 12 weeks of treatment (PFS-12 of 20%). In breast cancer, AI resistance involves the mTOR pathway, with clinical studies showing the benefit of everolimus in combination with AI. Here, we report preliminary data of a phase 2 clinical trial on combination treatment with everolimus and letrozole in patients with relapsed estrogen receptor (ER)–positive ovarian cancer. The primary endpoint of this trial was the proportion of patients with relapsed ER-positive ovarian cancer alive and progression free after 12 weeks of therapy with everolimus and letrozole (PFS-12). Historical data from Bowman et al (PFS-12 of 20% with letrozole as a single agent) was used for comparison. A PFS-12 of 45% was considered a positive result.

Methods: Eligibility criteria included patients with relapsed ER-positive ovarian, fallopian tube, or primary peritoneal carcinomas with measurable disease not previously treated with everolimus or AIs. Both platinum-resistant and -sensitive tumors were included.

Results: The study enrolled 19 eligible patients with a median age of 60 years (range, 52–76 years) and an ECOG PS of 0 (47%) or 1 (53%). Data on 16 subjects are currently evaluable. Eleven of 16 were alive and progression free at 12 weeks (PFS-12 of 69%) with a median PFS of 24 weeks. Nine patients experienced at least one grade 3 or worse adverse events (47%) and two grade 4 or worse adverse events (11%). One of these 2 patients experienced a grade 4 neutrophil count decrease that was probably related to treatment; the other patient died, believed to be unrelated to treatment. Grade 3 adverse events (occurring in >10% of patients) consisted of abdominal pain (16%), anemia (11%), oral mucositis (11%), and small intestinal obstruction (11%).

Conclusions: The combination of everolimus and letrozole is associated with a promising 69% PFS-12 in patients with ER-positive relapsed ovarian cancer. Acceptable toxicity was observed, consisting mainly of anemia and oral mucositis. This combination merits additional evaluation in relapsed ER-positive ovarian cancer.

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Feasibility of single-port laparoscopic surgery in primary ovarian cancer

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Objectives: The aim of this study was to evaluate the feasibility of single-port laparoscopic surgery (SPLS) in primary ovarian cancer patients who were assumed not to have intra-abdominal carcinomatosis in preoperative evaluations.

Methods: Medical records were reviewed for 51 patients who underwent SPLS for suspicious ovarian malignancy between April 2009 and July 2015 at Yonsei Cancer Center. Twelve patients with borderline and 16 patients with metastatic tumors were excluded.

Results: Twenty-three patients underwent SPLS for primary ovarian cancer. Median age was 52 years (range, 17–72 years) and median body mass index was 23.7 kg/m^2. In 21 patients (91.3%), complete surgical staging, including pelvic and para-aortic lymphadenectomy (LND), omentectomy, and peritonectomy for suspicious lesions, was performed. Two teenaged patients with stage IA immature teratoma had fertility-sparing surgery (bilateral ovarian cystectomy without hysterectomy or lymphadenectomy, with no evidence of recurrence for 57 and 6 months). Lymphadenopathy was not performed in 2 patients who had definite stage IIIC and IVB disease during operation and no evidence of lymph node enlargement in preoperative evaluation. One patient needed one more assistant port because of a huge cyst rupture that occurred when the umbilicus was punctured, but no patient was converted to open surgery. No macroscopic residual disease was seen. Postoperative hemoglobin decrease was 2.0 g/dL (range, −4.2 to 0.1 g/dL). No major postoperative complication was seen. Thirteen cases were at stage I (56.5%), 5 cases at stage II (21.7 %), 4 cases at stage III (17.4%), and 1 case was at stage IVb (4.3%). Among 19 patients who underwent LND, median pelvic LND yield was 12 (range, 1–26), and median para-aortic LND yield was 6 (range, 1–37). Median operative time was 192 minutes (range, 82–387 minutes) and median estimated blood loss was 150 mL (range, 10–1,900 mL). Median follow-up duration was 15 months (range, 2–59 months). Four patients (17.4%) experienced recurrence and 2 patients (8.7%) died of the diseases.

Conclusions: SPLS is a potential option for selected advanced ovarian cancer cases as well as cases of early-stage disease with improvements in techniques and instrumentations. Precise selection criteria could be established through a further study in SPLS for ovarian cancer.

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Survival impact of quality of lymphadenectomy in intermediate- or high-risk group of endometrioid type endometrial cancer: A multicenter retrospective cohort analysis

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Objectives: The aim of this study was to investigate whether quality of lymphadenectomy (LND) affects survival in patients with endometrioid-type endometrial cancer having intermediate- or high-risk factors.

Methods: Eligible patients were retrospectively enrolled from 4 tertiary centers in Korea. All patients underwent surgical staging, including hysterectomy with pelvic lymphadenectomy (PLND) with or without para-aortic lymphadenectomy (PALND) between 2000 and 2013 and finally diagnosed with FIGO stage IB to IIIC2 endometrioid adenocarcinoma. The numbers of lymph nodes (LNs) removed and positive LNs from the pelvic and para-aortic area were obtained from the

pathology report. Negative LN count was defined as positive LN count subtracted from total number of LNs removed. Recurrence-free survival (RFS) and overall survival (OS) were analyzed.

Results: A total of 476 patients were enrolled for analysis. PALND was performed in 298 patients (62.6%). Median pelvic LNs and para-aortic LNs removed was 23 (range, 2–74) and 7 (range, 1–58), respectively. Stage IIIC disease was seen in 164 (34.4%) patients (node-positive group). Positive LN detection rate was associated with both pelvic and para-aortic LNs removed. Isolated para-aortic lymph node metastasis presented in 6 (18.8%) of 32 patients in the group with 20 or less pelvic LNs removed, and in only 1 (1.5%) of 68 patients in the group with more than 20 pelvic LNs removed. In the node-negative group, patients who received only low-quality PLND (≤20 pelvic LNs removed) had lower RFS compared with those who received additional PALND (P = .025). In the node-positive group, total negative LN count was an independent prognostic factor as a continuous variable (RFS: HR 0.974, 95% CI 0.949–0.995; OS: HR 0.939, 95% CI: 0.899–0.981). In all patients, total negative LN count was an independent prognostic factor for RFS and OS as a continuous variable (RFS: HR 0.983, 95% CI 0.967–0.999; OS: HR 0.962, 95% CI 0.934–0.991). Quality of PLND assessed by pelvic negative LN count is the most important prognostic factor.

Conclusions: Both positive node detection rate and survival were affected by number of LNs removed. Negative LN count is a reliable marker for assessing quality of LND with prognostic value in patients with intermediate- or high-risk endometrial cancer regardless of node positivity. High-quality PLND is more important than performing PALND in such patients.

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Utility of routine postoperative hemoglobin testing after minimally invasive surgery for endometrial cancer

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Objectives: To determine if routine postoperative hemoglobin (Hgb) testing is useful in guiding care for women who undergo minimally invasive surgery (MIS) for endometrial cancer (EMCA).

Methods: A retrospective cohort study of patients who underwent MIS for EMCA from 2010 to 2015. We included patients who underwent standard laparoscopy (LSC) and robotic-assisted surgery. Baseline demographics and perioperative characteristics were collected. We defined clinical hemodynamic instability (HI) as development of at least one of the following: tachycardia, hypotension, low urine output, or dizziness.

Results: A total of 235 patients underwent MIS for EMCA: 138 (58.7%) underwent LSC and 97 (41.3%) underwent robotic-assisted surgery. Patients with a lower body mass index were more likely to have a greater decrease in Hgb (P < .01); however, surgical history, surgery/anesthesia time, blood loss, performance of and extent of lymphadenectomy, use of preoperative anticoagulation, and use of postoperative ketorolac were not associated with greater decreases in Hgb. Postoperatively, 52 patients (22.1%) had 1 or more sign or symptom of HI. Compared with asymptomatic patients, these clinically symptomatic patients were significantly older (68.6 vs 64.6 years old, P = .03) and had significantly greater decreases in Hgb (2.38 vs 1.96 g/dL, P = .048). Only 5 patients, all of whom were also symptomatic, required postoperative blood transfusions. No asymptomatic patients required transfusion. Symptomatic and asymptomatic patients did not differ with regard to rates of reoperation or readmission.

Conclusions: These results call into question the utility of performing routine Hgb testing after MIS for EMCA. Hgb testing may only be necessary for patients who develop signs or symptoms of HI. Omission of this routine test in asymptomatic patients could result in sizable health care cost savings. In addition, these results provide more data that could be used to support the safety of same-day discharge after MIS for EMCA in appropriately selected patients.

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Prognostic role of preoperative serum albumin in patients with advanced ovarian cancer undergoing primary debulking surgery

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Objectives: Hypoalbuminemia has been reported as a risk factor for postoperative complications and unfavorable survival in cancer patients. We aimed to evaluate the predictive value of preoperative serum albumin levels on the postoperative complication rate and the impact on overall survival (OS) in patients with advanced epithelial ovarian cancer (AEOC) who are undergoing primary debulking surgery (PDS).

Methods: The medical records of 276 patients with AEOC who underwent PDS at a tertiary medical center between 2009 and 2012 were reviewed. A serum albumin level less than 3.5 g/dL (35 g/L) was defined as hypoalbuminemia. All perioperative complications within 30 days after surgery, time to resumption of normal diet, and length of postoperative hospital stay were analyzed. Regression models were used to assess predictors of postoperative morbidity. Survival analyses were calculated using log-rank test and Cox regression models.

Results: Median age at diagnosis was 54 years (range, 20–80 years); and 258 patients received postoperative platinum-based chemotherapy. The incidence of preoperative hypoalbuminemia in the entire cohort was 32.6%. After adjusting for age, body mass index, performance status, and surgical complexity, hypoalbuminemia was independently associated with 30-day postoperative complications (OR 1.929, 95% CI 1.099–3.386, $P = .022$). In Cox regression analysis, hypoalbuminemia was independently associated with shortened overall survival (HR 1.700, 95% CI 1.179–2.451, $P = .005$) even after adjusting for established prognostic factors such as age, tumor stage, performance status, and postoperative residual disease.

Conclusions: Our results provide evidence that preoperative hypoalbuminemia can be used as both an independent predictive factor for 30-day postoperative complications and as a prognostic parameter regarding OS in AEOC patients. Therefore, albumin levels may be incorporated into future clinical trials as a stratification factor.

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Is surgical aggressiveness a determinant of prognosis in patients with advanced ovarian cancer?

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Objectives: Surgery followed by platinum-taxane chemotherapy is the current standard approach to treat advanced ovarian cancer. A major unproven concern is whether a long postoperative delay reduces the benefits of an extensive procedure and leads to disease progression. Our objectives were to evaluate the correlation between clinical and pathological variables and to evaluate the effect of the "time to chemotherapy" (TTC) interval on survival.

Methods: We retrospectively studied data from 276 patients with FIGO stage III or IV ovarian cancer who were consecutively treated between January 2006 and 2013. TTC was analyzed and correlated with outcome.

Results: Median age at diagnosis was 54 years (range, 20–80 years), and 258 patients received postoperative platinum-based chemotherapy. The 25%, 50%, and 75% quartiles of intervals from surgery to start of chemotherapy were 18, 22, and 28 days, respectively. TTC (≤28 days vs >28 days; HR 1.578, 95% CI 1.057–2.355, $P = .026$), complete debulking with no gross residual disease (HR 0.419, 95% CI 0.274–0.640, $P < .05$), and preoperative albumin level (HR 0.549 95% CI 0.382–0.791, $P = .001$) were significant prognostic factors for progression-free survival in multivariate analysis. Although delayed TTC (>28 days) did not have prognostic significance in patients without postoperative residual disease (n = 94), it significantly correlated with progression-free survival in patients with postoperative residual disease (n = 164, HR 1.893 95% CI 1.209–2.962, $P = .005$].

Conclusions: Our findings suggest that delayed initiation of chemotherapy might compromise progression-free survival in patients with advanced serous ovarian cancer, especially in cases of gross residual disease. A prospective study randomizing patients to different intervals could clarify the definitive relevance of the time between surgery and chemotherapy.

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Preoperative intrinsic factors affecting voiding recovery after radical hysterectomy for cervical cancer

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Objectives: The aim of this study was to assess risk factors for voiding difficulty after radical hysterectomy (RH).

Methods: From 2006 to 2008, data on patients who underwent RH performed by a single surgeon for stage 1A1 to 2B uterine cervical cancer were prospectively collected and analyzed. Urodynamic studies (UDS) were performed before and 10 days after RH. Urethral catheters were removed on postoperative day 8. If the postvoid residual (PVR) did not decrease to less than 100 mL until postoperative day 10, the patients were instructed to perform clean intermittent self-catheterization (CIC) after discharge.

Results: Median age was 47 years old and no patient complained of voiding difficulty before RH. Of 45 patients, 15 (33%) had failed to void until discharge day. Detrusor pressure at maximal flow (PdetQmax) and detrusor pressure at opening flow (Pdet,open) on preoperative UDS were significantly higher in the group with voiding failure than in the spontaneous voiding group. Receiver operating characteristic curve revealed that area under the curve of PdetQmax and Pdet,open are 0.68 and 0.74, respectively. For Pdet,open, 35 cm H_2O was determined to be the cutoff value. In multivariate analysis, after adjusting for age, mode of RH, and diabetes, Pdet,open values higher than 35 cm H_2O in preoperative UDS was an independent factor for predicting post-RH voiding failure (HR 9.54, 95% CI 2.0–44.3).

Conclusions: Preoperative intrinsic patient factors suggesting bladder outlet obstruction are significantly associated with voiding difficulty after RH. Individualized surgery such as nerve-paring RH should be considered in patients with high risk of having voiding difficulty after RH.

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Molecular response to neoadjuvant chemotherapy in high-grade serous ovarian carcinoma

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Objectives: To prospectively evaluate molecular responses to neoadjuvant chemotherapy in patients with high-grade serous ovarian carcinoma.

Methods: Between October 2013 and April 2015, 38 patients with suspected advanced ovarian carcinoma were enrolled in this single institution study. After obtaining informed consent, patients underwent a diagnostic laparoscopy. Eighteen patients were excluded—7 had nonserous histology, 3 were deemed suitable for debulking, and 8 did not have a subsequent specimen collected at interval cytoreduction. Analyses of pre- and posttreatment specimens was performed on the Nanostring platform using the nCounter® PanCancer Pathways Panel. Standard statistical tests were performed. Pathway analysis was performed with Ingenuity Pathway and nSolver Analysis Software (Fold change ^{3} ±2, $P < .05$).

Results: The analysis included 20 eligible patients with a median age was 74 years (range, 47–85 years). Stage IIIC disease (70%) was predominant, with median pretreatment CA-125 values of 540 (range 33–13,818). Patients received a median of 3 cycles (range, 2–6; mean 3.6) of neoadjuvant chemotherapy before their definitive surgery and collection of their second biospecimen. Based on the Ingenuity Pathway and Network Analysis, the top 5 pathways affected by neoadjuvant chemotherapy are Immune Signaling (*P* = 1.30E-09), Cell Growth and Proliferation (*P* = 5.03E-08), Cell-To-Cell Signaling and Interaction (*P* = 7.49E-06), DNA Damage Response and Repair (*P* = 1.78E-06), and Checkpoint Signaling (*P* = 2.54E-06). Upstream regulators of the pathways that were activated included phorbol myristate acetate, TNF, JUN, TGFB1. Consistent with these pathways being significantly altered after neoadjuvant chemotherapy, the top 10 upregulated genes (3-fold to 19-fold change) were *NR4A3*, *NR4A1*, *DUSP5*, *FOS*, *FOSL1*, *KLF4*, *OSM*, *SFRP2*, *IL12B*, and *NFATC1*, and the top 5 downregulated genes (all 2-fold change) were *RAD51*, *HIST1H3*B, *HIST1H3G*, *FANCA*, and *CCNA2*.

Conclusions: Genomic differences exist in ovarian cancer biospecimens from before to after therapy. Identification of these changes will be important not only to inform the potential response of targeted therapies, but also to allow improved patient selection for clinical trials.

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Primary chemoradiation for the treatment of locally advanced cervical cancer: Impact of treatment location and time on outcomes

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Objectives: Treatment of cervical cancer with primary chemoradiation (CRT) is a complex process requiring careful coordination. Treatment time has been shown to be an important prognostic factor in patients receiving radiotherapy for cervical cancer. We aim to determine whether location of treatment is associated with treatment time and whether it influences disease response, recurrence, and survival in women receiving primary CRT for locally advanced cervical cancer.

Methods: In this retrospective cohort study, patients with cervical cancer diagnosed between January 2000 and February 2014 undergoing primary CRT were identified using ICD-9 codes. Although all patients received brachytherapy at our academic center, chemotherapy and external beam radiation could be performed locally. Patients were stratified based on the location of treatment and treatment time (<56 vs >56 days). Continuous variables are presented as medians and compared using the 2-sample *t* test. Categorical variables are presented as frequencies and percentages and compared using the χ^2 test. Survival was estimated using the Kaplan-Meier method.

Results: A total of 201 patients met inclusion criteria. Of these, 63% received treatment exclusively at an academic center and 37% received a portion of their care locally. There were no differences in age at diagnosis, stage, or histology between these 2 groups. Patients treated exclusively at the academic center were more likely to have a lymph node dissection before chemoradiation ($P = .002$), have shorter median time to initiation of therapy (31 vs 39 days, $P = .029$), and shorter median treatment time (56 vs 63.5 days, $P = .003$). Response rates were similar between the 2 groups (complete response 91% vs 93%, $P = .63$) and there were no differences in progression-free and overall survival. In addition, when stratified by treatment time, we found no significant differences in response rates, and progression-free or overall survival.

Conclusions: In this study of women treated with primary CRT for cervical cancer, patients who split their care between a local institution and the academic center took longer to initiate and complete treatment. Although we were unable to demonstrate differences in progression-free or overall survival based on treatment location or treatment time, this warrants further investigation.

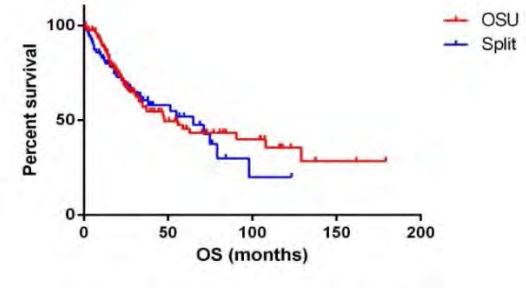

Fig. 1
OS Treatment Location.

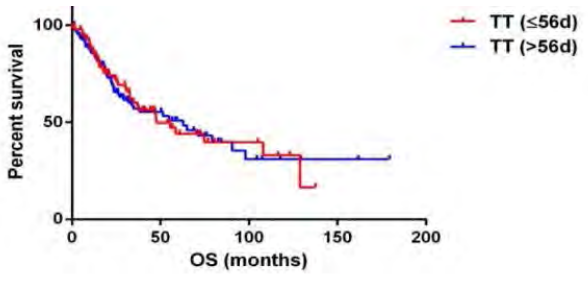

Fig. 2
OS Treatment Time.

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Sentinel lymph node mapping for early-stage cervical cancer: A single institution's experience

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Objectives: Lymph node assessment remains a key part of surgical evaluation for patients with early-stage cervical cancer, and provides important prognostic information to determine appropriate adjuvant therapy. We aim to compare our experience with sentinel lymph node (SLN) mapping in patients with early-stage cervical cancer with a historical cohort of patients at our institution.

Methods: We searched an institutional database for patients with cervical cancer between 1982 and 2014. Pertinent clinical and pathologic data were abstracted from the medical records. A historical cohort included patients from 1982 to 2009 who underwent selective lymph node (LN) sampling. An SLN mapping algorithm was performed according to institutional protocol in a cohort of patients from 2005 to 2014 (SLN cohort). Isolated tumor cells, micrometastases, and macrometastases were considered positive. Only patients with stage IB1 or IB2 squamous cell carcinoma or adenocarcinoma of the cervix were included. Appropriate statistical tests were performed.

Results: We identified 531 patients with cervical cancer who underwent surgical evaluation at our institution: 123 (23.2%) patients in the SLN cohort and 408 (76.8%) in the historical cohort. Median of the 2 groups was similar (SLN: median 36.5 years, range 20–77 years; historical cohort: median 40 years, range 20–92 years; $P = .052$). Most patients had stage IB1 disease (91.1% in the SLN and 90.4% in the historical cohort). More patients in the historical cohort had squamous cell carcinoma (43 [35%] in the SLN vs 208 (51%) in the historical cohort, $P = .002$). Patients received adjuvant radiation at a similar rate in both groups (28.5% in the SLN vs 27.2% in the historical cohort, $P = .05$). Fewer LNs were removed (19 [range, 2–70] vs 27 [range, 1–80], $P < .0001$) and more positive LNs were detected in the SLN cohort (23 [18.7%] vs 51 [12.5%], $P = .03$]. Median follow-up was similar between the 2 groups (51.6 months [range, 0.5–109] in the SLN vs 56.5 months [range, 1.0–338.8], $P = .22$ in the historical cohort). Median recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) was not reached in either group. Five-year RFS (100% vs 93.1% ± 1.4%, $P = .006$), DSS (97.7% ± 1.6% vs 91.3% ± 1.6%, $P = .047$), and OS (95.1% ± 2.2% vs 87.2% ± 1.8%, $P = .027$) were greater in the SLN cohort.

Conclusions: Patients undergoing SLN mapping have fewer total LNs removed but a higher detection rate of positive LNs compared with a historical cohort. In this single institution comparison, SLN mapping did not compromise the detection of positive LNs or outcome of patients with squamous cell or adenocarcinoma of the cervix.

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External validation of nomograms predicting survival of women with locally advanced cervical cancer

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Objectives: This study aims to externally validate a set of nomograms for predicting the 2-year progression-free survival (PFS) and 5-year overall survival (OS) of women with locally advanced cervical cancer in a predominantly African American and West Indian immigrant population.

Methods: After approval from an institutional review board, a database was constructed including patients diagnosed with cervical cancer at 2 major teaching hospitals in Brooklyn, NY, from January 1, 2005, to December 31, 2013. Predicted 2-year PFS and 5-year OS were calculated with the use of the nomograms. Kaplan-Meier survival analysis was then performed for both observed and predicted survival. These values were then compared using the Wilcoxon signed-rank test.

Results: The patient population in our study was predominantly black (89% African American or Afro-Caribbean), and had advanced stage (58% stage IIIB to IVA) and high-grade (74% moderately to poorly differentiated) disease. Seventeen (37%) were confirmed to have positive pelvic lymph nodes. The median follow-up for survivors was 40 months (range, 2–110 months). Observed versus predicted 2-year PFS differed significantly in the study population (34 months vs 68 months, $P < .0001$). There was a nonsignificant difference in 5-year OS with a trend toward shorter survival in the observed versus predicted OS (62 vs 78 months, $P = .09$).

Conclusions: The nomograms are not an adequate tool for predicting 2-year PFS and 5-year OS in a predominantly African American or West Indian immigrant population. The examined nomograms were constructed based on risk factors common to patients enrolled in clinical trials and may have failed to identify key risk factors present in a different population. This limits the application of these nomograms to our population.

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Clinical assessments of MELK immunohistochemical expression in uterine cancer patients: A Gynecologic Cancer Center of Excellence study

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Objectives: Higher transcript expression of *MELK*, a maternal embryonic leucine zipper kinase, has been observed in uterine cancers (UCs), particularly those with aggressive histotypes. Overexpression of MELK in nongynecologic cancers has been reported and phase I trials for MELK inhibitors in solid tumors are ongoing. Our objective was to evaluate the potential clinical value of MELK in well-annotated UCs, comparing cellular expression with outcome.

Methods: An optimized immunohistochemistry assay for MELK was performed in tissue microarrays representing primary tumor from UC patients and normal endometrium from healthy women. MELK staining was scored by intensity and localization pattern. The relationships of MELK staining with clinical characteristics and outcome were evaluated using logistic/Cox modeling and log-rank testing.

Results: A total of 478 UC patients (404 with outcome data) and 49 healthy controls were eligible. Of the cancer patients, 26% were in an advanced stage, 38% had nonendometrioid cancer, 16.4% experienced progression, 9.5% died of cancer, and 46% died of any cause. MELK intensity was consistently higher in UCs than in normal endometrium (83% vs 40%, $P = .0003$) but did not vary by surgicopathologic features ($P > .05$). UCs exhibited a diffuse cytoplasmic staining without versus with distinct perinuclear staining (Fig 1A). The perinuclear MELK staining pattern was more common in advanced stage (odds ratio [OR] 1.7, 95% CI 1.1–2.8, $P = .014$) and nonendometrioid UCs (OR 2.9, 95% CI 1.8–4.4, $P < .001$). Women with a distinct perinuclear MELK had worse progression-free survival (PFS, $P = .026$), cancer-specific survival (CSS, $P = .015$) (Fig 1B), and overall survival (OS, $P = .001$) with hazard ratios of 1.78, 2.25, and 1.68, respectively, and 95% CIs that excluded 1.0.

Conclusions: MELK staining was consistently more intense in UCs than in normal endometrial tissue. The presence of distinct perinuclear MELK staining was a marker of advanced-stage UCs, nonendometrioid UCs, and lower PFS, CSS, and OS rates. Additional studies are required to further evaluate MELK as a clinical biomarker and/or therapeutic target in patients with aggressive UC.

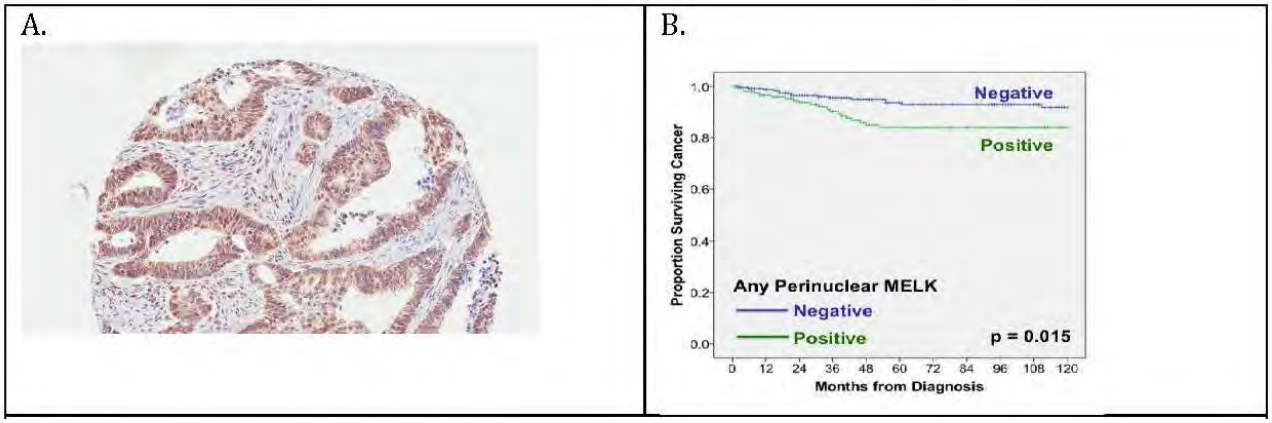

Fig.1

Intense perinuclear MELK staining (A) and worse uterine cancer-specific survival (B).

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What came first—the chicken or the egg? Ligand-independent activation of ERα in KRas mutant endometrial cancer

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Objectives: Approximately 20% of endometrial cancers (EC) harbor KRas mutations with downstream MAPK activation; however, the treatment of recurrent EC with MEK inhibitors (MEKi) has shown disappointing results in the phase II setting, with an objective response rate of 6%. Activation of estrogen receptor alpha (ERα) can occur through ligand-independent phosphorylation by several member kinases of receptor tyrosine kinase pathways, such as the PI3K/AKT and Ras/MAPK pathways, in the absence of estrogen. Our objective was to evaluate the role of ligand-independent activation of ERα in EC and to explore therapeutic implications for the treatment of KRas mutant EC.

Methods: The Cancer Genome Atlas (TCGA) was queried for RNA expression levels of estrogen-induced genes in endometrioid EC based on KRas mutation status. Western blot analysis and qualitative polymerase chain reaction were performed to evaluate estrogen signaling in KRas mutant EC cells after treatment with in vitro MEKi. Reverse-phase protein array was used to validate in vitro findings and identify relevant pathways. Cell viability assays were performed to address the functional consequence of differential estrogen signaling.

Results: Kras mutant tumors in TCGA had decreased expression of progesterone receptor ($P = .034$). This was mirrored in functional proteomic analysis where KRas mutant cells had decreased expression of ERα (*ESR1*, $P = .0001$) and progesterone receptor (*PGR*, $P < .0001$). In vitro KRas mutant cells had decreased total ERα expression. After treatment with a MEKi, Kras mutant cells had increased phosphorylation at ser167 and increased expression of estrogen-induced genes (*EIG121*, $P = .001$; *sFRP1*, $P < .0001$; *PR*, $P = .0003$; and *HOXA10*, $P = .002$). Treatment of mutant KRas cells with a MEK inhibitor in addition to estradiol depletion resulted in decreased cell viability compared with treatment with MEKi alone ($P = .0008$).

Conclusions: Treatment of EC with MEKi restores ligand-independent estrogen signaling in KRas mutant tumors and leads to increased expression of estrogen-induced genes. Treatment of EC cells with a MEKi in addition to estradiol depletion significantly decreases cell viability. Combination therapy with MEKi and hormonal therapy may increase response rates in the EC population with an acceptable toxicity profile.

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Does preoperative endometrial sampling method impact tumor size and the decision to perform lymphadenectomy in endometrial cancer?

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Objectives: Tumor size, in addition to depth of invasion and FIGO grade, may more accurately identify patients in whom lymphadenectomy may be safely omitted in endometrial cancer. We sought to determine if preoperative endometrial sampling method influenced overall tumor size, and whether this should be considered in the decision to perform lymphadenectomy.

Methods: All patients with endometrial cancer from 2009 to 2014 were identified from an institutional database after institutional review board approval was obtained and included in the analysis. Statistical analysis was performed using the Student *T* test.

Results: A total of 155 patients were identified. Preoperative diagnosis was as follows: 83 grade 1, 21 grade 2, 28 grade 3, and 11 hyperplasia. Of these, 73 underwent endometrial biopsy and 70 underwent dilatation and curettage (D&C). Twelve patients were found to have endometrial cancer on final pathology. Average specimen size (as determined by largest dimension of total specimen size) was 2.8 cm in patients who underwent endometrial biopsy and 3.2 cm for patients who had D&C ($P = .36$). Seventy-nine patients had hysterectomy and bilateral salpingo-oophorectomy, and 76 also had lymphadenectomy. Final pathology demonstrated 94 stage IA, 22 stage IB, 13 stage II, 9 stage IIIA, 2 stage IIIB, and 9 stage IIIC tumors. Average tumor size for each stage was as follows: stage IA: 2.4 cm, stage IB: 4.6 cm, stage II: 4.7 cm, stage IIIA: 4.9 cm, stage IIIB: 3.7 cm, and stage IIIC: 5.3 cm. Final pathologic tumor size was significantly smaller for patients who underwent D&C (2.9 cm) compared

with those who underwent endometrial biopsy (3.8 cm) (P = .04). Among stage IA patients with grade 1 or 2 tumors and final tumor size of 2 cm or less, with the addition of preoperative specimen size, 31 patients would have had total tumor size of 2 cm or larger and therefore require lymphadenectomy as recommended by the Mayo Clinic criteria.

Conclusions: Preoperative sampling method may influence intraoperative tumor size measurement, and therefore, the need for lymphadenectomy in endometrial cancer. In this series, patients who had preoperative D&C had smaller final tumor size than those who underwent endometrial biopsy. With the addition of preoperative specimen size to tumor size assessment, an additional 31 staging procedures would have been performed. Larger series are needed to determine whether these additional staging procedures would result in increased detection of lymph node metastasis and improved clinical outcomes.

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371 - Poster
MYB: A novel player in pathobiology of ovarian cancer
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Objectives: MYB is a cellular progenitor of v-MYB oncogenes, which confers its oncogenic activity by regulating the expression of several target genes. We aim to demonstrate that MYB is involved in ovarian cancer (OC) pathogenesis and is a novel site for targeted therapy.

Methods: The expression of MYB in OC tumor specimens and cell lines was evaluated by immunohistochemical and immunoblot analysis, respectively. shRNA/MYB models were used to determine its pathologic significance in tumor growth, clonogenicity, invasion, and responsiveness to chemotherapy.

Results: Immunohistochemistry demonstrated intense MYB staining in all histologic subtypes of OC, whereas no staining was observed in normal ovarian tissues. MYB was overexpressed in all the OC cell lines examined, particularly heightened in highly aggressive/chemoresistant OC cell lines SKOV3-ip and A2780-CP70. Densitometric analysis revealed that shRNA-mediated silencing resulted in more than 90% downregulation of MYB in all the 3 OC cell lines. Functional studies demonstrate that silencing of MYB led to decrease in growth (~46%, 37%, and 41%) and clonogenic ability (~2.5, 3.2, and 2.8 folds) in TOV112D, SKOV3-ip and A2780-CP70 cells, respectively, compared with their scrambled sequence-transfected (Scr) control cells. MYB-silenced TOV112D, SKOV3-ip and A2780-CP70 cells also exhibited reduced motility (~3.2, 4.1, and 3.7 folds, respectively) and invasion (~5.7, 7, and 6.2, respectively). Loss of mesenchymal and gain of epithelial markers was observed in MYB-silenced OC cell lines. IC_{50} dose response studies showed that TOV112D, SKOV3-ip and A2780-CP70-shMYB cells were more sensitive (IC_{50} values 2.3, 3.2, and 42 μM, respectively) to cisplatin cytotoxicity compared with TOV112D-Scr (IC_{50}:6.5 μM), SKOV3-ip-Scr (IC_{50}: 8 μM), and A2780-CP70-Scr (IC_{50}: 88 μM).

Conclusions: MYB is overexpressed in OC and demonstrates altered growth, malignant behavior, and chemoresistance of OC. These data provide the first experimental evidence for a functional role of the novel MYB oncogene in OC.

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372 - Poster
Endometrial cancer and Lynch syndrome: Immunohistochemical characterization of endometrial cancer associated with changes in mismatch repair protein expression
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Objectives: Lynch syndrome (LS) confers hereditary predisposition to multiple tumors. The incidence of endometrial cancer (EC) can match colorectal carcinoma, with a risk of up to 60%. The frequency of germline mutations of mismatch repair protein (MMR-P) in unselected patients with EC is 1.8% to 2.1%. Our objective was to analyze the expression of MMR-P (MLH1, MSH2, MSH6, and PMS2) with immunohistochemistry (IHC) in tumor tissue of unselected patients with EC at our institution, and describe morphologic features associated with altered expression of MMR-P.

Methods: We enrolled 84 patients with EC who were treated at the Hospital Italiano at Buenos Aires, Argentina, between April 2014 and August 2015. IHC for MLH1, MSH2, MSH6, and PMS2 was performed using the Ventana Benchmark XT system. The following variables were analyzed: expression of MMR-P, age, Lynch-associated morphologic characteristics, and tumor stage at diagnosis.

Results: The mean age of our population was 64.7 years (standard deviation 12.45), 12 patients (14.5%) were younger than 50 years. Twenty-eight patients had altered expression of at least 1 MMR-P (33.3%). Twenty-one patients (75%) had a deficit of MLH1/PMS2, 2 of PMS2 (7%), 1 of MSH2/MSH6 (4%), and 4 of MSH6 (14%). Among the patients with altered IHC, only 2 were younger than 50 years. Regarding histologic subtypes, there were 24 (86%) endometrioid carcinomas, 1 clear cell carcinoma, 1 serous carcinoma, and 2 undifferentiated carcinomas. The mean body mass index was 31. We performed a complete morphologic study of 26 surgical specimens. In 17 cases (65%), we found at least 1 characteristic associated with altered expression of MMR-P (TM-MMR-P). One patient in the subset that did not show TM-MMR-P features and one other met clinical criteria for LS. Of the 28 patients with altered expression, 25 were surgically treated at our hospital. FIGO stage distribution was as follows: 56% stage IA, 24% stage IB, and 20% stage III.

Conclusions: The deficit of expression of MMR-P is consistent with that reported in the literature. Preliminary results in our population might support the routine use of IHC in selected patients with EC. Further comparative studies are needed to define elements of suspicion for LS in these patients.

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373 – Poster
Locally advanced cervical squamous cell carcinoma (CSCC): Impact of the FDG PET/CT in the primary staging
Withdrawn at author's request

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374 - Poster
Impact of carcinoma involving adenomyosis on the survival of patients with endometrial endometrioid adenocarcinoma
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Objectives: Data are conflicting regarding the effect of the presence of adenomyosis on the prognosis of endometrial cancer patients. The prognostic value of adenocarcinoma colonizing adenomyosis has not been evaluated. We assessed the effect of both the presence of adenomyosis and carcinoma-colonizing adenomyosis on the outcome of patients with endometrial endometrioid adenocarcinoma (EEAC) in a large single institution cohort.

Methods: All patients who had primary surgical treatment of EEAC from 2000 to 2012 were identified from an institutional database. All pathology reports were reviewed by expert gynecologic pathologists. Adenocarcinoma involving adenomyosis did not influence reported depth of myometrial invasion. Relevant patient, clinical, and pathologic characteristics were collected, including the presence of adenomyosis in the hysterectomy specimen and the involvement of adenomyosis by endometrial adenocarcinoma. Appropriate statistical tests were used.

Results: Query of the available database identified 1,751 eligible patients. The median age at diagnosis was 60 (range, 25–92 years). The majority of tumors were grade 1 (n = 1,076, 62%) and stage I (n = 1,491, 85%). Adenomyosis was present in 808 cases (46%) and carcinoma was found to involve adenomyosis in 114 cases (114/808, 14%). Cases without adenomyosis were found to have deeper myometrial invasion ($P < .001$) and those patients had a lower body mass index ($P = .018$). Median follow-up was 57 months (range, 0–183 months). Median overall survival for the entire cohort was not reached. Five-year overall survival for those with and without adenomyosis was 94% and 90%, respectively ($P = .008$). After controlling for stage and grade, however, the presence of adenomyosis was not associated with improved survival (HR 1.1, 95% CI 0.8–1.5). Within the adenomyosis group, there was no difference in overall survival ($P = .54$), disease-specific survival ($P = .61$), or recurrence-free survival ($P = .84$) when carcinoma involved adenomyosis.

Conclusions: After controlling for other known prognostic factors, the presence of adenomyosis is not associated with survival in patients with endometrioid adenocarcinoma of the uterus. Adenocarcinoma involving adenomyosis does not alter the prognosis in patients with endometrial adenocarcinoma.

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375 - Poster

Trends in robotic surgery for endometrial cancer and the impact of hospital surgical volume on perioperative complications

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Objectives: We examine 5-year trends in robotic surgery for endometrial cancer and evaluate the impact of hospital robotic volume on surgical outcomes.

Methods: Using the Healthcare Cost and Utilization Project National (Nationwide) Inpatient Sample (HCUP-NIS) Database from 2008 to 2012, patients who underwent robotic surgery for endometrial cancer were identified. Surgical (intraoperative and perioperative) complications were abstracted. Medical comorbidity scores were calculated using the Charlson comorbidity index (CCI). High-volume centers were defined as hospitals that completed more cases than the median for each year in the dataset. We compared patient characteristics, procedures, and outcomes, and examined trends over the 5-year period. A multivariable analysis (MVA) was completed to identify independent predictors of surgical complications in the robotic cohort.

Results: A total of 7,066 patients were identified. Over the study period, rates of obesity increased ($P < .001$) as well as the CCI ($P = .001$). Lymph node dissection was less commonly performed ($P < .001$). Surgery volume increased in small or medium-sized ($P < .001$), private ($P < .001$), and teaching ($P < 0.001$) hospitals. High-volume centers were more likely to be large (74% vs 62%, $P < .001$), teaching hospitals (78% vs 58%, $P < .001$), located in the northeastern or western United States, and were less likely to be privately owned (22% vs 31%, $P < .001$). Patients treated at high-volume centers were similar in age ($P = .11$), but had higher CCI values (2.5 ± 0.9 vs 2.6 ± 1.2, $P = .002$) and were more likely to undergo lymph node dissection (73% vs 68%, $P = .007$). MVA models included age, race, CCI, obesity, lymph node dissection, hospital size, ownership, teaching status, location, and volume. Increasing age (adjusted odds ratio [aOR] 1.02; 95% CI 1.02–1.03), CCI (aOR 1.25, 95% CI 1.18–1.33), obesity (aOR 1.50, 95% CI 1.30–1.73), and teaching hospital (aOR 1.23, 95% CI 1.05–1.45) independently predicted having a surgical complication. Large (aOR 0.85, 95% CI 0.74–0.99) or high-volume (aOR 0.81, 95% CI 0.66–0.98) hospital and Caucasian race (aOR 0.84, 95% CI 0.71–0.99) were associated with lower risk of complication. With increasing year of the procedure, patients were less likely to have a surgical complication (aOR 0.86, 95% CI 0.81–0.91).

Conclusions: The strongest independent predictor of improved intraoperative and perioperative outcomes in robotic surgery for endometrial cancer is having surgery at a high-volume center.

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376 - Poster

AXL, a receptor tyrosine kinase, mediates platinum and taxane resistance in ovarian and uterine cancer

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Objectives: Expression of AXL is associated with a worse prognosis in ovarian cancer. We investigated the role of AXL expression in chemotherapy response in ovarian and uterine cancers, and sought to reverse chemoresistance through inactivation of AXL.

Methods: In vitro cell viability (XTT) assays were performed to confirm response to chemotherapy in SKOV3-S/R (platinum sensitive/resistant ovarian cell lines), OVCAR3/TP (taxane sensitive/resistant ovarian cell lines), and AN3CA/ARK1 (taxane sensitive/resistant uterine cell lines), and Western blotting was performed for AXL expression. XTT assays of ARK1 cells for paclitaxel resistance with AXL silencing by shRNA were performed. This was then repeated with selective small molecule inhibition of AXL with R428. AXL knockdown by siRNA was performed with either a traditional transfection reagent

(DharmaFECT) or with a novel serum-stable, cell-penetrating, endosomolytic amphipathic peptide delivery system (p5RHH). Cell viability assays were analyzed using paired *t* tests. $P < .05$ was considered statistically significant.

Results: Chemoresistance was validated with XTT assays for SKOV3-S/R, OVCAR3/TP, AN3CA/ARK1 ($P = .0666$, $P = .0005$, $P < .0001$, respectively). Western blotting confirmed overexpression of AXL in chemoresistant cell lines, and lack of AXL expression in their chemosensitive counterparts. Reversal of paclitaxel resistance was achieved in ARK1 cells genetically by silencing AXL with shRNA ($P = .0131$) or therapeutically by selective inhibition of AXL with R428 in combination with paclitaxel ($P = .0036$). The novel delivery system, p5RHH, conjugated to siAXL, was shown to inactivate AXL in ARK1 cells at the RNA and protein level to a similar extent as traditional transfection technique (8.4-fold vs 8.7-fold decrease for RNA, respectively; 67% vs 83% knockdown at 48 hours and 84% vs 97% knockdown at 96 hours for protein, respectively).

Conclusions: AXL expression is associated with chemoresistance in ovarian and uterine cell lines. Genetic inactivation of AXL or targeted therapy using R428 in taxane-resistant uterine cells reverses chemoresistance. To find a targeted therapy to mimic this genetic inactivation, both a novel AXL kinase inhibitor and a novel siRNA nano-particle delivery system were successfully used.

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377 - Poster

Preparing for a paradigm shift in the treatment of ovarian cancer: Effect of online CME on oncologists' knowledge and competence

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Objectives: We sought to determine the effect of online continuing medical education on the knowledge and competence of oncologists regarding the use of poly ADP ribose polymerase (PARP) inhibitors in ovarian cancer.

Methods: The effect of 2 educational interventions on the role of PARP inhibition in the treatment of ovarian cancer was analyzed to determine efficacy of online education. The activities launched online in August 2014 and April 2015, and data were collected through November 2014 and May 2015, respectively. The effects of education were assessed by comparing the same group of participants' responses to knowledge- and case-based matched pre- postassessments. A paired 2-tailed *t* test was used to assess whether the mean postassessment score was different from the mean preassessment score. The McNemar χ^2 statistic was used to measure changes in responses to individual questions. The effect size was calculated with the Cohen d.

Results: A total of 151 oncologist responses during the study period were included in this outcomes analysis. Significant improvements in the knowledge of the rationale for targeting PARP inhibition and its link to synthetic lethality were seen as a result of participation in video lecture (n = 62, large effect d = 1.287, $P < .05$) and case-based roundtable (n = 91, large effect d = 1.352, $P < .05$). After participation, 44% were more likely to recognize that all patients with ovarian cancer should be tested for *BRCA* mutations ($P < .05$), 27% were more likely to correctly counsel appropriate patients on the potential efficacy of PARP inhibitors in the management of their disease ($P < .05$), and 33% were more likely to identify the correlation among *BRCA* mutations, PARP inhibitors, and overall survival as reported in the literature. In a patient with ovarian cancer whose disease was *BRCA* wild-type, more oncologists were able to identify the potential clinical efficacy of combining a PARP inhibitor with vascular endothelial growth factor blockade in this patient population ($P < .05$).

Conclusions: This study demonstrates the effectiveness of online education that uses multiple formats and reinforces prior learning on improving knowledge and competence of oncologists regarding the use of PARP inhibitors in the management of ovarian cancer. Additional studies are needed to assess whether improved knowledge and competence translate to clinical practice.

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378 - Poster

Intimate partner violence and time to first treatment in women with gynecologic or breast cancer

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Objectives: Intimate partner violence (IPV) has been linked with cancer-related well-being. The potential of IPV or partner-interfering behavior (PIB) to affect the delivery of cancer treatment has not been well characterized. This study aims to evaluate the delay in primary treatment in women with gynecologic or breast cancer with a history of IPV/PIB.

Methods: Women, ages 18 to 79 years, with an incident, primary, biopsy-confirmed cancer were recruited from the Kentucky Cancer Registry within 12 months of their diagnosis (2009–2015). In a phone interview, consenting women reported current and past IPV, current PIB, sociodemographics, and cancer-related well-being indicators. The cancer registries provided stage, site, date of diagnosis, and age. Multivariable general linear regression models were used for time to first treatment, in days, by cancer site (cervical/vulvar, endometrial, ovarian, and breast) and self-disclosure of current or lifetime IPV and/or PIB while adjusting for age, stage, and insurance. Analysis was performed for time to first treatment and by type of primary treatment (surgery, chemotherapy, or radiation) among those receiving each treatment.

Results: Among 1,497 women interviewed, 1,223 had breast cancer, 152 endometrial cancer, 48 ovarian cancer, and 74 cervical or vulvar cancer. There were no statistically significant differences in overall time to first treatment by IPV history for any cancer site. When first therapy was surgery or chemotherapy, there were no statistically significant differences in time to first treatment for any cancer type when comparing those with and without lifetime history of IPV/PIB. Similarly for women with breast, endometrial, or ovarian cancer, IPV/PIB was not associated with a delay in first radiation treatment. However, in women with either cervical or vulvar cancer, time to first radiation treatment was significantly ($P = .05$) longer (average 55.19 days) among those with a history of IPV or PIB than in those not experiencing IPV/PIB (average 29.50 days).

Conclusions: Cervical or vulvar cancer patients experiencing current or past IPV/PIB had a significant delay in initiation of primary radiation treatment. Given the importance of early treatment, identifying patients at risk for delay may allow intervention with potential to improve cancer outcomes.

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Unique molecular signatures between high-grade and low-grade endometrial stromal sarcoma: An analysis of 96 cases

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Objectives: Endometrial stromal sarcoma (ESS) is a rare form of uterine cancer, traditionally categorized as high-grade (HG) or low-grade (LG) ESS. Molecular and genomic changes that underlie the distinct clinical characteristics associated with each subtype are largely uncharacterized. We aim to identify genomic and protein expression differences between HG and LG tumors in a large cohort of ESS.

Methods: Of 3,133 uterine cancers submitted for a molecular profiling test from March 2011 to July 2014, 143 ESSs were identified based on reported pathology. Testing was ordered based on physician request and included a combination of sequencing (Sanger or next-generation sequencing), protein expression (immunohistochemistry), and /or gene amplification (fluorescence/chromogenic in situ hybridization [FISH/CISH]).

Results: Of 144 ESSs, 52 (36%) were HG ESSs, 44 (31%) were LG ESSs, and 47 (33%) were unspecified. Compared with HG ESS, patients with LG ESS were on average 2 years younger (54.7 vs 56.9). In 1 of 47 genes sequenced, only 1 mutation, a variant of unknown significance in *JAK3*, was detected among LG ESSs, compared with16 mutations in HG ESSs. Among HG ESS, *TP53* was the most common mutation at 32%, compared with 0% in the LG ESS group ($P = .02$). Hormone receptor expression was significantly greater in LG ESS than in HG ESS: ERα (90% vs 21%), PR (86% vs 21%), and AR (60% vs 17%), respectively ($P < .001$). Sixty-nine percent of HG ESSs were ER and PR negative, whereas only 7% of LG ESSs were ER and PR negative. Epidermal growth factor receptor (EGFR) expression was common in both LG and HG ESSs (88% and 73%). Loss of phosphatase and tensin homolog (PTEN) was more common in HG ESS (40% vs 17%, $P = .01$), suggesting a potential use for inhibitors of the PI3K pathway. Increased TOP2a expression, associated with higher proliferation and anthracycline efficacy, was more common in HG ESS (87% vs 26%, $P < .001$). A significant higher proportion of HG ESS patients expressed TS and RRMI, known to confer resistance to folate analogue and gemcitabine, respectively (75% vs 28% TS, $P < .001$ and 52% vs 26% RRM1, $P = .025$, respectively).

Conclusions: Our findings suggest that HG and LG ESSs have distinct molecular signatures. LG ESSs rarely carry mutations and are hormonally active, suggesting potential usefulness with fertility preservation and endocrine therapy. HG ESSs are largely hormonally independent with frequent *TP53* mutation. Anthracyclines and drugs targeting the PI3KCA pathway may warrant consideration in a subset of patients with HGESS.

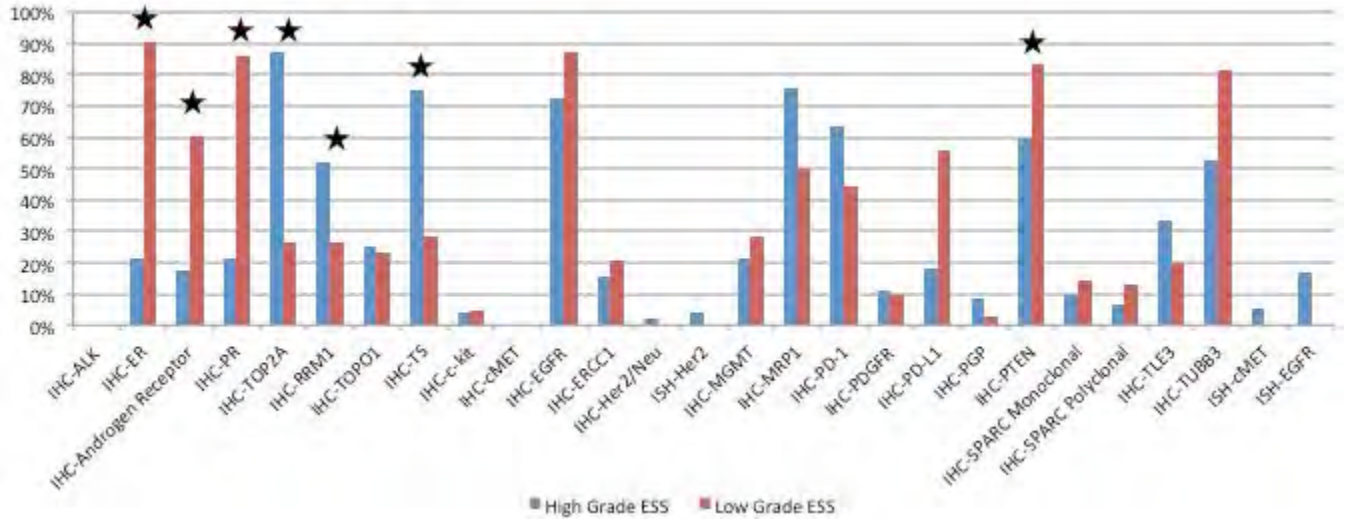

Fig. 1
Comparison of Molecular differences between HG and LG-ESS.

Table 1
Summary of Significant Molecular Distinictions between HG and LE-ESS.

Marker (IHC)	Pos	Neg	Total	High Grade ESS	Pos	Neg	Total	Low grade ESS	P value
IHC-ER	11	41	52	21%	38	4	42	90%	<0.0001
IHC-Androgen Receptor	9	43	52	17%	26	17	43	60%	<0.0001
IHC-PR	11	41	52	21%	36	6	42	86%	<0.0001
IHC-TOP2A	40	6	46	87%	10	28	38	26%	<0.0001
IHC-RRM1	24	22	46	52%	10	28	38	26%	0.025
IHC-TS	36	12	48	75%	11	28	39	28%	<0.0001
IHC-PTEN	31	21	52	60%	35	7	42	83%	0.0138
IHC-TUBB3	11	10	21	52%	13	3	16	81%	0.0912

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380 - Poster
The impact of obesity on the 30-day morbidity and mortality after surgery for ovarian cancer
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Objectives: To examine the effect of body mass index (BMI) on postoperative 30-day morbidity and mortality after surgery for ovarian cancer (OC).

Methods: Patients with OC were identified from the American College of Surgeons National Surgical Quality Improvement Program from 2005 to 2011. Women were divided into 3 groups: nonobese (BMI <30), obese (30–<40), morbidly obese (≥40). Multivariable logistic regression models were performed.

Results: Of 2,061 women included in this study, 1,336 (65%) were nonobese, 560 (27%) were obese, and 165 (8%) were morbidly obese. The overall 30-day mortality and morbidity rates for the entire cohort were 2% and 31%, respectively. In multivariate analyses, after adjusting for confounders, both obesity (OR 0.9, 95% CI 0.4–2.0, *P* = .87) and morbid obesity (OR 0.8, 95% CI 0.1–3.0, *P* = .73) were not significant predictors of increased 30-day postoperative mortality. Likewise, rates of any 30-day complications were comparable among nonobese, obese, and morbidly obese patients (31% vs 28% vs 33%, respectively, *P* = .35) in multivariate analysis. Obese and morbidly obese patients were more likely to have diabetes, hypertension requiring medications, cardiac morbidities, higher American Society of Anesthesiology class, and leukocytosis, and less likely to have weight loss before surgery.

Conclusions: With appropriate control for confounding comorbidities, the 30-day morbidity and mortality rates for obese and morbidly obese patients undergoing surgery for ovarian cancer do not appear to differ. Therefore, reported inferior long-term survival for these patients is likely related to a different phase of their disease and treatment process, and is deserving of further investigation.

Table 1
Multivariate regression analysis for 30-day morbidity following surgery for ovarian cancer.

Variable	OR (95% CI)	*P*-value
BMI <30	Reference	
BMI 30-39	0.9 (0.7-1.1)	0.26
BMI 40 or more	1.1 (0.7-1.6)	0.70
Age <60 years	Reference	
Age 60-69 years	1.3 (1.0-1.7)	0.04
Age 70-79 years	1.4 (1.0-1.8)	0.04
Age ≥ 80 years	1.7 (1.1-2.6)	0.02
Surgical complexity score ≥ 4	3.7 (2.7-5.0)	<0.001
Alcohol use	0.9 (0.3-2.5)	0.84
Ascites	1.9 (1.5-2.5)	<0.001
Dependent functional status	1.6 (0.8-3.0)	0.17
Albumin ≤ 3 g/dl	1.4 (1.0-2.0)	0.03
ASA class 3	1.4 (1.1-1.8)	<0.001
ASA class 4-5	2.1 (1.3-3.6)	<0.001
Operative time 60-119 min	2.1 (0.9-5.7)	0.10
Operative time 120-180 min	3.7 (1.7-9.8)	<0.001
Operative time >180 min	7.0 (3.2-18.4)	<0.001
Anemia (HCT <35)	2.0 (1.7-2.5)	<0.001
Thrombocytosis	1.3 (1.0-1.6)	0.05
Chemo before surgery	1.6 (1.1-2.4)	0.03

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381 - Poster
Anti-Angiogenic treatment of cervical cancer: Significant tumor regression with severe toxicity
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Objectives: Anti–vascular endothelial growth factor monoclonal antibodies inhibit tumor angiogenesis, consequently impeding the recruitment of new vasculature to existing and new tumor lesions. The addition of bevacizumab (BEV) to combination chemotherapy in patients with recurrent cervical cancer results in significant improvement in median overall survival. We sought to compare the patterns of disease progression and toxicity in women with recurrent cervical cancer after receiving BEV versus non-BEV combination chemotherapy.

Methods: A single-institution retrospective chart review was conducted of women with recurrent and metastatic cervical cancer who were treated with salvage chemotherapy with or without BEV between 2005 and 2015. All patients were on first- or second-line salvage treatment. Demographics and clinicopathologic data were obtained. Disease progression was defined by RECIST criteria. Reasons for treatment discontinuation were also recorded. Statistical analysis was performed using the Fisher exact test and Kaplan-Meier survival analysis.

Results: Seventy-four patients were identified. Twenty-nine patients were treated with BEV + chemotherapy and 45 patients with chemotherapy alone. Disease progression solely attributed to increase in existing target lesions was 7% in the BEV + chemotherapy group versus 27% for the chemotherapy group ($P = .04$). New target lesions were identified in 3% of the BEV + chemotherapy group compared with 38% of chemotherapy group ($P = .0006$). Interestingly, the patient who experienced a progression to new disease in the BEV + chemotherapy group had acquired immunodeficiency syndrome. Cessation of treatment secondary to severe toxicities was seen in 48% of the BEV + chemotherapy compared with 13% of the chemotherapy group ($P = .001$). About 24% of patients who were receiving BEV and stopped for toxicities were because of fistula formations. The progression-free survival was significant ($P = .0001$) and the overall survival showed a trend toward significance ($P = .07$). However, no significant difference in survival was seen between the 2 groups after disease progression ($P = .8$).

Conclusions: Antiangiogenic treatment of recurrent cervical cancer significantly decreases progression by inhibiting growth of both existing and new disease. Toxicity is a major reason for cessation of antiangiogenic treatment. Yet, no survival advantage is seen after progression on antiangiogenic therapy.

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382 - Poster

Cited rationale for variance in use of primary intraperitoneal chemotherapy following optimal cytoreduction for stage III ovarian, fallopian tube, and primary peritoneal carcinoma

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Objectives: Studies have demonstrated improved ovarian cancer survival with the administration of intraperitoneal (IP) chemotherapy after optimal cytoreduction. Despite this, IP chemotherapy is not uniformly used. We evaluated the rate of IP chemotherapy administration and the documented reasons for giving intravenous (IV)–only chemotherapy in a single large cancer center.

Methods: All patients who had optimal primary cytoreductive surgery for stage III ovarian, fallopian tube, and primary peritoneal carcinoma and subsequently received primary chemotherapy at our institution between 2006 and 2013 were identified. Primary cytoreduction was defined as optimal if residual disease was 1 cm or less. Patients who received at least 1 cycle of adjuvant IP therapy were included in the IP group. Pertinent patient characteristics, treatment information, and reason for not administering IP therapy were collected. Appropriate statistical tests were used.

Results: Of the patients evaluated, 392 met inclusion criteria. Most patients (n = 292, 74.5%) received at least 1 IP cycle (median 5, range 1–6) and 45.2% completed 6 cycles. Those who received IP chemotherapy were younger ($P < .001$) and had fewer baseline comorbidities ($P = .001$) and a higher performance index at chemotherapy evaluation visit ($P < .001$). Most (n = 300, 76.5%) had an IP port placed at the time of primary cytoreductive surgery; of the 92 patients who did not, 50 subsequently had one placed for IP therapy. The most common reason for giving IV-only therapy was postoperative status (complication, performance status, etc), accounting for 36 (36%) non-IP patients. The main postoperative reason cited was delayed wound healing (42% [4% of the total group]). Other commonly cited reasons in this subgroup were baseline comorbidities (14%) and IP port problems (11% [3% of those with an IP port]). The median follow-up for all patients was 47 months (range, 12–116 months). Five-year overall survival was 48% and 69% in the IV and IP groups, respectively ($P < .001$).

Conclusions: Potentially modifiable factors identified as leading to the use of IV-only chemotherapy were postoperative status and IP port problems. A focus on altering the frequency of these factors could potentially lead to higher rates of IP chemotherapy use.

Table 1
Reasons Cited for Giving IV Only Chemotherapy.

Reason	N (% of All Patients)
Post-operative status	36 (9%)
Delayed wound healing	15 (4%)
Post-operative infection (other than IP port)	7 (2%)
Other post-operative complication	11 (3%)
Low post-operative performance status	3 (1%)
Baseline comorbidities	14 (4%)
IP port problem	11 (3%)
Malfunction	7 (2%)
Infection	4 (1%)
Early disease recurrence/suspected stage IV disease	8 (2%)
Patient refused	7 (2%)
Ileostomy	6 (2%)
Clinical trial	6 (2%)
Intra-operative adhesions	3 (1%)
Other	9 (2%)
Not stated	3 (1%)
Severe taxane allergy with first infusion	2 (<1%)
Ascites	1 (<1%)
Stage III by positive para-aortic lymph nodes	1 (<1%)
Apparent localized disease intra-operatively	1 (<1%)
Avoid treatment delay for IP port insertion	1 (<1%)

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Genetic inactivation of the receptor tyrosine kinase AXL inhibits invasion and metastasis in metastatic endometrial cancer

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Objectives: AXL overexpression promotes migration and invasion in multiple cancers; similarly, genetic and therapeutic inhibition of AXL prevents metastasis in ovarian cancer xenograft models. Our objective was to evaluate the role of AXL in metastatic uterine serous carcinoma.

Methods: Immunohistochemical staining of AXL was performed in malignant and benign endometrial specimens. Uterine serous carcinoma cell lines, ARK1 and Hec50a, were used. shRNA was used to genetically inactivate AXL (shAXL) and scrambled control (shControl). Invasion assays were performed using extracellular matrix–coated semipermeable membranes (ie, Matrigel). Proliferation was measured using a XTT-based assay and protein expression was evaluated using Western blot analysis. Uterine serous cancer xenograft models were developed using luciferase-tagged ARK1 cells injected intraperitoneally into NOD/SCID mice. Tumor growth was assessed via imaging as well as tumor burden at necropsy. The Student unpaired *t*test was used for analysis.

Results: High immunohistochemical expression of AXL was found in 58 (74%) of 78 advanced-stage and 121 (77%) of 158 high-grade specimens, whereas benign tissues demonstrated minimal AXL expression. AXL expression was seen in metastatic uterine serous cancer cells, ARK1 and Hec50a. AXL was also found to regulate invasion and migration, but not proliferation. Matrigel invasion assays showed a decrease in tumor cell invasion in shAXL compared with shControl in ARK1 and Hec50a

cells (32 vs 117 cells per high power field [hpf], $P = .0001$ and 3 vs 9 cells/hpf, $P = .0486$, respectively). In Boyden chamber migration assays, ARK1 shAXL cells migrated significantly less than ARK1 shControl cells (10 vs 35 cells/hpf, $P < .0001$). We found a profound inhibition of p-AKT expression and PI3K signaling in shAXL cells compared with shControl cells. The in vivo metastasis model showed that bioluminescence was significantly greater in ARK1 shControl vs shAXL (5.95×10^8 vs 5.10×10^7, $P = .0085$) as was tumor count (36 vs 7, $P = .0016$), and tumor weight (706 vs 287 mg, $P = .004$).

Conclusions: AXL is highly expressed in serous uterine cancers and regulates migration, invasion, and metastasis. The receptor tyrosine kinase AXL is a therapeutic candidate for treatment of metastatic endometrial cancer.

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Widespread failure to adhere to National Comprehensive Cancer Network guidelines adversely impacts survival for patients with locally advanced cervical cancer

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Objectives: To examine compliance with category 1 National Comprehensive Cancer Network (NCCN) guidelines and utilization of surgical staging in the management of stage IIB–IVA cervical cancers using a large national cancer registry

Methods: Using the National Cancer Data Base (NCDB), patients with stage IIB–IVA cervical cancers were identified from 2003 to 2012 (n = 24,952). Cochran-Armitage tests were used to examine trends over time and receipt of guideline-recommended care was assessed using generalized estimating equations, after adjusting for patient and clinical characteristics.

Results: Only 5,935 patients (23.8%) met the criteria for compliance with NCCN guidelines by receiving concurrent chemoradiation followed by brachytherapy Patients older than 70 years ($P < .0001$), of African American race ($P < .0001$), of Hispanic origin ($P = .0023$), having no insurance ($P < .0001$), having low household income ($P = .0019$), and low education ($P = .0005$) were less likely to receive category 1 recommended treatment. Only 5,777 patients (23.5%) underwent surgical lymph node assessment, with overall use decreasing from 2003 to 2012 (24.4% to 21.8%, $P = .01$). Patients younger than 50 years, of Caucasian race, treated at a comprehensive community or academic cancer center, with private insurance, higher household income, and higher education were most likely to undergo lymph node assessment ($P < .0001$ for all variables). Patients who received category 1 NCCN treatment had an improved median survival (99.7 vs 52.5 months, $P < .001$). Surgical staging with regional lymph node assessment was also associated with an improved median survival (126.2 vs 46.4 months, $P < .001$).

Conclusions: Patients who receive category I treatment and/or surgical lymph node assessment show a significant survival advantage. Very low adherence to NCCN guidelines has not significantly improved over the past 10 years. Our study demonstrates opportunities to improve quality of care for women with locally advanced cervical cancer.

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Personalizing surgical therapy for advanced ovarian cancer: CT imaging may not predict disease resectability

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Objectives: To determine the ability of computed tomography (CT) to characterize peritoneal disease distribution and determine resectability in a prospective cohort of patients with advanced ovarian cancer (OC).

Methods: All patients with suspected stage 3 or 4 OC undergo a triage algorithm to determine who is likely to achieve R0 resection. Each patient undergoes preoperative CT followed by diagnostic laparoscopy (LS) according to the Anderson algorithm (those with Fagotti score >8 are triaged to neoadjuvant chemotherapy). Trained radiologists, blinded to the clinical outcome of the patient, prospectively evaluated each CT scan. A structured radiology report (SRR) outlines the presence or absence of disease on the liver, mesentery, gastric wall, subdiaphragm, supracolic or infracolic omentum, and bowel. Agreement between individual and composite SRR and LS points of disease was determined using the k statistic. Concordance

between surgeons and radiologists with respect to assessment of the extent of disease was estimated. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the SRR with respect to LS was evaluated.

Results: A total of 120 patients who were suspected to have advanced OC had both SRR and LS. Composite radiology scores correlated with surgeon assessment of disease distribution 66.7% (95% CI 57.5%–75%) of the time (k = 0.35 [95% CI 0.21–0.49]), with disease being classified as resectable, based on composite LS and SRR scores, 73.3% and 46.7% of the time, respectively. The sensitivity, NPV, specificity, and PPV of the SRR were 87.5%, 92.9%, 59.1%, and 43.8%, respectively. Correlation of LS and SRR for specific sites (particularly opposing surfaces, i.e., subdiaphragm and liver or bowel and mesentery) of disease demonstrated poor agreement, with k < 0.4 for all. In general, the SRR overestimated disease presence compared with LS in every area except bowel infiltration, for which the SRR appeared to underestimate the disease presence.

Conclusions: CT imaging is useful for gross disease detection but is limited in determining overall resectability of advanced OC. Although SRR is important for overall patient care, alternative modalities are important to determine disease resectability. LS for peritoneal disease assessment remains a critical component of personalizing surgical therapy for advanced OC.

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Interval cytoreductive surgical outcome following administration of standard versus dose-dense neoadjuvant chemotherapy in patients with advanced-stage ovarian cancer

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Objectives: Given the benefit of dose-dense platinum/taxane chemotherapy compared with standard every-3-week treatment after primary cytoreductive surgery, we sought to evaluate the utilization of dose-dense chemotherapy (DDC) in the neoadjuvant setting.

Methods: With institutional review board approval, we identified all stage III/IV ovarian cancer patients who received initial treatment at our institution, and received neoadjuvant chemotherapy (NACT) from January 2008 to May 2013. We excluded cases treated with upfront surgery, low-grade histology, and early-stage disease. Clinicopathologic data were abstracted from medical records. DDC was defined as receiving at least 1 cycle of platinum with weekly paclitaxel. Standard chemotherapy (SC) was defined as receiving no DDC, and at least 1 cycle of an every-3-week platinum/taxane regimen. Appropriate statistical tests were performed.

Results: A total of 154 patients received NACT. Of these, 5 (3%) did not undergo interval cytoreductive surgery (IDS) because of progression of disease; all 5 received SC. Of the remaining 149 cases, 23 (15%) received DDC and 126 (85%) received SC. There were no differences in age, CA-125 levels at diagnosis, or baseline albumin between the 2 groups. Seventy-three (49%) of 149 patients had stage IV disease: 64 (51%) of 126 who received SC and 9 (39%) of 23 who received DDC (P = .37). During NACT, the median number of DDC cycles administered was 3 (range, 1–7) compared with 4.5 cycles for the SC patients (range, 3–7) (P = .03). Carcinomatosis was present before IDS in 19 (83%) of 23 DDC patients compared with 109 (87%) of 124 SC patients (P = .74). At the time of IDS, 1 (4%) of 23 DDC patients exhibited a complete clinical response intraoperatively compared with 15 (12%) of 126 SC patients (P = .5). All 7 complete pathologic responses were in the SC group. All patients treated with DDC achieved less than 1 cm visible residual disease at IDS compared with 108 (86%) of 126 who received SC (P = .08). At IDS, 14 (61%) of 23 DDC patients achieved complete gross resection compared with 68 (54%) of 126 SC patients (P = .14).

Conclusions: DDC patients had similar clinical features, but received fewer NACT cycles before IDS compared with standard dosing. DDC patients had a similar rate of optimal and complete gross resection at IDS compared with SC, and all DDC patients achieved less than 1 cm visible residual disease. Our data support the consideration of dose-dense neoadjuvant chemotherapy, and future investigation of the long-term oncologic outcomes with this approach.

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Differences in obesity and comorbidity profiles by age in uterine cancer patients and their impact on surgical outcomes

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Objectives: To identify differences in the epidemiologic profile of uterine cancer patients by age, and to evaluate the effect of age, body mass index (BMI), and comorbidities on surgical outcomes.

Methods: Using the National Surgical Quality Improvement Project (NSQIP) database, we reviewed all cases of uterine cancer between 2006 and 2012. Demographics, comorbidities, BMI, operative time, postoperative hospital days, and postoperative outcomes within 30 days of surgery, including major complications and readmission, were collected. Women were stratified into 3 groups: young (age <40 years), middle (age 40–70 years), and old (age >70 years). Descriptive statistics and multivariable logistic regression models were used. Institutional review board exemption was obtained.

Results: A total of 6,728 women were identified. The median age was 62 years (interquartile range 55–70 years), with 3% young and 24% old. Seventy-seven percent were white. Median BMI was highest in the young (40.4 kg/m^2) and decreased with age (middle: 33.6; old: 29.7). Of the young women, 51% were morbidly obese compared with only 28.6% in the middle-aged and 11% in the old age group ($P < .001$). Overall, 62% (n = 4,147) had 1 or more comorbidities. Twice as many old patients had 2 or more comorbidities compared with the young patients (32% vs 14%, $P < .001$). Comorbidities such as heart disease, hypertension, chronic obstructive pulmonary disease, and neurovascular disease were significantly more prevalent in the old patients (5.1%, 73.6%, 12.0%, 4.6%, respectively). In multivariable analysis, the old were 13 times more likely to have a greater number of comorbidities when adjusted for race and BMI (OR 12.96, $P < .001$). The young underwent fewer lymphadenectomies than did middle-aged and older women (25.0%, 37.5%, 37.1% respectively, $P < .001$). For surgical outcomes, the old had twice the likelihood of readmission as that of the young (OR 2.01, $P = .069$) and more major complications (OR 2.37, $P = .068$). Within the middle age group, those with morbid obesity were more likely to have longer hospital stays ($P = .0001$), major complications ($P = .01$), and operative time ($P = .0001$).

Conclusions: Young uterine cancer patients had almost 5 times the prevalence of morbid obesity as the old patients. Older women had more comorbidities, and trended toward increased readmission, longer hospital stay, and increased complications compared with younger women. Morbid obesity was associated with longer operative times, hospital stay, and major complications.

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Full inguinofemoral lymphadenectomy after positive sentinel inguinofemoral lymph node is associated with greater overall survival in patients with stage III squamous cell vulvar cancer

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Objectives: The use of sentinel lymph node (SLN) evaluation is increasingly popular for cases of vulvar squamous cell carcinoma (SCC) because of the reduction in postoperative morbidity and potential increase in detection of positive lymph nodes afforded by SLN evaluation. However, when inguinofemoral SLNs are positive, it is not known whether full lymph node dissection (LND) with or without radiation therapy (RT) is of benefit to patients. We sought to review our experience of SLN evaluation in patients with vulvar SCC and determine if full LND is associated with survival benefit in women with positive SLNs.

Methods: All patients who underwent primary SLN mapping for vulvar SCC from January 1, 1990, to September 1, 2015, were identified. Pertinent demographic, pathologic, and treatment data including age, race, body mass index, and medical and treatment history was abstracted. Survival was calculated using the log rank and Kaplan-Meier tests, and categorical variables were compared using c^2 analysis.

Results: A total of 467 patients received treatment for vulvar SCC at our institution during the study period and a total of 76 patients underwent SLN evaluation. Thirteen (17.1%) of 76 patients were found to have positive SLNs. Of these 13 patients, 7 (53.8%) had SLN evaluation alone and 6 (46.2%) had full LND after SLN (SLN + LND). Two of 7 patients who had SLN alone had recurrence in the groin, whereas none of 6 patients with SLN + LND had a recurrence in the groin. Median overall survival for patients who had SLN + LND was 49 months and 41 months for patients with SLN alone (P = .05) (Figure). Mean size of lymph node metastasis was 13.33 mm in the SLN + LND group and 13.16 mm in the SLN alone group (P = .97). Three (50%) of 6 patients who had SLN + LND received adjuvant groin RT and 6 (85.7%) of 7 patients who underwent SLN evaluation alone had adjuvant groin RT (P = .217). In patients who underwent SLN + LND, a median of 4.5 (range, 2–17) additional non-SLNs were removed. Two patients were found to have positive non-SLNs after full LND, and in each case only 1 non-SLN was positive.

Conclusions: Patients selected to undergo full LND after positive SLN for vulvar SCC may have an improved OS over those patients who had SLN evaluation alone, irrespective of postoperative radiation therapy.

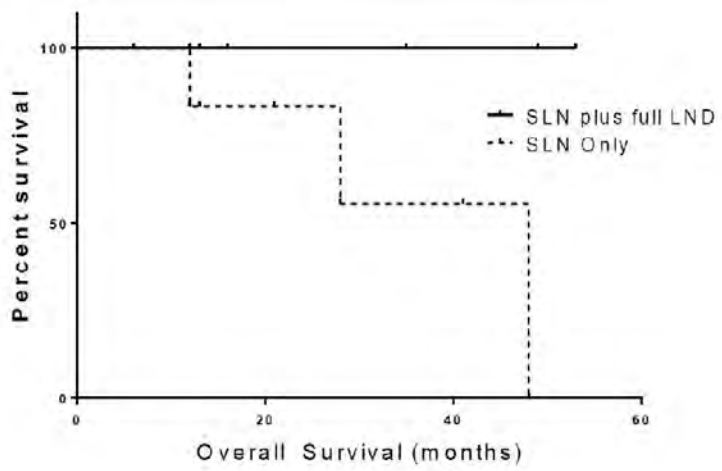

Fig. 1
Overall Survival from Time of Postive SLN.

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Robotically assisted laparoscopy for the evaluation of nodal status in early-stage cervical and endometrial cancer: The fluorometric and isotopic technique on a face-to-face
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Objectives: Sentinel node biopsy is an accepted option for nodal staging of patients with early cervical and endometrial cancers. A combined technique using blue dye and an isotope is generally used. Fluorescence appears as an alternative. We conducted a prospective study to compare the detection performance of the near-infrared fluorescence technique with that of the conventional isotopic technique, and to determine the anatomic distribution of sentinel lymph nodes, thus evaluating the feasibility of this new method.

Methods: Twenty eight patients diagnosed with early-stage cervical cancer FIGO stage IA with lymphovascular space invasion to IB1 (n = 15) and FIGO stage IA and IB endometrial cancer (n = 13) were enrolled. All patients received both technetium 99m and indocyanine green injections. Robotically assisted laparoscopic technique was implemented for completing the procedure. The number and exact anatomic location of the sentinel lymph nodes were documented for both techniques and the outcomes were compared.

Results: Fluorescence had similar overall detection rates as the isotopic technique or the combination of the 2. Indocyanine green was significantly superior in bilateral detection compared with technetium 99m (78.57 % vs 53.57 %; *P* = .049), and the results were equal to those seen with the combination of the 2 techniques. It also provided a striking outcome in cervical cancer patients, with a bilateral detection rate of 93.33%.

Conclusions: Indocyanine green/near-infrared fluorescence appears to be a promising technique in the detection and anatomic mapping of sentinel lymph nodes in early-stage cervical and uterine cancers because it has a relatively safe profile, with concomitant high bilateral detection rates.

Table 1
Sentinel lymph node detection according to Technetium 99m and Indocyanine green.

	Cervical cancer group (N=15)		**Endometrial cancer group (N=13)**		**Total population (N=28)**	
	No	%	No	%	No	%
Lymphoscintigraphy	6	40	2	12	8	29
At least one sentinel lymph node detection	4	66.66	1	50	5	62.5
Bilateral detection	2	33.33	0	0	2	25
Technetium 99m	15		13		28	
At least one sentinel lymph node detection	13	86.66	6	46.15	19	67.85
Bilateral detection	10	66.66	5	38.46	15	53.57
Number of sentinel lymph nodes per patient	2.2		0.92		1.64	
Indocyanine green	15		13		28	
At least one sentinel lymph node detection	14	93.33	8	61.53	22	78.57
Bilateral detection	14	93.33	8	61.53	22	78.57
Number of sentinel lymph nodes per patient	4.33		1.76		3.14	
Technetium 99m + Indocyanine green	15		13		28	
At least one Sentinel lymph node detection	14	93.33	8	61.53	22	78.57
Bilateral detection	14	93.33	8	61.53	22	78.57

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Surgical specialty affects the risk of postoperative complications in ovarian cancer: An analysis of the ACS-NSQIP datasets
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Objectives: To determine if the rate of postoperative complications in ovarian cancer patients differs by primary surgeon specialty.

Methods: We inspected the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective surgery for ovarian cancer. We compared rates of death, morbidity, and return to the operating room between those who underwent surgery performed by gynecologists versus general surgeons. The NSQIP participant use files do not discriminate between gynecologists and gynecologic oncologists. Rates were adjusted for demographic and preoperative comorbidities. Relative risks were determined using logistic regression.

Results: We identified 4,926 patients who underwent elective surgery for ovarian, fallopian tube, or primary peritoneal carcinoma. Rates of NSQIP complications were 414 per 1,000 surgeries for general surgeons and 357.3 per 1,000 surgeries for gynecologists (relative risk [RR] 1.16, 95% CI 1.04–1.30). In a comparison of general surgeons and gynecologists, the RR was 1.68 (95% CI 1.28–2.20) for surgical site infections (SSI), 4.47 (95% CI 2.66–7.52) for death, and 2.89 (95% CI 2.06–4.04) for return to the operating room. After adjusting for hypertension, diabetes, preoperative dyspnea, disseminated cancer, ascites, and sepsis on entry to the operating room, the risk of complications remained higher for general surgeons, but without statistical significance (RR 1.15, 95% CI 0.95–1.40). Rates of SSI, return to the operating room, and death remained significantly higher for general surgeons than for gynecologic oncologists.

Conclusions: Patients undergoing surgery for ovarian cancer at NSQIP hospitals by gynecologists are at lower risk for mortality, morbidity, and return to the operating room than those undergoing surgery by general surgeons. Patients should be encouraged to undergo ovarian cancer surgery with gynecologic oncologists when their services are available.

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A comparative analysis of prediction models for complete gross resection in secondary cytoreductive surgery

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Objectives: Many retrospective studies support secondary cytoreductive surgery (SCS) for selected patients with recurrent ovarian cancer; however, the criteria for case selection are variable and often surgeon dependent. In 2006, we published an institutional model (IM) for SCS case selection. The objective of this study is to examine our compliance and current outcomes using IM to predict complete gross resection (CGR), and compare the performance with 2 internationally validated models, the Tian model and AGO DESKTOP.

Methods: With institutional review board approval, all SCS cases for recurrent platinum-sensitive epithelial ovarian cancer were identified from May 2001 to June 2014. Patient and tumor characteristics, operative findings, outcomes of SCS, progression-free survival (PFS), and overall survival (OS) were documented. The AGO and Tian models were both applied to this population, and positive predictive value, negative predictive value, sensitivity, specificity, accuracy, k coefficient, and McNemar test computed to determine their performance.

Results: A total of 214 SCS cases were identified. Since implementation of IM, the compliance has been 97%, with an 87% CGR rate. The AGO model had an accuracy of 49% in this population, with a k coefficient of 0.002. Fifty-one percent of patients were AGO negative; however, CGR was achieved in 86% of these patients. The Tian model had 88% accuracy and a k coefficient of 0.269. Four percent were scored as Tian high risk, of which CGR was achieved in 33%. Using the McNemar test, $P = .366$ between the Tian model and IM, and $P < .001$ between AGO and IM; $P > .05$ represented agreement between models. Median PFS after SCS was 21.3 months (range, 18.2–24.5 months) for the entire cohort, 22.5 months (range, 19.4–25.3 months) for CGR patients, and 14.1 months (range, 9.7–22.1) for patients with residual disease ($P = .013$). OS from the time of SCS was 82.2 months (range, 60.2–123.3 months) for the entire cohort, 95.6 months (range, 63.6-NE) for CGR patients, and 57.5 months (range, 27.5–113.9 months) for patients with residual disease ($P = .014$).

Conclusions: CGR at the time of SCS is associated with extended PFS and OS. We report a high rate of institutional compliance and CGR with IM. For our population, the AGO criteria were strict, and application would preclude 51% of cases from SCS. There is good concordance of the Tian model to IM; however, IM has fewer variables required for calculation, which underscores its ease of use. Consideration can be given to stratify intermediate IM cases using the Tian criteria.

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Development and validation of a fluorescent reporter system for ovarian cancer stem cells

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Objectives: To create a fluorescence-based cancer stem cell (CSC) reporter for ovarian cancer cells.

Methods: We used a lentiviral construct to attach green fluorescent protein (GFP) to the promoter region of the stem cell transcription factor NANOG in an ovarian cancer cell line A2780, and its cisplatin-resistant derivative CP70. Cells were sorted into GFP-high and GFP-low groups using flow cytometry. Protein and mRNA levels were validated with Western blot analysis and reverse transcriptase polymerase chain reaction. Self-renewal was demonstrated using tumorsphere-limiting dilution analysis (LDA) at doses of 1 to 20 cells/well. Injections of 500k, 50k, and 5k sorted cells were made into NSG mice to demonstrate in vivo CSC frequency. Formed tumors were excised, dissociated, and underwent flow cytometry to demonstrate in vivo asymmetric division. A high-throughput flow cytometry screen (HTS) was conducted of 242 cell surface proteins to identify differences in cell surface signature between CSC and non-CSC in the cisplatin-sensitive and cisplatin-resistant cell lines.

Results: In A2780, GFP-high cells express higher levels of 3 CSC transcription factors (NANOG, SOX2, OCT4) in protein and mRNA levels. In CP70, levels are higher but the difference is nonsignificant. The in vitro tumorsphere frequency was 1:88.8 versus 1:136 for GFP-high versus low in A2780, and 1:5.37 versus 1:10.54 for CP70 (P £ .01). In vivo, GFP-high cells were more tumorigenic in the mice injected with A2780 cells (P < .01). No difference in tumorigenesis was seen in the CP70 injections. In dissociated tumors from the GFP-high group in both cell lines, flow cytometry showed reconstitution of a mixed population, thus demonstrating asymmetric division in vivo. The HTS identified novel cell surface targets for follow-up.

Conclusions: Our fluorescent reporter system can identify CSC in A2780 cells both in vitro and in vivo using the assays described here. We were not able to demonstrate an in vivo tumorigenesis difference in CP70, but this may be because of the fact that both GFP-high and GFP-low cells were highly self-renewing in the CP70 cell line. We also identified a potential novel marker for cisplatin resistance; further study is under way in our laboratory.

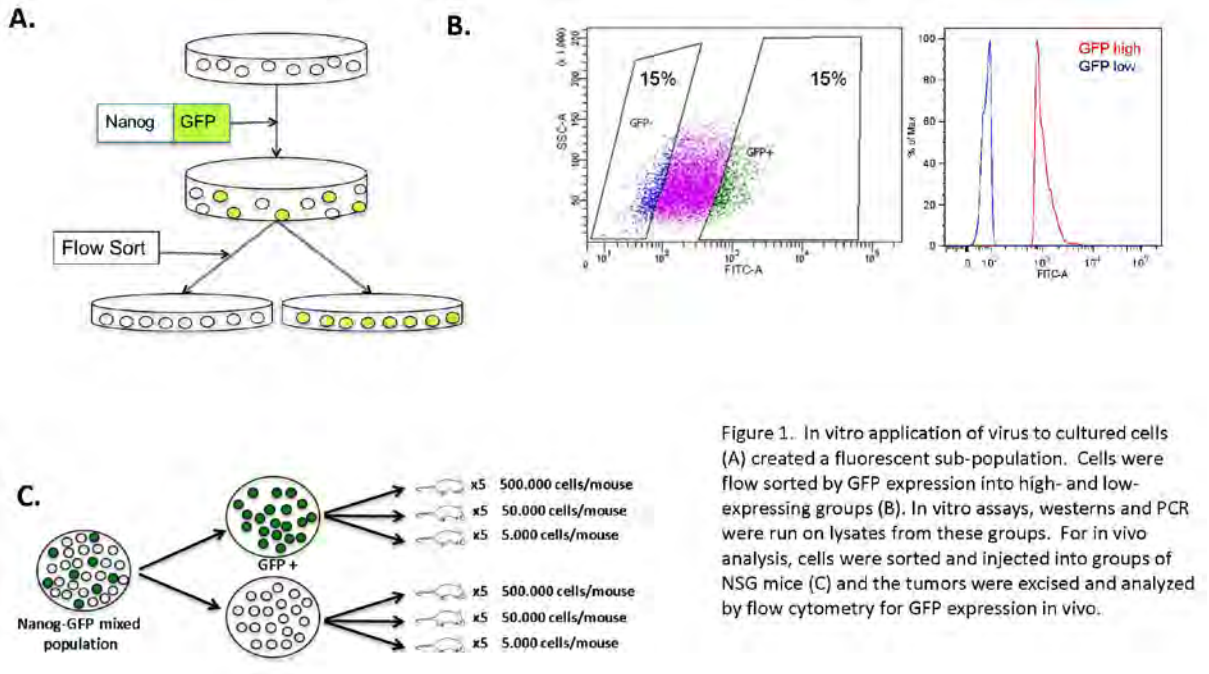

Figure 1. In vitro application of virus to cultured cells (A) created a fluorescent sub-population. Cells were flow sorted by GFP expression into high- and low-expressing groups (B). In vitro assays, westerns and PCR were run on lysates from these groups. For in vivo analysis, cells were sorted and injected into groups of NSG mice (C) and the tumors were excised and analyzed by flow cytometry for GFP expression in vivo.

Fig. 1
Experimental Schematic.

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Upregulation of the extrinsic apoptosis pathway by docetaxel, panobinostat, and volasertib may potentiate synergy with birinapant in high-grade serous ovarian cancer

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Objectives: Birinapant, a second mitochondrial activator of caspases (SMAC) mimetic, which functions to potentiate tumor cell death, has demonstrated preclinical activity against solid tumors, including ovarian cancer. We have identified synergy between birinapant and 3 distinct classes of anticancer agents—taxanes, HDAC inhibitors, and PLK inhibitors. This study sought to uncover potential mechanisms of synergy through differential gene expression in ovarian cancer cell lines treated with each of 3 synergistic drugs.

Methods: A high-throughput screening matrix identified distinct drug classes as synergistic with birinapant. Candidates were evaluated by XTT assay in 8 high-grade serous ovarian cancer cell lines. Further in vitro testing verified synergistic activity between birinapant and 3 selected drugs: docetaxel, panobinostat, and volasertib. Microarray analysis of Caov4 treated individually with docetaxel, panobinostat, and volasertib was completed to interrogate common patterns of differential gene expression. Microarray results were validated using polymerase chain reaction (PCR).

Results: A high-throughput drug screen identified synergistic activity of birinapant in combination with docetaxel, panobinostat, or volasertib. Four high-grade serous ovarian cancer cell lines (Caov3, Caov4, Ovcar4, and Ovcar8) consistently showed sensitivity to birinapant, and synergism with the combination. Gene expression was profiled in Caov4 cell line treated individually with each of the 3 synergistic drugs, and confirmed with PCR analysis. Interestingly, 8 commonly upregulated genes (*FADD*, *CASP6*, *TNFRSF1A*, *TNFRSF12A*, *BAG4*, *PIAS1*, *SOCS5*, and *IFNGR2*) and 8 downregulated genes (*CCNE*, *CYLD*, *CXCR4*, *RB1*, *TNF*, *CDKN1A*, *CDKN2B*, and *TNFAIP3*) are noted to be involved in regulating extrinsic apoptosis.

Conclusions: Gene expression profiling in the birinapant-sensitive cell line Caov4 treated with docetaxel, panobinostat, or volasertib was validated with PCR. The therapeutic activity of birinapant appears to be augmented by activation of the extrinsic apoptosis pathway by other agents. Cotherapy has the potential to overcome drug resistance and improve outcomes. Our findings support further investigation into the use of birinapant as a targeted, combination treatment for ovarian cancer.

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Knowledge and confidence in gynecologic oncology care among women with ovarian cancer

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Objectives: Not all women diagnosed with ovarian cancer (OC) receive care from gynecologic oncologists (GOs). Little is known about the reasons for the low uptake. One factor may be related to women's knowledge of, and the perceived survival advantage associated with, GO care.

Methods: We conducted phone surveys with 170 women with OC (response rate 66%), recruited from 3 hospitals in Alabama and Georgia, and from the Alabama Statewide Cancer Registry. Questions were adapted from Cancer Care Outcomes Research and Surveillance Consortium's questionnaire. We asked women about the specialty of the physicians they saw, knowledge about GO care, and confidence in their physicians.

Results: Overall, 95% had seen 1 or more GO: 91% for surgery, 79% for decisions about treatment, 63% for diagnosis, and 59% for chemotherapy. Fewer (81%) reported that they had seen 1 or more GO. Women not reporting seeing GOs were more likely to be African American (36% vs 21% of those reporting GO care) , to have high school education or less (58% vs 36%), to be within 6 months of diagnosis (30% vs 17%), and to have stage III disease (36% vs 29%). Results on knowledge and confidence are in Table 1. Most important differences in knowledge were: 19% of women not reporting GO care vs 6% women reporting GO care strongly agreed/agreed that there are no clear benefits to receiving GO care; 72% women not reporting GO care versus 82% of women reporting GO care strongly agreed/agreed that GOs follow women from diagnosis to end of life, and 91% of women not reporting GO care versus 97% of women reporting GO care strongly agreed/agreed that some women

clearly benefitted from receiving treatments from GOs. Most important differences in confidence were: 73% of women not reporting GOs versus 87% of women reporting GOs thought it was very likely or likely that their physicians will cure OC.

Conclusions: One in five OC cases was not aware of the specialty of the physicians. These women were less likely to be aware of the advantages of receiving GO care or to have confidence in their physicians.

Table 1
Knowledge about GOs and beliefs about doctors.

	All	Reporting GOs	
Understanding about services of GOs		Yes N = 137	No N = 33
		% Strongly Agree/Agree	
There are not clear benefits from receiving care from them, it is just another surgeon	8.3	5.8	18.8
I am not sure why I should see one of them	4.7	5.1	3.1
Gynecologic oncologists follow-up women with ovarian cancer from diagnosis through end of life	80.5	82.5	71.9
Gynecologic oncologists are surgeons dedicated to cancer surgery	91.7	92.7	87.5
Gynecologic oncologists provide all treatments, i.e., perform surgery, prescribe chemotherapy and any other appropriate treatment	92.3	92.7	90.6
Gynecologic oncologists specialize in the treatment of gynecologic cancers	98.2	99.3	93.7
Some women have clearly benefitted from receiving treatment from these specialists	95.8	97.1	90.6
Beliefs about doctors How likely did you think it was that:		**% Very Likely/Likely**	
Doctor/s would help you live longer?	97.6	98.5	93.9
Doctor/s would cure your cancer?	84.1	86.9	72.7
Doctor/s would help you with problems you were having because of your cancer?	93.5	94.9	87.9

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Evaluating determinants of prolonged hospitalization following minimally invasive surgery for endometrial cancer
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Objectives: To use a centralized multi-institutional dataset to determine the pre- and intraoperative factors associated with prolonged hospitalization after minimally invasive surgery for endometrial cancer.

Methods: We inspected the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective minimally invasive hysterectomy (CPT codes 58500–58599) for endometrial cancer. Length of stay was defined as normal for 0 to 1 days and prolonged for discharge 2 or more days after surgery. Pre- and intraoperative factors were compared using a χ^2 test of independence with a nominal value of $P < .05$ as a threshold for significance.

Results: We identified 6,150 patients who underwent minimally invasive hysterectomy for endometrial cancer. Of those, 4,698 patients (76.4%) were discharged home by the first postoperative day. NSQIP-tracked postoperative complications were 3 times more common among women staying in the hospital longer than 1 day versus those discharged on time (relative risk [RR] 3.65, 95% CI 3.00–4.34). Factors associated with prolonged hospitalization included: not-independent functional

status (RR 4.4, 95% CI 2.86–6.78), age over 70 years (RR 2.03, 95% CI 1.79–2.31), dyspnea before surgery (RR 1.72, 95% CI 1.38–2.15), diabetes (RR 1.55, 95% CI 1.35–1.78), hypertension (RR 1.54, 95% CI 1.36–1.74), class III obesity (RR 1.17, 95% CI 1.03–1.34). Surgery longer than 4 hours was also associated with an almost 3-fold increase in risk of prolonged hospitalization (RR 2.97, 95% CI 2.59–3.41), and lymph node dissection (CPT 58548) increased the risk of prolonged hospitalization by 34% (RR 1.34, 95% CI 1.22–1.49).

Conclusions: Some preoperative comorbidities, long surgical duration, and lymph node dissection are significant risk factors for prolonged hospitalization after minimally invasive surgery. Although class III obesity cannot be significantly altered in the weeks before surgery, improving poor functional status with prehabilitation may reduce the complications and costs associated with treating endometrial cancer.

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Preoperative hyponatremia in women with ovarian cancer: An additional cause for concern?

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Objectives: An association between preoperative hyponatremia and postoperative 30-day morbidity and mortality has been reported. To date, no studies have assessed the association between hyponatremia and postoperative complications among women with gynecological cancer. Our objective was to determine if preoperative hyponatremia in women with ovarian, fallopian tube (FT), and primary peritoneal cancers (PPC) is associated with postoperative mortality and complications.

Methods: We performed a retrospective population-based cohort study of women with a postoperative diagnosis of ovarian, FT, or PPC who had a cytoreductive procedure in the National Surgical Quality Improvement Program (NSQIP) database from 2005 to 2013. Women with a missing preoperative serum sodium measurement (n = 354) or hypernatremia (n = 350) were excluded. The primary exposure, preoperative sodium, was classified as normal (135–142 mEq/L) or hyponatremic (≤134 mEq/L). Where appropriate, categorical preoperative characteristics were compared using the χ^2 and Fisher exact tests. Estimates of risk for 30-day postoperative mortality and complications were determined with logistic regression.

Results: A total of 4,009 subjects met inclusion criteria. Subjects had similar body mass index (P = .21), functional status (P = .07), and comparable operative times (P = .31). Those with preoperative hyponatremia (n = 365) were older (P < .001) and more likely to have disseminated cancer (P < .001), ascites (P < .001), and chronic hypertension (P < .001) than women with normal serum sodium. Thirty-day mortality was higher in the hyponatremic group than in the normal serum sodium group (3.56% vs 1.18%). After adjusting for serum albumin and other confounders, preoperative hyponatremia was associated with an increased risk of hospital stay of more than 14 days (adjusted OR [aOR] 1.69, 95% CI 1.11–2.57) and 30-day postoperative mortality (aOR 2.28, 95% CI 1.13–4.59) (Table 1).

Conclusions: Hyponatremia is associated with postoperative 30-day mortality and morbidity in women with ovarian, FT, and PPC. Serum sodium in conjunction with other markers has the potential to identify candidates for neoadjuvant chemotherapy. Furthermore, work is needed to determine if correction of hyponatremia in the preoperative period alters outcomes.

Table 1

Multivariate Logistic Regression of Hyponatremia on 30-day Postoperative Complications.

	OR *	95% CI	*P*-value
Outcome			
Wound infection/dehiscence	0.51	0.27 - 0.94	0.03
Pneumonia	1.05	0.45 - 2.42	0.92
Myocardial Infarction	6.31	1.18 - 33.57	0.03
^LOS >14 days	1.70	1.11 - 2.57	0.01
30 day mortality	2.37	1.13 - 4.98	0.02
Any post-op complication	1.29	0.92 - 1.81	0.14

* Adjusted for age, body mass index, race, tobacco use in the past year, chronic obstructive pulmonary disease, ascites, congestive heart failure, chronic hypertension, diabetes, blood transfusion 72hrs prior to surgery, serum creatinine, and serum albumin

^ Length of hospital stay

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Symptom management in women with recurrent ovarian cancer: Do patients and providers agree on what symptoms are most important?

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Objectives: Symptom management requires communication, documentation, and intervention, yet little is known about how this occurs within gynecologic oncology. This study analyzes concordance between patient-reported symptoms within a randomized controlled trial and those documented by providers during the same time period.

Methods: The WRITE Symptoms Study (NIH/NR010735; GOG 259) is a randomized controlled trial of web-based ovarian cancer symptom management that included 497 women with recurrent ovarian, fallopian tube, or primary peritoneal cancer from 68 GOG sites. This analysis includes 50 women from a single institution. Women completed the Symptom Representation Questionnaire for 28 symptoms and selected 3 priority symptoms (PS). Electronic medical records were reviewed for provider documentation of symptoms and interventions pursued.

Results: Table 1 describes PS reported, documented, and intervened for. Providers documented at least 1 PS in 92% of patients and intervened in 58% of patients. Of 150 PS, 53% were never documented. Providers never documented PS of sexuality concerns, hot flashes, or memory problems. When documented, the mean number of visits in which a PS was documented was 2.3. Twenty-nine patients (58%) had at least 1 PS intervention. On average, PS intervened for were documented at 2.58 visits (1–7) versus 0.50 visits (0–5) for PS not receiving intervention ($P \leq .0001$).

Conclusions: The 4 most common PS were also the 4 most commonly documented PS, showing that providers are identifying and documenting symptoms important to patients. Symptoms documented by providers but not reported by patients tended to be related to physiologic effects of disease and acute treatment toxicity, whereas symptoms reported by patients but not documented by providers tended to be more psychosocial in nature. The number of visits documenting a PS correlated with intervention, suggesting that improving physician-patient communication could improve intervention rates. The etiology of discordance between patient and provider-report is likely multifactorial and requires further investigation; this study illustrates the need to improve identification of PS and increase intervention rates to enhance quality of life in women with recurrent ovarian cancer.

Table 1

Priority Symptoms (PS) Reported, Documented and Intervened for.

Most common PS	fatigue (29), neuropathy (17), sleep disturbance (13), pain (11)
Most documented PS	fatigue (21), neuropathy (12), pain (9), sleep disturbance (5)
Most frequently intervened for PS	neuropathy (8), fatigue (7), pain (5), sleep disturbance (4)
Non-PS symptoms commonly documented	musculoskeletal pain (28), abdominal or pelvic pain/bloating (26), neuropathy (17), nausea/vomiting (15)
PS symptoms never documented	sexuality concerns (3), hot flashes (3), and memory problems (6)

( ) = number of patients

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Inbound referral patterns for ovarian cancer patients at a National Comprehensive Cancer Network (NCCN) institution

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Objectives: We evaluated the referral patterns that ovarian cancer (OVCA) patients experience from the initial recognition of a pelvic mass to consultation with a gynecologic oncologist (GO) and seek to define quality of care and identify areas for improvement.

Methods: A retrospective review was performed on all OVCA patients managed at a National Cancer Institute–designated comprehensive cancer center from 2000 to 2014. Subjects were excluded for a prior personal history of cancer, no pelvic mass on imaging, borderline histology, inadequate medical records, or chemotherapy before GO consultation. Using NCCN guidelines, 6 adherent referral patterns were defined, starting with the physician subspecialty that identified the pelvic mass. To measure adherence to NCCN guidelines, we used 4 categories. In addition to referral patterns, the other criteria were abdominal/pelvic imaging, chest imaging, and tumor marker utilization (Table 1).

Results: In the 345 patients who met inclusion criteria, 24% of the masses were identified by an OB/GYN, followed by internists (20%), family medicine, and emergency medicine (18%), with the remaining 19% by other subspecialties. Overall, 41.7% of patients experienced 1 or more inpatient admission or ED visit before GO referral. Two hundred forty-one patients (70%) were referred to GO via an adherent pattern defined as above. The other 104 patients (30%) were referred via 1 of 40 highly variable nonadherent referral pathways. There was no difference in early- versus late-stage distribution between the 2 groups (P = .05137). Patients with adherent referral patterns had better overall survival (P = .0349) and shorter median delay in referral to a GO (14 vs 18.5 days, P = .034). Only 197 patients (57.1%) received NCCN-adherent care in all 4 categories examined

Conclusions: While referral guidelines focus on OB/GYN care paths, most OVCA patients had pelvic masses identified by other subspecialties. A significant number experienced inpatient or EM episodes where referral guidelines may not be well known. We have identified referral patterns and delay as potentially useful quality metrics of prereferral care.

Table 1

Forty Non-Adherent Referral Patterns.

- Obstetrician/Gynecologist (OB/GYN) → GO
- NON-OB/GYN → GO
- NON-OB/GYN → OB/GYN → GO
- NON-OB/GYN → Gastroenterologist (GI)* → GO
- NON-OB/GYN → GI* → OB/GYN → GO
- NON-OB/GYN → OB/GYN → GI* → GO

*if indicated by symptoms

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Investigating the impact of asymptomatic leukocytosis on postoperative outcomes in ovarian cancer

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Objectives: The purpose of this study is to identify the relationship between asymptomatic preoperative leukocytosis and postoperative complications in elective ovarian cancer surgery.

Methods: We inspected the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective surgery for ovarian cancer. Patients were excluded if they had an infection present at the time of surgery (PATOS). We compared rates of death, NSQIP-tracked morbidities, infectious morbidity (surgical site infection, pneumonia, urinary tract infection, or sepsis), and return to the operating room. Patients were stratified based on leukocytosis (white blood cell [WBC] count > 11×10^9/L). Rates were adjusted for demographic and preoperative comorbidities. Relative risks were estimated using logistic regression.

Results: We identified 7,535 patients who underwent surgery for ovarian cancer. Of these, 484 patients were excluded for emergency surgery or PATOS infections. Another 926 were excluded for no WBC value listed. Of 6,125 evaluable patients, 518 (8.5%) had a leukocytosis before surgery. The rate of complications in those patients was 440 per 1,000 surgeries, compared with 341 per 1,000 surgeries in patients who did not have leukocytosis (relative risk [RR] 1.29, 95% CI 1.16–1.43). Patients with leukocytosis also had increased risk of death (RR 2.41, 95% CI 1.34–4.32) and infectious morbidity (RR 1.34, 95% CI 1.05–1.70), but not return to the operating room (RR 1.23, 95% CI 0.82–1.85). After adjustment for extent of disease, prior chemotherapy treatment, and other preoperative factors, the risk of any NSQIP-tracked complication remained associated with leukocytosis, but infectious morbidity (RR 1.08, 95% CI 0.62–1.89) and death (RR 2.29, 95% CI 0.71–7.40) were no longer statistically significant.

Conclusions: Patients going to surgery for ovarian cancer with pre-existing leukocytosis are at increased risk of NSQIP-tracked complications in the 30 days after surgery, especially the risk of infectious morbidity. The interaction between the immune system and long-term ovarian cancer outcomes is well established. Paraneoplastic leukocytosis does not appear to increase the risk of postoperative death or return to the operating room within 30 days.

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Risk prediction model for surgical site infections in patients undergoing gynecologic cancer surgery

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Objectives: Surgical site infections (SSIs) remain a substantial cause of morbidity, prolonged hospitalization, and death in patients undergoing gynecologic cancer surgery, especially in those undergoing colorectal procedures. In addition, there is growing evidence that SSIs negatively impact oncologic outcomes. The objective of our study was to establish a risk prediction model for SSIs in patients undergoing complex gynecologic cancer surgery.

Methods: We searched our institutional database for patients who underwent any COLO National Health Safety Network (NHSN) operative procedure category for a gynecologic malignancy as defined by ICD-9-CM codes from 2012 to 2015. Superficial, deep incisional and organ/space SSIs were captured as defined by the Centers for Disease Control and Prevention (CDC) within 30 days after surgery. Patient, preoperative, and intraoperative characteristics were assessed. A logistic regression model was built by performing backward stepwise variable selection based on Akaike Information Criterion (AIC).

Results: We identified 365 patients who underwent COLO NHSN operative procedures. An SSI was detected in 95 patients (26.03%). Total blood loss, total/maximal relative value unit (RVU), the performance of a bowel resection, body mass index (BMI), preoperative low serum albumin levels, preoperatively elevated white blood cell (WBC) count, the performance of a lymphadenectomy, operative time, diabetes, and smoking were significantly associated with SSI. The optimal prediction model included the following variables: performance of a bowel resection, BMI, operative time, and preoperative serum albumin. A receiver operating characteristic curve was generated for the model, showing an AUC of 0.63 and an accuracy of 73.4%.

Conclusions: We have developed and internally validated a risk prediction model for SSIs in patients undergoing complex gynecologic cancer surgery. Identifying patients at high risk for SSIs will allow for individualized perioperative interventions. This SSI risk prediction model will be used prospectively to stratify and evaluate SSI reduction initiatives at our institution.

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Evaluation of smoking as a risk factor for adverse postoperative outcomes in endometrial cancer: A study of the NSQIP database

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Objectives: The purpose of this study is to determine the impact of smoking on surgical outcomes in endometrial cancer patients.

Methods: We evaluated the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective surgery for endometrial cancer. Patients were classified as current smokers (regular smoking within 1 year of surgery) or nonsmokers. Other variables including preoperative comorbidities, such as hypertension, diabetes, and functional status; intraoperative variables, including operative time, extent of surgery (based on CPT code), and surgical approach; and postoperative complications, including death, return to the operating room (ROR), and infectious morbidity (surgical site infection [SSI], pneumonia [PNA], urinary tract infection [UTI], or sepsis), were recorded and compared using χ^2 test of independence. Crude and adjusted relative risks (RRs) were estimated using logistic regression. $P <$ .05 was used as a threshold of significance.

Results: We identified 10,302 patients who underwent elective surgery for endometrial cancer. Of these, 939 patients were current smokers at the time of surgery. The rate of complications in those patients was 50 per 1,000 surgeries, compared with 41 per 1,000 surgeries in patients who were not current smokers (RR 1.22, 95% CI 0.91–1.64). Smokers had an increased risk of ROR (RR 1.67, 95% CI 1.08–2.58), but the risks of SSI, PNA, UTI, sepsis, and death were not significantly different from nonsmokers. After adjusting for surgical approach, disease spread, lymphadenectomy, and operative time, smokers remained at significantly increased risk of ROR, but were not at increased risk for other complications.

Conclusions: In this multicenter patient database, smoking does not increase the risk of infectious morbidity after elective surgery for endometrial cancer. This paradoxical finding may be because of altered host response to cigarettes in patients who develop endometrial cancer despite smoking. Patients are at higher risk of returning to the operating room, but this does not appear to affect 30-day mortality after surgery.

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Endometrial evaluation in adult granulosa cell tumors: Is it really necessary?

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Objectives: Adult granulosa cell tumors are known as estrogen producers, and therefore, patients with these tumors may be at risk of developing endometrial hyperplasia and cancer. Our aim was to determine the safety of omitting endometrial evaluation adult granulosa cell tumor patients.

Methods: We retrospectively analyzed a series of 56 patients treated at A.C. Camargo Cancer Center from April 1980 to April 2014.

Results: Median age was 52 years (range, 23–84 years). Median follow-up time was 48 months (range, 1–272 months). Seven patients (12.1%) had fertility-sparing surgeries. Only 3 patients (5.3%) had synchronous endometrial cancer diagnosed, with previous vaginal bleeding symptoms seen in 2 of them. The endometrial cancers were all low grade and had superficial myometrial invasion. One patient had endometrial hyperplasia, also with vaginal bleeding. The diagnosis of endometrial cancer or hyperplasia did not have a negative impact on disease-free survival (P = .22) and overall survival (P = .43). No patient who received fertility-sparing treatment had preoperative endometrial thickening on transvaginal ultrasound, and none of the patients developed endometrial cancer after fertility-sparing surgery during follow-up.

Conclusions: Our data suggest that endometrial evaluation may not be mandatory in asymptomatic patients.

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Knowledge about the HPV vaccine among employees at a tertiary cancer center: Room for improvement

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Objectives: Despite the availability of several US Food and Drug Administration–approved vaccines that prevent human papillomavirus (HPV)–related cancers, vaccination rates for girls and boys in the United States remain low. The aim of this study was to determine the knowledge and attitudes of employees at a tertiary cancer center toward HPV vaccination.

Methods: We surveyed 20,673 employees of The University of Texas MD Anderson Cancer Center using a 19-item institutional review board–approved online survey. Participants were recruited via email and employee newsletter that included a link to the survey. The survey included questions about HPV vaccination of participants and their families as well as reasons for not vaccinating.

Results: A total of 4,366 employees completed the survey (response rate, 21%). Of those responding, 36% were health care providers, 11% provided care for pediatric patients, and the majority was women (73%). Most responders did not know it was covered by the Adult Safety Net program (79%); however, more than half knew that the HPV vaccine is covered under the Affordable Care Act and the Vaccines for Children program (58% and 57%, respectively). Seven percent of men and 16% of women had completed the vaccine series. Of those who had not been vaccinated, only 41% were within the right age range for eligibility. The main reasons for not personally being vaccinated were not knowing it was needed and the vaccine not being recommended by a health care provider. The majority of children of responders had not completed the vaccine series despite being eligible (65% girls and 70% boys). The main reasons for not vaccinating children was not knowing it was needed (16% girls and 33% boys), the vaccine not being recommended by pediatrician (13% girls and 19% boys), and not vaccinating because their child was "not sexually active" (16% girls and 2% boys). Among those with children too young to vaccinate, 82% of those with daughters and 79% of those with sons planned to vaccinate when the child was old enough.

Conclusions: HPV vaccination rates remain low in the United States and knowledge about the vaccine is poor even among health care workers in a major cancer hospital. Increasing vaccination rates will require increased awareness about the benefits of the HPV vaccine and an effort to increase the number of health care providers who recommend the vaccine to their patients. We plan to use targeted education to increase the knowledge base of the employees and resurvey 2 years from now.

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Evaluation of risk factors for readmission following surgery for ovarian cancer: A NSQIP database analysis

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Objectives: Characterize risk factors for hospital readmission within 30 days of surgery for ovarian cancer.

Methods: We evaluated the National Surgical Quality Improvement Program (NSQIP) participant use files from 2011 to 2013 for patients undergoing elective surgery for ovarian cancer. Patients were classified as having been readmitted to the hospital if they were classified as "inpatient" by the readmitting hospital or were reported as such by the patient or their family. Other variables including age, body mass index (BMI), preoperative comorbidities, and length of surgery were recorded and compared using the χ^2 test of independence. Adjustments were performed using the Mantel-Haenszel method. Logistic regression was performed to identify risk associated with surgical duration. $P < .05$ was used as a threshold of significance.

Results: Of 3,633 patients identified with complete information, 344 were readmitted to the hospital within 30 days of surgery. Age greater than 70 years was not a significant risk factor for readmission (RR 1.19, 95% CI 0.95–1.48). Significant risk factors for readmission included being underweight (BMI <18.5 kg/m^2, RR 1.68, 95% CI 1.07–2.63), history of severe chronic obstructive pulmonary disease (RR 1.64, 95% CI 1.02–2.65), hypertension (RR 1.28, 95% CI 1.05–1.56), chronic steroid use (RR 1.79, 95% CI 1.24–2.61), disseminated cancer found at the time of surgery (RR 1.36, 95% CI 1.10–1.67), or if the surgery lasted longer than 4 hours (RR 1.52, 95% CI 1.23–1.88). For patients undergoing surgery longer than 4 hours, the risk of readmission was 12.7% per additional hour of surgery (RR 1.13, 95% CI 1.01–1.25). The risk of readmission for patients hospitalized longer than 5 days after surgery was 55% higher than those hospitalized for less time (RR 1.55, 95% CI 1.27–1.90).

Conclusions: Medical comorbidities, chronic steroid use, and low body weight are associated with an up to 79% increased risk of hospital readmission after surgery for ovarian cancer. Patients with these medical problems, disseminated cancer, surgeries lasting longer than 4 hours, or hospitalized more than 5 days after surgery may benefit from additional discharge planning and care coordination to avoid hospital readmission.

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Bone marrow–derived fibroblasts are a functionally distinct stromal cell population in breast cancer and lung metastases

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Objectives: Breast tumors are characterized by an extensive desmoplastic stroma, abundantly populated by fibroblasts. Cancer-associated fibroblasts (CAFs) are a heterogeneous cell population found in the microenvironment of solid tumors, shown to promote tumor growth in various mechanisms, including stimulation of tumor cell proliferation, enhancement of angiogenesis, and mediation of tumor-promoting inflammation. Here we set out to characterize CAF subpopulations during progression of mammary carcinoma and lung metastasis.

Methods: We used the MMTV-PyMT transgenic mouse model of human breast carcinogenesis for adaptive bone marrow transplantation (BMT).

Results: We show that bone marrow (BM)–derived mesenchymal stromal cells are specifically recruited to breast tumors and to spontaneous lung metastases, where they differentiate to CAFs, but not to normal mammary glands or lungs. Detailed analysis of this unique population revealed that BM-derived CAFs express α-SMA, but do not express PDGFRα, implying that the latter is a marker of resident tissue fibroblasts. Furthermore, we show that BM-derived CAFs are functionally distinct from resident fibroblasts in various tumor-promoting activities. We isolated the different CAF subpopulations from primary tumors and lung metastases and analyzed their immunologic transcriptome. This analysis revealed distinct gene expression signatures of resident and BM-derived CAFs, as well as genes that are commonly expressed by both subpopulations. Interestingly, the distinct inflammatory profile exhibited by BM-derived cells depended on the location to which they were recruited. Furthermore, BM-derived CAFs induced significantly more angiogenesis than resident mammary CAFs in a plug assay in vivo. Analyzing 792 human breast tumors, we found a significant decrease in the expression of PDGFRα that was evident in multiple other human tumors, suggesting that it may be a general phenomenon. Moreover, decrease in PDGFRα in human breast tumors was associated with worse outcome, suggesting that recruitment of PDGFRα– CAFs affects survival.

Conclusions: CAF populations in the tumor microenvironment are unique in marker expression and function. Our findings may form the mechanistic basis for novel therapeutic manipulations and cotargeting of BM-derived CAFs.

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Metabolic effects of metformin treatment in ovarian cancer cell lines

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Objectives: Metformin is being actively repurposed for the treatment of gynecologic malignancies. It is known to alter the cancer cell metabolism, primarily inhibit oxidative phosphorylation, and induce glycolysis. Our aim was to investigate the metabolite changes occurring in response to metformin treatment in ovarian cancer (OvCa) cell lines.

Methods: A2780, C200, SKOV3ip cell lines were treated with metformin (10 mM) for 48 hours and subjected to untargeted global metabolites by ultra–high performance liquid chromatography and gas chromatography mass spectroscopy. Per-metabolite comparisons were made. Interpretive analysis was performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) and the Ingenuity molecule library.

Results: Metformin treatment caused alterations in metabolites in all treated lines: A2780 showed 132 alterations (72 up; 60 down), C200 showed 135 (77 up; 58 down), and SKOV3ip showed 135 (84 up; 51 down); (FDR ≤ 0.1). The 3 cell lines revealed

57 common altered metabolites, of which 30 had consistent direction change. KEGG analysis of these 30 metabolites showed that the amino acid metabolism (alanine, aspartate, glutamate and glycine, serine, threonine metabolism; adjusted $P < .0001$) was the most significantly affected. Interestingly, metformin affected the energy pathways of glycolysis and oxidative phosphorylation differentially across the 3 cell lines. Cellular proliferation and signaling was the top common network pathway on Ingenuity analysis.

Conclusions: Metformin treatment had a significant and widespread effect on metabolism of OvCa cell lines. Although metformin resulted in certain consistent metabolic changes in amino acid metabolism across cell lines, its modulation of glycolysis and oxidative phosphorylation was varied. These differential metabolic changes could indicate the degree of metformin response and suggest it to be context-dependent. Such information about the cancer metabolism may aid in preclinical and clinical assessment of metformin therapy in ovarian and other cancers.

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Changing the balance between personal and professional life among female gynecologic oncologists: 1998 versus 2015

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Objectives: To describe changes in mentoring and work-life issues faced by female gynecologic oncologists between the years 1998 and 2015.

Methods: We conducted a cross-sectional survey of female and male gynecologic oncology physician members of the Society of Gynecologic Oncology (SGO). A survey originally sent to female gynecologic oncologists in 1998 was expanded, piloted in 10 volunteers, and administered in electronic format (DatStat Illume) in February 2015. Our revised instrument contained 75 fixed response questions regarding 4 domains including: (1) demographics; (2) mentoring issues; (3) work-life balance; and (4) caregiving responsibilities. We compared our survey responses to the previous 1998 raw survey data. Data were analyzed using Stata 10 (Statacorp, College Station, TX) with χ^2 analysis and Fisher exact test using aggregate data functions.

Results: A total of 268 gynecologic oncologists completed our survey (response rate 21.5%). Of these, 172 (64%) were women and are included in this analysis. The historical comparison group included 81 female respondents who completed the 1998 survey (response rate 57%). The mean age of survey respondents did not differ between groups (39 vs 40, $P = .4$). No difference was found between the proportion of respondents in academic practice, private practice, and fellowship, with the majority being in academic practice (55%) ($P > .05$). More women reported having a female mentor in 2015 compared with 1998 (59% vs 35%, $P < .0001$); however, 30% of female respondents in 2015 did not feel that the mentor's gender was important compared with 6% in 1998 ($P < .0001$). In work-life balance issues, more women in 2015 reported starting a family during residency/fellowship training compared with 1998 (58% vs 36%, $P < .009$). Overall, women reported taking longer maternity leave (7–12 weeks) in 2015 compared with 1998 (46% vs 16%, $P < .0001$). An increased proportion of women reported that their spouses were the primary caregivers in 2015 compared with 1998 (59% vs 12%, $P < .0001$).

Conclusions: The trends in mentoring, work-life balance, and caregiving responsibilities have changed significantly for female gynecologic oncologists between 1998 and 2015.

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Uptake and outcomes associated with neoadjuvant chemotherapy in the elderly: A population-based analysis

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Objectives: Randomized trials have demonstrated similar survival between neoadjuvant chemotherapy (NAC) and primary debulking surgery (PDS) as initial therapy for ovarian cancer (OC). In the United States, however, a bias towards PDS persists. We evaluated patterns of use and outcomes in a population-based cohort of elderly women with OC.

Methods: A cohort of patients older than 66 years diagnosed between 2002 and 2011 with pathologically confirmed stage II–IV epithelial OC who underwent surgery and platinum/taxane chemotherapy as primary treatment was identified from the Surveillance, Epidemiology and End Results Program (SEER)–Medicare database. Demographic and clinical variables were used to develop a propensity score of the probability of receiving NAC using a multivariate logistic regression model. Based on the propensity score of 13 covariates (age, stage, histology, grade, marital status, comorbidity, year of diagnosis, tumor size, and 5 demographic variables), we performed a 1:1 match of NAC and PDS patients. Kaplan-Meier analysis was performed to compare overall survival in the matched sample. Cox proportional hazards model was used to determine factors associated with survival.

Results: A total of 4,799 women met cohort criteria, including 1,038 treated with NAC (22%) and 3,761 (78%) with PDS. Adoption of NAC significantly increases over time, with a peak of 29% in 2010 ($P < .0001$). A total of 1,888 patients were matched for outcomes analysis. Overall survival of the matched cohort favored patients who underwent surgery ($P < .0001$). Analyzed by stage, median survival was shorter for patients with stage III disease who received NAC (30 vs 41 months, $P < .001$) and similar for patients with stage IV disease (30 vs 33 months, $P = .51$) regardless of treatment modality. Intensive care unit admissions did not differ 30 days after surgery between women who had NAC or PDS (2.4% vs 2.8%), but patients who underwent NAC had fewer emergency department visits (13% vs 22%, $P < .0001$) and hospitalizations (22% vs 27%, $P < .02$) within 30 days of surgery.

Conclusions: Careful consideration should be given to which elderly patients undergo PDS. For women with stage IV disease, survival outcomes are similar and fewer postoperative acute care services are associated with NAC. There may be a survival advantage for select individuals in a geriatric OC population with stage III disease who undergo primary debulking surgery, although residual confounders may exist despite matching.

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Evaluation of the impact of chronic steroid use on outcomes in gynecologic cancer patients: A NSQIP database analysis

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Objectives: To determine the effect of chronic steroid use on postoperative outcomes.

Methods: We evaluated the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for patients undergoing elective surgery for gynecologic cancers (ICD 9 codes 179–184). Patients were categorized as users of steroids according to NSQIP standards. Postoperative outcomes including venous thromboembolism (VTE), surgical site infection (SSI), pneumonia (PNA), urinary tract infection (UTI), sepsis, return to the operating room (ROR), and death were recorded. Postoperative outcomes were compared using the χ^2 test of independence. Adjustments were performed using the Mantel-Haenszel method. $P < .05$ was used as a threshold of significance.

Results: We identified 17,380 patients with complete data who underwent elective surgery for gynecologic malignancy. Before surgery, 369 patients (2.12%) used chronic steroids. The rate of postoperative complications for patients taking steroids was 325.2 per 1,000 surgeries, compared with 204.5 per 1,000 surgeries in patients not taking chronic steroids (RR 1.59, 95% CI 1.37–1.85). Chronic steroid users were more likely to have SSI (RR 1.56, 95% CI 1.09–2.23), UTI (RR 1.72, 95% CI 1.11–2.65), and sepsis (RR 2.80, 95% CI 1.81–4.35), but not PNA (RR 1.30, 95% CI 0.54–3.13). Patients using chronic steroids are also at risk for ROR (RR 2.71, 95% CI 1.77–4.17), but despite associations in other surgical specialties, VTE (RR 1.11, 95% CI 0.53–2.34) and death (RR 1.81, 95% CI 0.67–4.88) were not associated. After adjusting for primary site, the risk of sepsis remained significantly elevated, 2.7-fold more likely in steroid users than nonusers (RR 2.73, 95% CI 1.76–4.23).

Conclusions: Chronic steroid use before surgery is not a common risk factor among gynecologic cancer patients, but those taking steroids are at increased risk for infectious complications and ROR. Although some differences in risk can be explained by primary cancer site, the risk of sepsis among all patients is elevated. Surgeons should pay extra attention to the signs and symptoms of sepsis after surgery in patients taking chronic steroids.

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Immunohistochemical expression of estrogen and progesterone receptors and clinical outcomes among uterine and nonuterine leiomyosarcomas

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Objectives: Little is known about the molecular differences between uterine and nonuterine leiomyosarcomas (LMS). We conducted a clinicopathologic review including an assessment of the immunohistochemical (IHC) expression patterns of key biomarkers among patients with uterine and nonuterine LMS.

Methods: All cases of uterine and nonuterine LMS treated at our institution from January 2004 to August 2014 were identified. Formalin-fixed, paraffin-embedded tissues obtained from each tumor were reviewed and protein expression was performed using IHC.

Results: Sixty-three patients were identified (49 [77.8%] women, 14 [22.2%] men; 39 [61.9%] uterine LMS, 24 [38.1%] nonuterine LMS). There were 47 (74.6%) high-grade LMS and 16 (25.4%) low-grade LMS. Overall expression rates of estrogen receptor (ER) and progesterone receptor (PR) were 17% and 21%, respectively. Among male patients, the expression rate was 0% for ER and 21.4% for PR, and in female patients, the rates were 34.7% for ER and 36.7% for PR. Uterine LMS expressed ER, 30.8% (vs 20.8% in nonuterine LMS; OR 1.69, 95% CI 0.51–5.59, *P* = .391) and PR, 43.6% (vs 16.7%; OR 3.86, 95% CI 1.11–13.43, *P* = .034] compared with nonuterine LMS. Low-grade LMS were significantly more likely to express ER (50% vs 19.1%; OR 4.22, 95% CI 1.25–14.30, *P* = .021). PR expression was 43.8 in low-grade LMS compared with 29.8 in high-grade LMS (OR 1.83, 95% CI 0.57–5.90, *P* = .309). ER expression was not associated with improvement in progression-free survival (PFS) (HR 1.01, 95% CI 0.51–2.01, *P* = .974) or overall survival (OS) (HR 0.70, 95% CI 0.32–1.57, *P* = .392] on univariate analysis. PR expression was not significantly associated with PFS (HR 0.68, 95% CI 0.34–1.35, *P* = .264), but it was positively associated with OS (HR 0.33, 95% CI 0.13–0.85, *P* = .022). Using multivariate analysis, the cases were adjusted for stage, grade, and uterine versus nonuterine origin, and PR status remained positively associated with OS (HR 0.26, 95% CI 0.10–0.73, *P* = .010). On univariate analysis, Ki-67 was negatively associated with PFS (HR 2.02, 95% CI 1.05–3.9, *P* = .036) and OS (HR 1.96, 95% CI 0.95–4.07, *P* = .069). On multivariate analysis, p53, WT-1, and Ki67 were not significantly associated with PFS or OS.

Conclusions*:* ER staining was exclusive to female patients, and did not have significant influence on PFS or OS. PR expression was seen in both male and female patients, and overall was positively associated with OS. IHC expression of p53, WT-1, and Ki67 were not significantly associated with PFS or OS.

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What is the impact of a career in gynecologic oncology on personal life?

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Objectives: Training, academic responsibilities, and clinical practice in gynecology oncology are demanding. Our objective was to describe work-life balance issues for gynecologic oncologists (GO) in 2015.

Methods: We conducted a cross-sectional survey of physician members of the Society of Gynecologic Oncology. A survey originally sent to female GOs in 1998 was expanded, piloted in 10 volunteers, and administered in electronic format (DatStat Illume) in February 2015. Our revised instrument contained 75 fixed response questions regarding 4 domains: (1) demographics; (2) mentoring issues; (3) work-life balance; and (4) caregiving responsibilities. Data were analyzed using Stata 10 (Statacorp, College Station TX) with χ^2 analysis and the Fisher exact test using aggregate data functions.

Results: Of 1,246 GOs, 268 completed the survey. Of these, 172 (64%) were female and 96 (36%) were male; 69 (26%) were 30 to 40 years of age, 75 (28%) were 41 to 50 years of age, and 55 (21%) were older than 50 years. Two hundred thirty-five (88%) were married or living with a partner and 38 (14%) were divorced. One hundred forty-four (54%) were in academic practice and 56 (21%) were in fellowship. Seventy-four respondents (28%) had no children, 45 (17%) had 1 child, and 149 (56%) had 2 or more children. Of the 63 without children, 11 (18%) do not plan on becoming a parent in the future. Of these, 6

(55%) felt their career had a moderate or large impact on the decision to not become a parent. One hundred thirty-two (68%) respondents felt that their career somewhat or very much affected the timing of having children, and 64 (33%) felt that their career plans somewhat or very much affected their decision to become a parent. Of those who are parents, 140 (72%) thought residency or fellowship was the best time to become a parent. One hundred thirty-five (70%) reported that children decreased their academic productivity, and 40 (21%) felt that children decreased their clinical performance. Most relied on a spouse, relative, or nanny for childcare, and 55 (28%) bring their children to work occasionally or frequently. Among the female respondents, 33 (19%) had used assisted reproductive technology; of women without children, 20 (44%) would consider cryopreservation to delay childbearing. Forty-seven participants (18%) reported being the primary caregiver for an elder and 16 (34%) of those have taken family leave for this purpose.

Conclusions: Among GOs, career choices influence decision-making surrounding personal lives.

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Positron emission tomography–computed tomography in the preoperative assessment of vulvar cancer

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Objectives: To determine the utility of preoperative positron emission tomography–computed (PET-CT) in detecting groin and distant metastases in vulvar cancer patients.

Methods: A single institution retrospective chart review was conducted of all patients with vulvar cancer treated from 2000 to 2014. Patients with vulvar cancer who received a PET-CT during their initial assessment were included. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated based on PET-CT correlation with each groin surgically and pathologically evaluated.

Results: We identified 240 patients with vulvar cancer in our institution's tumor registry from 2000 to 2014, of which 179 had data available for analysis. Of these, 43 patients underwent PET-CT during their initial evaluation, 39 subsequently underwent surgery, and 56 inguinofemoral lymphadenectomies were performed. The mean age at diagnosis was 64.1 years (range, 22–90 years), and all patients had squamous cell carcinoma. The average standard uptake value (SUV) was 10.16 (range, 0–29.8) for the vulvar lesions and 5.8 (range, 1.9–19.1) for the groin lesions. Preoperative PET-CT had a sensitivity of 66.67% and specificity of 92.68% in detecting groin lymph node metastasis. The PPV and NPV were 76.9% and 88.3%, respectively. In the 5 patients who had a false-negative PET-CT, the mean size of lymph node metastasis was 4.4 mm (2–10 mm). Preoperative PET-CT identified distant metastases in 1 patient (2.3%), whereas distant disease was diagnosed in 2 patients (1.5%) after primary surgery.

Conclusions: Preoperative PET-CT does not appear to be reliable in predicting stage III vulvar cancer and may not be cost-effective in detecting the rare event of distant disease before surgery. Further studies are warranted to investigate the role of PET-CT in the preoperative management of vulvar cancer.

Table 1
Demographics.

		PET-CT (N=43)	No PET-CT (N=135)
Variable	**Level**	**Value [Mean (SD), N (%)]**	
Age at diagnosis		64.07 (22-90)	65.79 (35-94)
BMI		32.47 (10.3)	29.16 (6.11)
Smoking status	Never	23 (53.5%)	68 (44.4%)
	Current	12 (27.9%)	42 (27.5%)

		PET-CT (N=43)	No PET-CT (N=135)
Variable	**Level**	**Value [Mean (SD), N (%)]**	
	Past	8 (18.6%)	38 (24.8%)
	Unknown	0 (0%)	5 (3.3%)
Race/Ethnicity	Caucasian	41 (93.2%)	127 (85.2%)
	African American	1 (2.3%)	2 (1.3%)
	Hispanic	0 (0%)	0 (0%)
	Unknown	1 (2.3%)	16 (10.7%)
	Other	1 (2.3%)	4 (2.7%)
Stage	I	25 (58.1%)	113 (66.1%)
	II	2 (4.7%)	6 (3.5%)
	III	12 (27.9%)	41 (23.9%)
	IV	4 (9.3%)	11 (6.4%)
ASA score	1	1 (2.5%)	8 (6.2%)
	2	25 (62.5%)	86 (66.7%)
	3	13 (32.5%)	33 (25.6%)
	4	1 (2.5%)	2 (1.6%)
History of DM	No	31 (70.5%)	136 (88.9%)
	Yes	13 (29.5%)	17 (11.1%)
History of HTN	No	20 (45.5%)	73 (47.7%)
	Yes	24 (54.5%)	80 (52.3%)

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Ovarian cancer debulking by gynecologic oncologists alone versus multidisplinary surgical specialties: Is there a difference in outcomes?

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Objectives: To evaluate the surgical outcomes of ovarian cancer complex debulking surgeries (CDS) performed by gynecologic oncologists alone (GYNO) versus those performed by multidisciplinary surgical specialties (MSS) (gynecologic oncologists plus gastrointestinal, colorectal, urology, surgical oncology, or vascular).

Methods: We identified patients who underwent ovarian CDS in the National Surgical Quality Improvement Program database from 2006 to 2012 by GYNO versus MSS. CDS procedures were defined by having 2 concurrent CPT codes (gynecologic plus

associated abdominal pelvic code). We excluded patients who had CPT codes mutually exclusive to other surgical specialties (i.e., MSS CPT codes with no match to GYNO CPT codes). Procedures considered more complex included those with upper abdominal surgery (UPAB). Clinical and surgical outcomes were abstracted. *T* test, χ^2 test, Fisher exact test, and univariable and multivariable regression models were used.

Results: Of 2,601 ovarian cancer surgeries, 49.4% (n = 1,285) underwent CDS, 90% (1,166) by GYNO and 10% (119) by MSS. MSS cases had longer operative times (246 vs 195 minutes, $P < .001$), longer hospital stay (9 vs 6 days, $P < .001$), and more complications (18% vs 10%, $P = .04$). However, readmission (10% vs 9%) and 30-day mortality (1.7% vs 1.2%) were similar. After controlling for age, body mass index, preoperative disease status, and UPAB, the MSS group had longer operative times ($P < .001$) and longer hospital stays ($P < .001$). In adjusted models, complication rates did not differ between groups. In a subset analysis of patients who underwent UPAB, of which 80% (127/159) were by GYNO and 20% (32/159) by MSS, there were no differences in operative times (286 vs 258 minutes), complications (22%), hospital length of stay (12 vs 9 days), readmission rate (9.4% vs 12%), and 30-day mortality rate (3.1% vs 1.6%), ($P > .05$ for all).

Conclusions: Complex ovarian cancer debulking procedures done by GYNO had shorter operative times and hospital stays, and similar complication rates compared with those performed by MSS. Surgical outcomes seem to favor procedures performed by GYNO alone. Future studies should consider physician factors influencing optimal patient outcomes, and include multifaceted cost-benefit analyses.

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Strategic cotargeting in epithelial ovarian cancer: FOXM1

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Objectives: Despite the dynamic armamentarium of chemotherapies and biological agents available for epithelial ovarian cancer (EOC), the last 4 decades have witnessed only slight improvements in survival rates. The Cancer Genome Altas (TCGA) identified Foxhead box protein M1 (FOXM1) as a leading therapeutic target for high-grade serous ovarian cancer (HGSOC). The identification of synthetic interactions between therapeutic targets offers a novel approach to designing treatments that may be less susceptible to the evolution of resistance. The aim of this study was to use molecular profiles from TCGA to identify rational co-targets that could be used in combination with a FOXM1 inhibitor (thiostrepton) to increase antitumor activity. Targets identified in silico were then tested in vitro using biologically relevant models of EOC.

Methods: We interrogated TCGA data using 3 approaches to identify specific cotargets: (1) gene coexpression analyses that were both gene specific and pathway based using Ingenuity pathway analysis; (2) reverse phase protein array (RPPA) analysis; (3) mutual exclusivity analyses. Five EOC cell lines exhibiting high FOXM1 expression were used to evaluate the inhibition of FOXM1 in combination with the specified cotarget in 2D culture: A2780, CAOV3, OVCA429, Tyk-Nu, OVISE. Cell lines were plated onto 96-well plates and the small molecular inhibitors were added alone and in combination with thiostrepton. The colorimetric MTT assay was used to quantify the cytotoxicity of the combination regimens. Each experiment was repeated at least 3 times and the mean calculated to determine statistical significance.

Results: Table 1 outlines the results of the in silico analyses as well as the respective small molecular inhibitor. The combination of thiostrepton with dexrazoxane, olaparib, gefitinib and semagacestat potentiated the effect of a single inhibitor alone. Synergy between thiostrepton and olaparib was observed in 3 of the 5 cell lines.

Conclusions: Thiostrepton plus olaparib is a promising cotreatment strategy for EOC. Other promising cotargets were also identified and importantly, many of the drugs used in this study are already shown to be safe in humans, which means that these results could be rapidly translated into clinical practice.

Table 1

Candidate FOXM1 co-targets identified using TCGA data for HGSOC.

Co-Target	*In-silico* approach	Small molecular inhibitor
TOP2A	Gene Co-Expression: Gene Specific	Dexrazoxane
PARP	Gene Co-Expression: Pathway Based	Olaparib

EGFR	RPPA	Gefitinib
KRAS	Mutual Exclusivity	U0126
NOTCH3	Mutual Exclusivity	Semagacestat

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Intraperitoneal chemotherapy administered on an outpatient basis for optimally cytoreduced epithelial ovarian, primary peritoneal, and fallopian tube cancers

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Objectives: To examine the tolerability of outpatient administration of intraperitoneal (IP) chemotherapy for optimally cytoreduced epithelial ovarian (EOC), peritoneal (PC), and fallopian tube cancers (FTC), and to identify predictors of noncompletion.

Methods: Retrospective cohort study of patients with EOC, PC, and FTC who underwent optimal cytoreductive surgery, followed by a modified outpatient Gynecologic Oncology Group (GOG) 172 IP chemotherapy regimen at a single institution between 2006 and 2014.

Results: A total of 106 patients met the eligibility criteria and 98 were included in the final analysis. Mean age was 57.9 (± 10.05), body mass index was 27.3 (± 6.46) and CA-125 level at start of treatment was 570 (± 1,073.55). Overall, 72 patients (73%) completed the prescribed number of IP chemotherapy cycles. Eighty-three patients were prescribed 6 cycles and 59 (71%) completed them. Reasons for discontinuation included port complications (n = 12) and toxicities (n = 14). The most frequently reported toxicities were fatigue, gastrointestinal, and neuropathy. Severe toxicities occurred in 5.7% of patients on average per cycle, the most frequent being fatigue, neuropathy, and pain. As cumulative severe toxicities increased, there was a lower odds of starting the next cycle, but this was not significant (OR 0.832, *P* = .49). The probability of starting each cycle was lower if the patient had experienced severe toxicities in the prior cycle (OR 0.414, *P* = .044).

Conclusions: IP chemotherapy has been shown to improve overall and progression-free survival and yet is not universally prescribed. Outpatient administration of IP chemotherapy is feasible, with acceptable toxicities and high completion rates. Discontinuation of IP chemotherapy is most frequently secondary to port complications and grade 3 or higher toxicities.

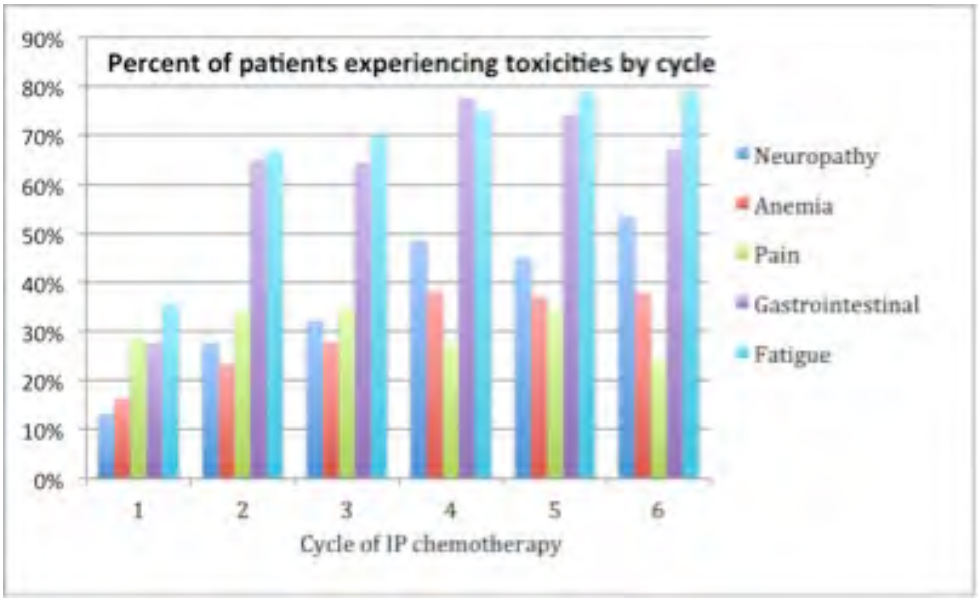

Fig. 1
Percent of Patients Experiencing Toxicities by Cycle

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Is there a role for weekly paclitaxel dosing regimen in patients with advanced epithelial ovarian cancer receiving neoadjuvant chemotherapy?

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Objectives: To examine the efficacy of weekly paclitaxel compared with the standard 3-weekly paclitaxel dosing regimen in patients with advanced ovarian cancer who underwent neoadjuvant chemotherapy followed by interval debulking surgery.

Methods: One hundred and twenty-eight patients were identified. Two cohorts were created: patients treated with paclitaxel (175 mg/m^2) and carboplatin every 3 weeks (n = 104), and patients treated with either 80 mg/m^2 or 60 mg/m^2 paclitaxel each week and carboplatin every 3 weeks (n = 24). Statistical analysis for categorical and continuous covariates was conducted using the X^2 and student *t* test, respectively, and regression models were used.

Results: No significant differences were seen in the clinical characteristics between the 2 cohorts. Kaplan-Meier curve for overall survival (OS) showed no difference between the weekly and every-3-week paclitaxel regimen groups (37 months vs 36.5 months, $P = .54$). There was a trend toward improved progression-free survival (PFS) in the weekly paclitaxel group compared with the every-3-week paclitaxel group (median not reached vs 18.4 months, $P = .09$). In multivariable analysis adjusting for age, race, histology, and extent of cytoreduction, weekly paclitaxel was associated with significant improvement in PFS (HR 0.34, 95% CI 0.12–0.96, $P = .04$) but not OS (HR 0.46, 95% CI 0.18–1.18, $P = .10$).

Conclusions: In this analysis, weekly paclitaxel dosing was associated with improved PFS compared with traditional dosing every 3 weeks, with no difference in OS in patients with advanced ovarian cancer receiving neoadjuvant chemotherapy, followed by interval debulking surgery. Future studies should be performed to further delineate the role of weekly paclitaxel in neoadjuvant chemotherapy.

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417 - Poster

Endometrial expression of hormonal and insulin/IGF receptors in relation to cancer risk factors

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Objectives: The aim was to investigate, in a prospective cohort of postmenopausal women, endometrial tissue expression of hormonal and insulin/insulin like growth factor (IGF) receptors in relation to cancer risk factors.

Methods: This institutional review board–approved prospective study enrolled 50 postmenopausal women undergoing hysterectomy. Clinical data were obtained using a study questionnaire. Immunohistochemical (IHC) staining was done on formalin-fixed paraffin-embedded endometrial tissue sections using primary antibodies specific for estrogen receptor alpha (ERα), progesterone receptor (PR), type 1 IGF receptor (IGF1R), insulin receptor (IR), and phosphorylated IR/IGF1R (p-IR/IGF1R). The study pathologist evaluated staining intensity and percentage of positive cells; receptor expression was categorized as positive or negative, as previously described. Statistical significance of receptor expression differences according to risk factor categories was evaluated with the Fisher exact test. $P < .05$ was considered significant; analyses were performed using R version 3.1.1.

Results: Patients completing the study questionnaire and from whom sufficient endometrial tissue was obtained were eligible for analysis (n = 29). The mean age was 60.9 years. The mean body mass index was 29.3 kg/m^2. The primary indications for hysterectomy were uterine prolapse or leiomyomata. Twenty-eight percent were diabetic. Diabetics were more likely to have positive endometrial glandular expression of p-IGF1R/IR ($P = .02$). Forty-eight percent reported NSAID use. Women reporting NSAID use were more likely to have positive PR expression in the endometrial stromal tissue ($P = .01$).

Conclusions: This is the first study to evaluate the relationship of hormonal and insulin/IGF receptor expression in normal postmenopausal endometrium, in relation to cancer risk factors. Our finding of increased insulin/IGF receptor activation in diabetics suggests that detectable signaling alterations in the endometrium may precede neoplastic transformation in these at-risk women. NSAID usage has been linked to decreased endometrial cancer risk in epidemiologic studies. The increased PR expression observed in the endometrial stromal tissue of NSAID users may be associated with a novel mechanism of cancer

protection. In summary, clinical cancer risk factors are associated with altered receptor expression in nonmalignant endometrium, and should be further investigated as biomarkers in cancer risk assessment and prevention studies.

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Highlighting the need for intervention: Long-term evaluation of change in BMI in endometrial cancer survivors

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Objectives: To evaluate change in body mass index (BMI) over time in long-term endometrial cancer survivors in the absence of a formal weight loss intervention program and to describe the relationship between BMI change and patient characteristics.

Methods: A retrospective cohort analysis was conducted of endometrial cancer patients in our institutional database who underwent surgery as the primary treatment for endometrial cancer from 2000 to 2009 with approximate 5-year follow-up. Weight and BMI values at the time of surgery were compared to values 5 years later. Patients who underwent weight loss surgery were excluded. Longitudinal analysis was performed using generalized estimating equations (GEE) to model BMI over time as a function of clinicopathological variables.

Results: We identified 437 endometrial cancer survivors with data after 42 to 78 months of follow-up. At the time of diagnosis, 18% of patients were of normal weight based on BMI, 20% were overweight, and 62% were obese (BMI of ≥30). More than a quarter of patients (26%) were class III obese, with a BMI of 40 or greater. Overall mean BMI for this cohort was 34. Mean BMI was comparable for patients with type I and II disease, with BMIs of 35 and 31, respectively. Although 44% of all patients had an increase in BMI over time, there was no overall change in mean BMI from time of initial encounter to long-term follow-up ($P = .53$). An increase in BMI was significantly associated with presence of hypertension ($P < .001$) or diabetes ($P < .001$). A decrease in BMI was significantly associated with older age ($P < .001$) and performance of lymphadenectomy ($P < .001$). Histologic type and stage were not associated with change in BMI over time.

Conclusions: In a large single institution cohort of endometrial cancer survivors, nearly half the patients gained weight over the follow-up period, whereas mean BMI from time of diagnosis to long-term follow-up was unchanged. Given the large percentage of patients with elevated BMI at diagnosis and the lack of useful disease-related characteristics to predict weight gain, this study confirms the need for weight loss intervention in the entire endometrial cancer survivor population. The presence of hypertension and diabetes was significantly associated with BMI increase over time, and may represent a group of patients to more aggressively target for weight loss intervention.

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419 - Poster

Surviving vulvar cancer, does obesity matter?

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Objectives: To determine the relationship between obesity and progression-free survival (PFS) and overall survival (OS) in vulvar cancer patients.

Methods: A single-institution retrospective chart review was conducted of patients with vulvar cancer treated from 2000 to 2014. Demographic, clinical, pathologic, recurrence, and survival data were collected. Patients were identified as obese based on body mass index (BMI) of 30 or higher. Univariate and multivariable Cox proportional hazards models were used to determine the association of age at diagnosis, obesity, smoking, diabetes mellitus (DM), hypertension (HTN), stage, grade, and tumor size with PFS and OS.

Results: A total of 240 patients with vulvar cancer were identified in our institution's tumor registry from 2000 to 2014, of whom 169 had data available for analysis. Significantly more obese patients had a history of DM and HTN compared with nonobese patients, but no differences in age, smoking status, stage, grade, and tumor size were noted between the 2

groups. The mean number of lymph nodes removed per inguinofemoral lymphadenectomy was not significantly different between the 2 groups (obese vs nonobese: right—7.22 [standard deviation, SD, 3.92] vs 8.16 (SD 9.19), *P* = .194; left—7.6 (SD 3.53) vs 8.22 (SD 3.76), *P* = .367). Median time to recurrence was 5.4 years (95% CI 4–10.2 years) and median time to death was 11.2 years (95% CI 8.3–NR) for the entire cohort. Age, DM, and stage were significantly associated with PFS on univariate and multivariable analyses. Obesity, smoking, HTN, grade, and tumor size were not associated. OS was significantly associated with age, DM, stage, grade, and tumor size on univariate analysis, but only age remained significantly associated with OS on multivariable analysis.

Conclusions: Obesity was not associated with PFS and OS in vulvar cancer patients. However, DM, a common comorbidity of obesity, was significantly associated with worse PFS.

Table 1
Clinical and pathologic characteristics of obese v. non-obese patients with vulvar cancer.

Variable	Level	Non-Obese (BMI<30) N=96	Obese (BMI≥30) N=73	P-value*
Age (years)		66.39 (16.42)	65.26 (12.82)	0.618
Smoking	Current	26 (27.1%)	21 (28.8%)	0.991
	Past	23 (24%)	18 (24.7%)	
	Never	44 (45.8%)	32 (43.8%)	
	Unknown	3 (3.1%)	2 (2.7%)	
History of DM	Yes	5 (5.2%)	19 (26%)	<0.001*
History of HTN	Yes	44 (45.8%)	48 (65.8%)	0.010*
Tumor size (cm)		3.19 (2.38)	3.59 (2.81)	0.355
Stage	I	69 (71.9%)	44 (60.3%)	0.106
	II	4 (4.2%)	4 (5.5%)	
	III	15 (15.6%)	22 (30.1%)	
	IV	8 (8.3%)	3 (4.1%)	
Grade	1	51 (53.1%)	33 (45.2%)	0.708
	2	26 (27.1%)	21 (28.8%)	
	3	8 (8.3%)	9 (12.3%)	
	Unknown	11 (11.5%)	10 (13.7%)	
Median time to recurrence (years)		5.5 (4.1-11.2)	4.2 (2.7-NR)	
Median time to death (years)		11.2 (7.5-NR)	11.3 (6.2-NR)	

Displaying Mean (SD) for continuous variables and p-value via Student's t-test.
Displaying N (%) for categorical variables and p-value via chi-square test.

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Risk of venous thromboembolism following major laparoscopic surgery for gynecologic malignancy

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Objectives: To determine the incidence of venous thromboembolism (VTE) after laparoscopic surgery for uterine, cervical, and ovarian cancers from a national surgical registry.

Methods: Patients who underwent at least 1 major laparoscopic surgery for uterine, ovarian, and cervical cancers were identified from the American College of Surgeons National Surgical Quality Improvement Program database from 2005 to 2011. VTE was defined as deep venous thrombosis (DVT) requiring therapy and pulmonary embolism (PE) within 30 days of surgery. Statistical analysis for categorical and continuous covariates were assessed using the χ^2 and Student *t* test, respectively, and regression models were used to identify risk factors for VTE.

Results: Of the 2,219 patients included in the final analysis, 15 patients (0.7%) were diagnosed with VTE. Six patients (0.3%) were diagnosed before discharge, and 9 patients (0.4%) were diagnosed after discharge. The median time from surgery to diagnosis was 6 days (range, 0–28 days). For patients who had a diagnosis of VTE within 30 days, the 30-day mortality was significantly higher than in those who did not have VTE (7.0% vs 0.3%, $P < .001$). No difference was noted based on the site of cancer ($P = .95$). There was no difference in VTE rate when stratified by age ($P = .10$), body mass index (BMI; $P = .68$), diabetes ($P = .22$), smoking ($P = .60$), respiratory morbidities ($P = .55$), cardiac disease ($P = .22$), hypertension ($P = .13$), preoperative blood transfusion ($P = .90$), or American Society of Anesthesiology class ($P = .10$). There was a trend toward higher risk of VTE among patients with disseminated cancer compared with those with early cancers ($P = .05$). No difference was found in the risk of VTE based on operative time ($P = .96$). No difference was noted in the risk of VTE among those who underwent lymphadenectomy compared with those who did not ($P = .35$). Using multivariable logistic regression analysis, after adjusting for age ($P = .12$), BMI ($P = .90$), operative time ($P = .71$), and lymphadenectomy status ($P = .30$), none of these variables was significantly associated with risk of VTE. In multivariable analysis, after adjusting for other confounders, VTE within 30 days was a significant predictor of higher 30-day morality (OR 24.7, 95% 1.0–345.2, $P = .022$).

Conclusions: The VTE rate is low after major laparoscopic surgery for gynecologic cancers but is associated with increased 30-day mortality. Higher rate was noted in those with disseminated cancer who might benefit from VTE prophylaxis.

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421 - Poster

Recurrent ovarian cancer: Can second clinical remission surpass the first?

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Objectives: Most patients with ovarian cancer will have a recurrence, and the second remission is traditionally shorter than the first. Among patients who achieve second remission, we sought to evaluate those with a progression-free survival (PFS2) greater than their first remission (PFS1), and identify associated clinical factors.

Methods: With institutional review board approval, all patients with recurrent platinum-sensitive epithelial ovarian cancer who underwent secondary cytoreductive surgery (SCS) from May 2001 to June 2014 were identified. Patient and tumor characteristics, operative findings, PFS, and overall survival (OS) were documented. The incidence of PFS2 > PFS1 was identified, and statistical analysis performed to identify associated clinical factors for this cohort.

Results: Among 214 SCS cases, 52 (24%) had a second remission longer than the first remission. Of these 52 patients, 20 (38%) subsequently sustained disease progression, 10 of whom died of disease. The remaining 32 (62%) were without disease recurrence at a median follow-up of 62.8 months (range, 19.1–147.9). When comparing PFS2 > PFS1 patients with the PFS1 > PFS2 patients, age, performance status, stage, grade, histologic subtype, and number of sites of recurrent tumor were similar between the 2 groups. The outcome of primary debulking surgery (PDS) to residual disease of less than 0.5 cm was 78% for prolonged PFS2 patients compared with 69.4% for PFS1 > PFS2 patients ($P = .034$). Method of recurrent disease detection for prolonged PFS2 patients compared with PFS1 > PFS2 patients was CA-125 level (30.8% vs 49.4%, respectively), imaging (59.6% vs 35.8%), and physical examination/symptoms (9.2% vs 14.8%) ($P = .012$). Among patients in both groups, 86% achieved CGR at SCS. There was no difference in type of chemotherapy used for recurrence; however, more than 70% of all patients received a platinum doublet.

Conclusions: Among patients who underwent SCS, 24% achieved a second remission greater than their first. Although many clinical and tumor characteristics are similar between the 2 groups, prolonged PFS2 patients had a higher rate of optimal PDS to less than 0.5 cm, and had tumor recurrence identified by serologic or radiographic markers. Recognition and characterization of prolonged PFS2 patients is pertinent for clinical trial design, and for effective treatment selection among patients with recurrent disease.

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Comprehensive genomic profiling of ovarian clear cell carcinomas identifies clinically relevant genomic alterations and targeted therapy options

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Objectives: Loss of the SWI/SNF chromatin remodeling gene, *ARID1A*, and frequent PI3K pathway activation has been previously observed in ovarian clear cell carcinomas (OCCCs). Recently, co-occurrence of these 2 mutations was shown to promote tumorigenesis in an OCCC mouse model and tumor growth halted by a pan-PI3K inhibitor. We present the comprehensive genomic profiling (CGP) of 125 advanced/recurrent stage OCCCs to highlight co-occurring clinically relevant genomic alterations (CRGAs) to predict subsets of patients who may similarly benefit from targeted therapies.

Methods: DNA was extracted from 125 formalin-fixed, paraffin-embedded OCCC clinical specimens. Hybridization captured libraries of 236 (n = 73) or 315 (n = 52) genes, plus select introns frequently rearranged in cancer were sequenced to high (avg 609X), uniform coverage (FoundationOne). All classes of genomic alterations (GAs; base subs, small in/dels, rearrangements, and copy number alterations) were evaluated and reported. Microsatellite instability (MSI) was additionally assessed. CRGAs were defined as GAs associated with on-label targeted therapies and targeted therapies in mechanism-driven clinical trials.

Results: A total of 125 OCCCs, 44% from primary site tissue and 55% from metastatic sites, were included. The patients were women aged 30 to 76 years (median, 53 years) with predominantly advanced-stage OCCC. One hundred and twelve cases (89.6%) had at least 1 CRGA (mean 2.2 CRGA/tumor). The most common CRGAs observed were: *PIK3CA* (52.8%), *ARID1A* (51.2%), TP53 (21.6%), ZNF217 amp (17.6%), *ERBB2 (12.8%), CCNE1 (7.2%), CRKL* (4.8%). In the 52% of cases with ARID1A loss, *PIK3CA* activating GA co-occurred in more than half (56%) and *TP53* LOF in 20%. *AKT* amplification, previously reported to correlate with shorter survival, was identified in 12 OCCCs (10%). *BRCA1/2* alteration rates were low (2.4%). In contrast to previously published studies, this cohort of OCCC had lower rates of focal *MET* amplification (1.6%), *PTEN* loss (5.6%), and MSI-H status (4%). OCCC cases with *ERBB2* and *PIK3CA* mutations responding to anti-HER2 or *PI3K/AKT/mTOR* targeted therapies are presented.

Conclusions: More than three quarters of OCCCs demonstrate CRGA, most commonly in the *PI3K/Akt/mTOR* pathway, but also in *ERBB2, CCNE1,* and *CRKL.* Further investigation of the combined effect of co-occurring alterations in *SWI/SNF* components and *PI3K/Akt/mTOR* or other targetable pathways on clinical response to therapies is warranted.

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Electronic patient-reported outcomes from home in patients recovering from major gynecologic cancer surgery: A prospective study measuring symptoms and health-related quality of life

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Objectives: A pilot study suggested that the use of a web-based system to capture patient-reported outcomes (PROs) is feasible and highly accepted by patients in the acute postoperative period. The objective of this study was to further demonstrate its feasibility, measure patient assessments of its usefulness, and clinician perceptions of its value.

Methods: This is a prospective cohort study of patients scheduled for laparotomy for presumed gynecologic malignancy. Patients completed a web-based Symptom Tracking and Reporting ("STAR") questionnaire preoperatively and weekly during a 6-week postoperative period. The survey consisted of the patient adaptation of the National Cancer Institute's CTCAE 3.0 and EORTC QLQ-C30 3.0. Email alerts were sent to clinicians when concerning patient responses were entered. The patient and the clinician assessments of STAR's usefulness were measured via an exit survey.

Results: The study enrolled 120 patients. Of these, 69 patients (57.5%) completed at least 4 of 7 total sessions. The CTC generated 84 alerts, which resulted in 28 contacts and 2 ED referrals. One hundred and twelve patient-reported symptoms generated an alert; the most common were poor performance status (15%), nausea (14%), and fatigue (12%). Fifty-one patients (42.5%) completed the exit satisfaction survey; 86% found STAR easy to use and 73% found it useful; 63% reported that STAR improved the ability to remember symptoms at office visits; 57% reported improved discussions with the provider; 43% reported overall improved quality of care; 63% felt more in control of their care by using the STAR system; and 71% would recommend it to other patients and 61% would like to continue use. Most clinicians did not find STAR helpful. Seventy-five percent did not find the self-assessments of pain and quality of life accurate. All clinicians surveyed reported that the STAR system increased their workload.

Conclusions: Application of an electronic program for PROs in those recovering from major gynecologic cancer surgery is feasible and acceptable for most patients with a computer and home internet access. Poor performance status, nausea, and fatigue were the most common distressing symptoms reported. The majority of patients reported a positive experience with the system and would recommend its use. The program helped many to feel more empowered in their postoperative recovery. Clinicians reported a less positive experience, possibly associated with the increased work.

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424 - Poster

Postmenopausal endometrial cancer patients have significantly higher expression of GLUT6 in the endometrium

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Objectives: Risk factors for the development of endometrial carcinoma include unopposed estrogen, anovulation and absence of progesterone, obesity, and diabetes. Case control data reveal blood glucose, but not sex hormones or lipids, to be significantly elevated in obese endometrial cancer patients. Published data examining obesity-related endometrial cancer reveal genes related to glucose metabolism to be among the most altered, with GLUT6 to be the most overexpressed among the glucose transporter genes. We wish to further our understanding of the relationship between glucose and sex hormones in endometrial cancer proliferation in both lean and obese women with uterine cancer.

Methods: Retrospective chart review identified lean (body mass index [BMI] <25 kg/m^2) and obese (BMI >30 kg/m^2) patients who had undergone hysterectomy for endometrial carcinoma. A tissue microarray (TMA) was created with both tumors and normal adjacent endometrium from cancer patients as well as uterine specimens from age- and weight-matched controls with benign indications for hysterectomy. Immunohistochemical staining for GLUT6, phosphorylated AKT (PAKT; a marker of PI3K pathway activation), estrogen receptor (ER), progesterone receptor (PR), and metabolic regulator LKB1, in endometrial glands was scored by a gynecologic pathologist in a blinded fashion. Fisher exact test was used to compare groups.

Results: GLUT6 was expressed at a significantly higher frequency in postmenopausal endometrial tumor than benign control endometrium (30 of 47 vs 6 of 25 patients, $P = .003$), but not in premenopausal cancer patients (5 of 15 tumors vs 3 of 10 benign, $P = 1$). Additionally, the frequency of tumoral GLUT6 expression was significantly higher than normal adjacent endometrium in obese, postmenopausal women (23 of 33 vs 14 of 33, $P = .046$). GLUT6 expression did not differ between lean postmenopausal and obese premenopausal women. ER, PR, P-AKT, and LKB1 were expressed at high frequencies in benign and malignant endometrium and expression was not significantly altered by menopausal status or obesity.

Conclusions: Significantly increased expression of GLUT6 in the endometrium of obese postmenopausal endometrial cancer patients suggests a role for GLUT6 in endometrial cancer growth. Further characterization of the role of GLUT6 in endometrial cancer is warranted, perhaps allowing for the development of therapeutic strategies targeting glucose metabolism.

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Comprehensive genomic profiling of ovarian carcinomas identifies both ERBB2 amplifications and activating point mutations as biomarkers for anti-HER2 targeted therapy

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Objectives: Clinical trials of anti-HER2 therapies in ovarian cancer (OC) have not demonstrated sufficient gains in clinical outcomes in unselected or single biomarker-evaluated cohorts to achieve drug registration. Herein, all classes of *ERBB2* genomic alterations (GAs) and co-occurring clinically relevant GAs (CRGAs) are assessed using comprehensive genomic profiling (CGP) in a large cohort of serous and nonserous OCs to identify a subset of patients who might benefit from anti-HER2 targeted therapy.

Methods: DNA was extracted from 2,045 formalin-fixed paraffin-embedded OC clinical specimens. Hybridization captured libraries of up to 315 genes, plus select introns frequently rearranged in cancer were sequenced to high (avg 588X), uniform coverage (FoundationOne). All classes of GA (base subs, small in/dels, rearrangements, and copy number alterations) were evaluated and reported. CRGAs were defined as GA associated with on-label targeted therapies and targeted therapies in mechanism-driven clinical trials.

Results: Eighty-one (3.9%) of 2,045 predominantly advanced-stage OC clinical samples from women (median age, 58 years) demonstrated an *ERBB2* alteration. Prevalence of *ERBB2* alteration correlated with mucinous (25.6%; $P < .0001$) and clear cell (13.6%; $P < .0001$) OC subtypes compared with endometrioid (5.8%; $P = .46$), serous (2.8%; $P = .09$), or mixed/NOS (2.4%; $P = .13$) OCs. *ERBB2*amp (range, 6 to >50 copies) was present in 62 OCs (77%), activating base subs in 18 OCs (26%), and both in 3 OCs (4%). Nonamplifications (*ERBB2*mut) were primarily in the TK domain (50%) and extracellular domain (32%), with rare transmembrane domain (9%) and splice site (9%) mutations. The most common co-occurring GAs observed were *TP53* (75%), *PIK3CA* (27%), *CCNE1* (19%), ARID1A (17%), *CDKN2A* (10%), and *MYC* (9%). *CCNE1* amp was only seen to co-occur with *ERBB2*amp, whereas *FBXW7, GNAS,* and *MSH6* GAs were much more common (10%–15%) in *ERBB2*mut cases. Clinical responses to anti-HER2 therapy in patients with different *ERBB2*amp levels and co-occurring GA, including one near-complete response to trastuzumab in a patient with high level *ERBB2*amp, will be presented

Conclusions: More than one-fourth of *ERBB2* GAs are caused by sequence changes rather than amplification, are detectable on CGP and potentially targetable, but are missed on immunohistochemistry or fluorescence in situ hybridization. Given the clinical benefit of anti-HER2 targeted therapy demonstrated in this study, further investigation of the potential impact of *ERBB2* GA class, amp level, and co-occurring GA on OC response to anti-HER2 therapy is warranted.

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426 - Poster

Ovarian granulosa cell tumors: The role of GATA4 in predicting tumor behavior

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Objectives: Granulosa cell tumors (GCTs) of the ovary are rare. Late recurrences are characteristic, with 10% to 30% of stage I GCTs recurring, many more than 5 years after the original diagnosis. There is a subset of GCTs with more aggressive behavior. Given their unpredictable clinical course, there is interest in identifying prognostic biomarkers to optimize appropriate adjuvant therapy. Recent evidence has identified immunohistochemistry (IHC) for the transcription factor GATA4 as a potentially useful predictor of recurrence; however, this has not been validated. This study sought to correlate GATA4 positivity with clinical outcomes.

Methods: All patients with GCTs treated at a tertiary care hospital from 1980 to 2012 who had adequate tumor samples banked were eligible for inclusion. A representative whole histologic section of tumor was immunostained for GATA4 (Santa Cruz Biotechnology); recut H&E slides were reviewed. Two pathologists reviewed all H&E and IHC slides. GATA4 staining was

graded based on extent (percentage positive nuclei, focal: 0%–33%, moderate: 33%–66%, diffuse: >66%) and intensity (strength of nuclear staining, 0 = none, 1+ = weak, 2+ = moderate, 3+ =strong). Clinical follow-up was obtained.

Results: We identified 33 patients for the study, with an average age of 49 years (range, 13–77 years). Tumors ranged in size from less than 1 cm to 35 cm. Follow-up was available for 28 cases with an average length of 77 months (range, 5–330 months). Of these, 18% experienced a recurrence, with an average time to recurrence of 50 months, (range, 11– 90 months). Half the recurrences were in patients with greater than stage I disease. GATA4 immunostaining was diffuse in the majority (94 %), with only 6% showing a moderate extent of staining and no cases showing only focal positivity. Staining intensity ranged from weak in 6 % (2) to moderate in 58% (19) and strong in 36% (12). Of the 6 recurrences, 1 had strong and diffuse GATA4 positivity. The odds ratio of strong and diffuse GATA4 positivity and recurrence was nonsignificant at 0.29, (95% CI 0.03–2.8).

Conclusions: GATA4 did not show discriminatory value in this series because of its widespread positivity in almost all tumors, irrespective of clinical outcome. However, given the high frequency of GATA4 in these tumors, this marker may have diagnostic usefulness in cases when the differential diagnosis includes other entities. Evaluation of various gynecologic tumor types may therefore be of interest.

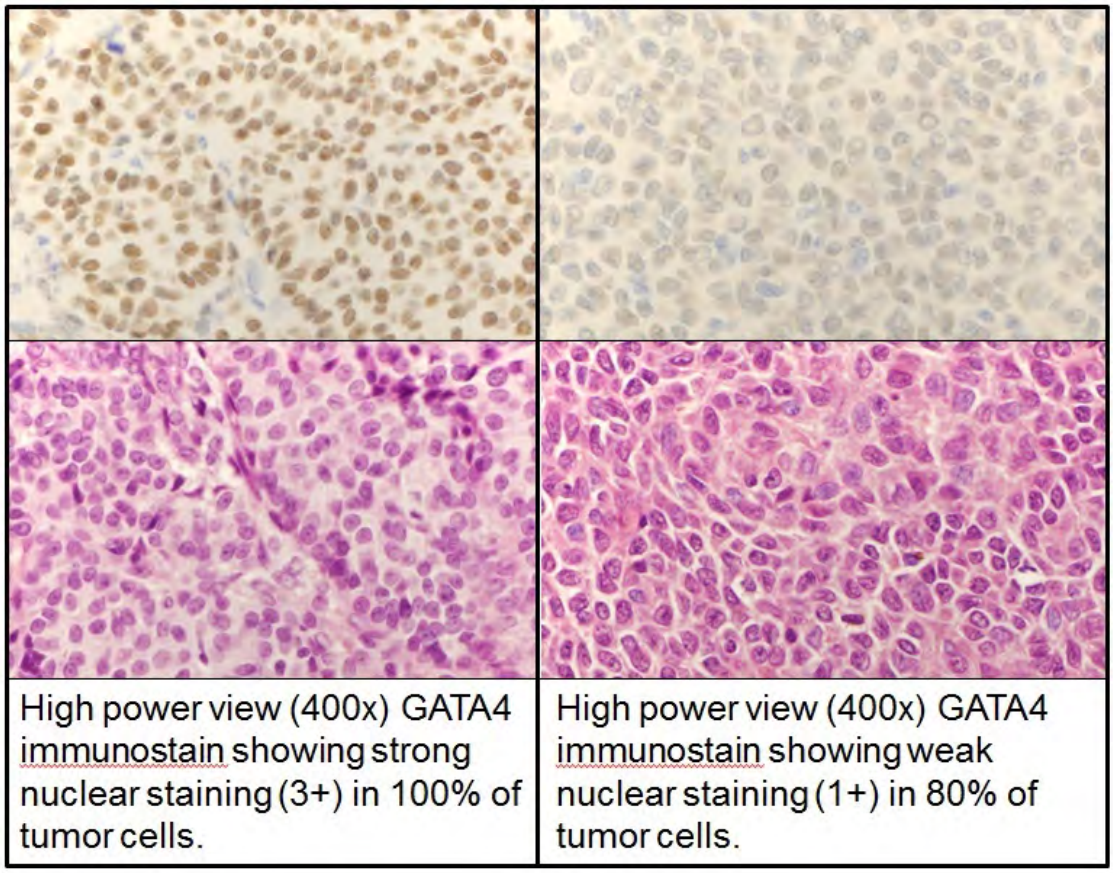

Fig. 1

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Combination of a patient symptom index and MIA2G, a second-generation multivariate biomarker test, for the preoperative prediction of ovarian cancer in patients presenting with pelvic masses

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Objectives: To determine whether the combination of a symptom index (SI) and biomarker panel can improve the identification of ovarian cancer in women presenting for surgery with a pelvic mass.

Methods: This was a prospective study of patients seen at a tertiary care center. Following consent, patients completed an SI and preoperative serum specimens were collected for individual serum markers (CA-125), a US Food and Drug Administration–cleared multivariate biomarker test (MIA), and its validated second-generation test (MIA2G). Results for the symptom index, CA-125, and MIA2G were correlated with operative findings and surgical pathology. Logistic regression modeling was performed to assess the combined contribution of the SI with MIA2G to determine the risk of malignancy (ROM).

Results: For the 218 patients enrolled, the mean age was 53.6 years (range, 18–86 years). One-hundred and forty-seven patients (67.4%) were postmenopausal. Of these, 124 patients (56.9%) had benign disease and 94 (43.1%) had borderline tumors or carcinoma. Sixty-four patients (29.4%) had epithelial ovarian cancer or fallopian tube cancer (EOC/FTC), two (0.9%) had nonepithelial ovarian cancer, 17 (7.8%) had borderline ovarian tumors, and 11 (5.0%) had metastases to the ovaries. The SI and MIA2G correctly identified 98.5% of patients with EOC/FTC. Using logistic regression, we found that both SI and MIA2G score were significantly associated with ROM. In a multivariate model, SI stratification strongly affected ROM based on the MIA2G score, such that patients with a negative SI and a MIA2G score of 3 had a ROM of 4%, whereas patients with the same MIA2G and positive SI had a 20% ROM, a 5-fold higher risk (Table 1).

Conclusions: The combination of a patient-reported SI and biomarker panel allows for improved accuracy in the assessment for ovarian cancer when patients present for operative management of a pelvic mass. This strategy could offer a personalized approach to addressing ROM in patients presenting for surgery with a pelvic mass to triage patients to appropriate care.

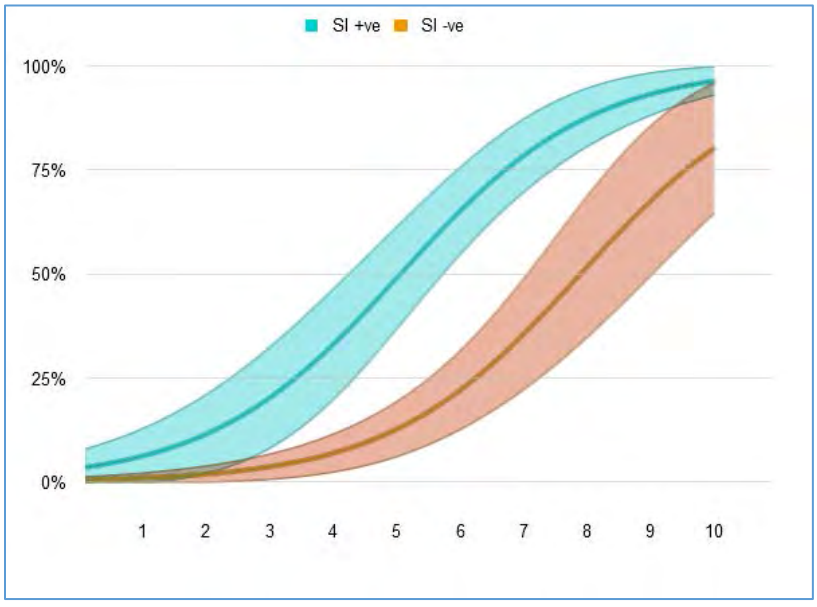

Fig. 1
ROM by MIA2G Score.

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Exploring further the poor outcomes of elderly patients with platinum-sensitive recurrent ovarian cancer using a contemporary application of the SOCRATES study

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Objectives: Older patients with epithelial ovarian cancer have been shown to have a poorer prognosis than younger patients; the SOCRATES study found that older patients (≥70 years) with primary platinum-sensitive ovarian cancer (PPSOC) received less treatment and had poorer treatment responses and overall survival (OS). This study aimed to characterize contemporary patterns of care and prognosis in elderly patients with PPSOC.

Methods: Patients receiving care at an academic practice with a diagnosis of PPSOC (>6 months platinum-free interval) between January 2000 and July 2013 were included. Demographic and clinical data were retrospectively collected from the electronic medical record. Descriptive statistics and univariate and multivariate analyses were performed using SAS version 9.3.

Results: Of the 249 patients who met inclusion criteria, 29% were 70 years of age or older. Both age groups had similar baseline characteristics, including stage, histology, primary treatment modality, residual disease, and type of primary chemotherapy (see Table 1); however, performance status (PS) was better in younger patients ($P = .02$). At recurrence, patients were similar with regard to secondary debulking surgery, receipt of second-line chemotherapy, and choice of second-line agent, but older patients more frequently had recurrence-free intervals (RFI) of 12 months or longer ($P = .01$) and showed a trend toward worse PS ($P = .08$). Older patients received fewer lines of chemotherapy (median 2 vs 4, $P < .01$) and had shorter OS from first recurrence (17.9 vs 25.9 months, $P = .05$). On multivariate analysis, older age at recurrence (HR = 1.82, $P = .02$), RFI less than 12 months (HR 1.77, $P = .02$), secondary debulking (HR 0.24, $P = .04$), and PS of 2 or greater (HR 14.17, $P < .01$) were independently associated with OS.

Conclusions: In our population, patients aged 70 years or older received similar primary treatments, including surgery and chemotherapy; however, patients aged 70 years or older had longer median RFI. Despite improved RFI, which has been shown to predict better responses to chemotherapy, and OS, patients 70 years or older with recurrent disease received fewer lines of chemotherapy and had shorter OS. In contrast to SOCRATES, our patients aged 70 years or older received similar treatments to patients younger than 70 years in the primary setting with better RFI, but patients 70 years or older still received less chemotherapy with recurrence and had shorter OS. Best practices in treatment of PPSOC in older patients require additional study.

Table 1
Patient Characteristics.

	Age at recurrence < 70	**Age at recurrence ≥ 70**	**P-value**
Number of patients	176(70.97%)	72(29.03%)	
FIGO stage at diagnosis			P = 0.13
I	8(4.60%)	0(0.00%)	
II	6(3.45%)	6(8.45%)	
III	125(71.84%)	58(81.69%)	
IV	35(20.11%)	7(9.86%)	
Histology			P = 0.20
HGSC	137(77.84%)	62(84.93%)	
LGSC	12(6.82%)	2(2.74%)	
CCC	6(3.41%)	1(1.37%)	
Endometrioid	13(7.39%)	4(5.48%)	
Mucinous	3(1.70%)	1(1.37%)	
Mixed	1(0.57%)	1(1.37%)	
Undifferentiated	3(1.70%)	2(2.74%)	
Unknown	1(0.57%)	0(0.00%)	
Primary Treatment			P = 0.78
Primary Chemo	5(2.84%)	1(1.37%)	
NACT/Surgery	19(10.80%)	8(10.96%)	
Surgery/Chemo	152(86.36%)	63(87.67%)	
None/Hospice	0(0.00%)	0(0.00%)	

Residual Disease			P = 0.29
Suboptimal	22(14.47%)	13(20.31%)	
Optimal, NOS	21(13.82%)	6(9.38%)	
Optimal, < 1 cm	55(36.18%)	13(20.31%)	
Optimal, NGRD	54(35.53%)	32(50.00%)	
Unknown	0(0.00%)	0(0.00%)	
Type of First Line Chemo			P = 0.50
Single agent platinum	1(0.57%)	1(1.37%)	
Platinum/taxane doublet	171(97.16%)	70(95.89%)	
Other platinum doublet	4(2.27%)	2(2.74%)	
Non-platinum-based cytotoxic	0(0.00%)	0(0.00%)	
Performance Status at diagnosis			P = 0.02
0	163(92.61%)	64(87.67%)	
1	3(1.70%)	7(9.59%)	
2	0(0.00%)	0(0.00%)	
3	1(0.57%)	0(0.00%)	
4	0(0.00%)	0(0.00%)	
Unknown	9(5.11%)	2(2.74%)	
Age at recurrence (years)			P = NA
Mean +/- S.D.	58.36 ± 8.15	76.73 ± 5.57	
Median	59.51	75.52	
Range	24.75 – 69.97	70.01 – 96.86	

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Survival disadvantage associated with delayed surgical treatment of endometrial cancers

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Objectives: To identify contributing factors and quantify survival disadvantage associated with delay in surgical treatment for endometrial cancers.

Methods: The National Cancer Data Base, capturing approximately 80% of cancers, was queried for endometrial cancers between 2003 and 2012. Cancers were grouped into type 1 (grade 1/2 endometrioid histology) and type 2 (nonendometrioid and grade 3 endometrioid) and analyzed separately. Patients receiving preoperative chemotherapy, radiation, or hormonal therapies were excluded. Demographic, clinicopathologic, and process factors (eg, hospital location and volume) were collected. Based on prior studies, delay was defined as surgery more than 12 weeks from diagnosis. Logistic regression was used for correlates of surgical delay; survival analyses were performed.

Results: A total of 88,256 type 1 and 40,009 type 2 cancers met inclusion criteria. For both types, 5% of cases were complicated by surgical delay of more than 12 weeks from diagnosis. Age, black race, Hispanic ethnicity, no/Medicaid insurance, stage 2/3 disease, comorbidity, low case volume at treating hospital, and eventual lymphadenectomy were significantly associated with delayed surgery for both type 1 and type 2 cancers. Surgical delay was associated with a significant survival disadvantage at 5 years for type 1 (86.6% vs 77.9%; $P < .001$) and type 2 (67.9 vs 60.5%; $P < .001$) cancers.

Conclusions: One in 20 patients with endometrial cancer experience a delay in surgical treatment that substantially decreases their likelihood of surviving 5 years postoperatively. Alongside patient- and disease-intrinsic factors, surgical delay likely reflects disparities in access to subspecialty care. There is a critical need to decrease the prevalence and effects of such disparities.

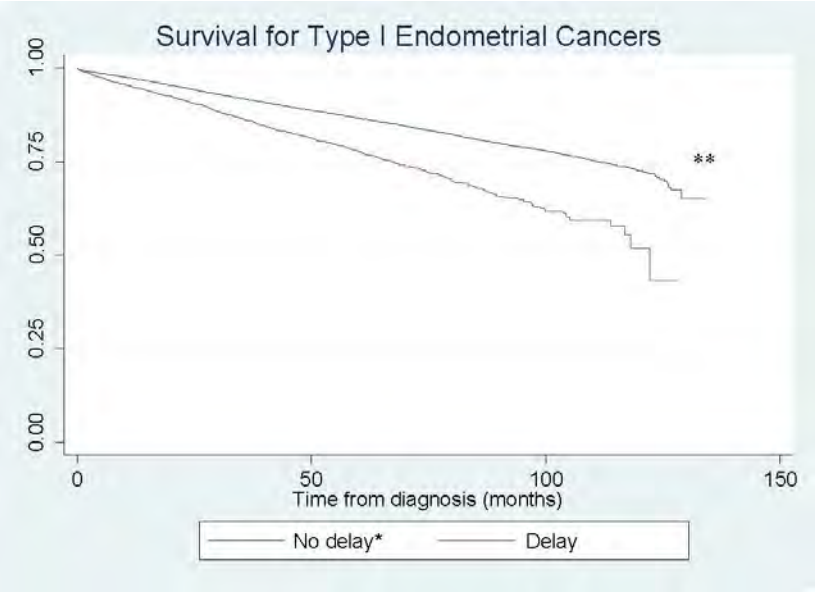
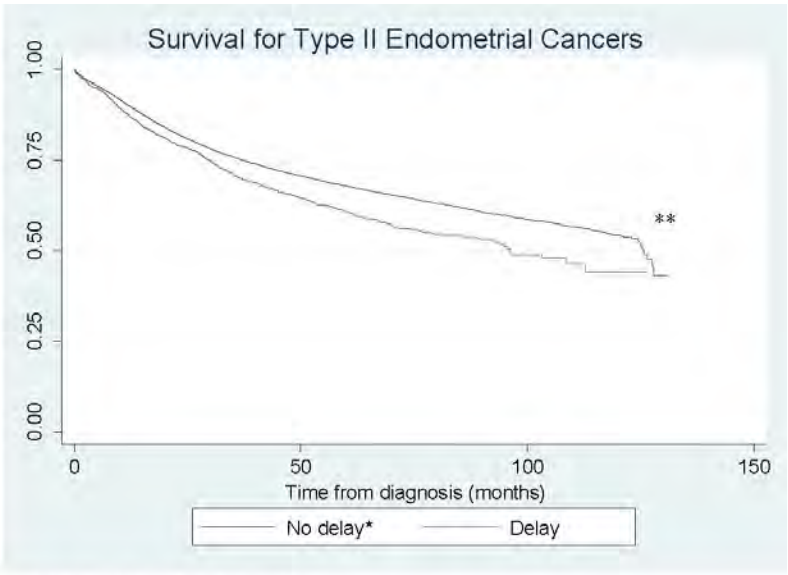


Fig. 1
Survival for Type 1 Endometrial Cancers.



*Delay defined as >12 weeks from diagnosis to surgery
** p<0.001

Fig. 2
Survival for Type II Endometrial Cancers.

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Factors associated with successful outpatient laparoscopic hysterectomy for women with endometrial cancer

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Objectives: Minimally invasive surgery is the preferred surgical method to treat women with endometrial cancer. Several single-institution reports have described the feasibility and safety of outpatient laparoscopic hysterectomies (LH) for both benign and malignant indications. The objective of this study is to identify patient and surgical factors associated with outpatient laparoscopic hysterectomies (OLH) and to compare outcomes between OLH and inpatient laparoscopic hysterectomies (ILH) in women with endometrial cancer.

Methods: Data were obtained from the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) database. All patients who underwent hysterectomies for endometrial cancer from 2007 to 2013 were identified by ICD-9 and CPT codes. These patients were then filtered for LH. Comparative analyses were performed and stratified by admission status to evaluate demographics, preoperative and intraoperative variables, and surgical outcomes. Statistical tests were performed with R Studio version 0.99.442.

Results: LH rates have been steadily increasing (see Table). Between 2010 and 2013, 5,851 patients underwent LH for endometrial cancer; of these, 3,428 (58.6%) were ILH and 2,423 (41.4%) were OLH. OLH rates increased each year from 30.0% in 2010 to 50.0% in 2013. OLH patients were on average 61.81 years old compared with 63.03 years for ILH patients ($P < .001$). Medical comorbidities were not different between the 2 groups. Total operating time and anesthesia time were both significantly shorter in the OLH group: average times were 161.3 and 187.0 minutes ($P < .001$) and 245.2 versus 256.3 minutes ($P = .002$), respectively. More lymph node dissections were performed in the ILH group than the OLH group: 2,074 (60.5%) versus 1,390 (57.4%, $P = .016$). There were more radical hysterectomies in the ILH group (n = 803; 23.4%) compared with the OLH group (n = 315; 13.1%) ($P < .001$). OLHs were assigned fewer relative value units than ILHs (mean 28.5 vs 30.6, respectively, $P < .001$). Postoperative complications were not different between the groups.

Conclusions: Younger age, fewer RVUs, shorter operating and anesthesia times were associated with successful OLH in patients with endometrial cancer. Lymph node dissection and radical surgery were associated with an increased rate of ILH. There were no differences in postoperative complications between OLH and ILH.

Table 1

Types of Hysterectomy by Year (%).

Type of hysterectomy	2007	2008	2009	2010	2011	2012	2013
Open	79 (79%)	230 (72.8%)	451 (79.1%)	445 (54.4%)	746 (38.8%)	889 (32.3%)	1143 (30.4%)
Laparoscopic	19 (19%)	83 (26.3%)	105 (18.4%)	341 (41.7%)	1139 (59.2%)	1822 (66.2%)	2550 (67.8%)
Vaginal	2 (2%)	3 (0.9%)	14 (2.5%)	32 (3.9%)	40 (2.1%)	41 (1.5%)	69 (1.8%)

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Chemotherapy use is a significant predictor for sexual dysfunction in women with gynecologic cancer

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Objectives: Sexual dysfunction is a significant survivorship issue in women with gynecologic cancer. Multiple modalities are used to treat these diseases but may have a detrimental affect on sexual function. We examined the association between chemotherapy and impaired sexual functioning.

Methods: A multi-institutional study of women with gynecologic cancer was conducted with a 181-item survey of validated instruments. A subanalysis of women with chemotherapy treatment was performed to examine factors associated with sexual function including age, menopause status, body mass index (BMI), diagnosis, stage, surgery/radiation use, active disease

status, number of regimens, and number of cycles. Sexual dysfunction was measured by change in the Female Sexual Function Index (FSFI) score from pretreatment values, with a significant decline in sexual function determined to be a 5.6-point decrease using a Reliable Change Index Statistic (RCIS). Standard statistical tools were used.

Results: A total of 107 (63%) of the women in the larger study had received chemotherapy as part of their treatment and were included in the substudy. Women undergoing chemotherapy were more likely to experience sexual dysfunction after treatment (51% vs 26%; OR 2.9, 95% CI 1.5–5.7). In bivariate analyses, sexual dysfunction after chemotherapy was associated with age less than 50 years (80% vs 42%; OR 5.6, 95% CI 1.9–16.6), premenopausal (30.8% vs 12.7%, OR 3.1, 95% CI 1.1–8.2) cervical cancer (25.5% vs 10.0%, OR 3.1, 95% CI 1.0–9.4), and low (I/II) stage (51.1% vs 24.5%; OR 3.2, 95% CI 1.4–7.7). Chemotherapy agent, number of regimens or cycles, radiation therapy, disease status, and BMI were not predictors of sexual dysfunction in women with chemotherapy.

Conclusions: Women treated with chemotherapy for gynecologic cancer are at a significant risk of impaired sexual function. Specifically, women with cervical cancer, early-stage disease, those who are premenopausal, and those younger than age 50 years are at highest risk. Providers should be aware of the potential impact of treatment methodologies on sexual function.

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A novel virotherapy-based immunotherapy approach to ovarian cancer using an IL-12–expressing oncolytic herpes simplex virus

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Objectives: Immunotherapy represents a promising approach to the treatment of ovarian cancer. We evaluated the antitumor activity of a conditionally replicative, oncolytic herpes simplex virus (oHSV) armed with murine cytokine, IL-12, and the ability of oHSV to elicit enhanced tumor-specific immune responses in ovarian cancer.

Methods: We evaluated the in vitro cytotoxicity, defined as the number of plaque-forming units required to kill 50% of the cells (PFU/TD50), of oHSV toward several ovarian cancer cell lines, including syngeneic transplantable murine and paired human chemosensitive (CS) and chemoresistant (CR) lines. We also evaluated the immune response and antitumor response in Fox Chase TgMISIIR-Tag mice after intraperitoneal injection with oHSV. Specifically, immune response was assessed in various abdominal organs by quantifying CD8-specific T cells to the NIH tetramers, SV40 antigen and mesothelin. Antitumor response was assessed by measuring total tumor burden in oHSV-treated mice versus control mice.

Results: The paired human CS & CR cell lines, syngeneic transplantable murine, and MISIIR cancer cells harvested and grown in tissue culture all demonstrated susceptibility to oHSV in vitro (see Table 1). Compared with controls, mice injected with oHSV demonstrated a more robust CD8-specific immune response to both SV40 antigen and mesothelin in all evaluated tissues. The mean difference in the number of SV40 antigen CD8-specific T cells was most pronounced in the omentum (471.6.cells oHSV vs 33.1 cells controls; $P = .02$) and the mean difference in mesothelin CD8-specific T cells was most pronounced in the peritoneal cavity (962.3 cells oHSV vs 179.5 cells control; $P = .05$). In the tumor burden experiment, 2 of 11 mice injected with oHSV died of disease compared with 9 of the 11 control mice. Five of 11 mice injected with oHSV showed no evidence of metastatic tumor when killed at 6 months.

Conclusions: oHSV demonstrated effective antitumor activity in vitro in several ovarian cancer cell lines. A vigorous intraperitoneal CD8-specific immune response was also demonstrated in mice injected with oHSV. Lastly, oHSV was well tolerated in MISIIR mice, and led to decreased rates of intraperitoneal metastasis and ultimately less deaths. Further development of this oHSV is warranted.

Table 1
4 and 8-hour susceptibilities to oHSV across all cell lines.

Cell Lines	4hr PFU/TD50 (SD)	8hr PFU/TD50 (SD)
Human Chemo-sensitive		
SKOV3ip1	11.5 (15.0)	8.4 (8.2)
HeyA8	15.2 (6.1)	26.5 (15)
A2780ip2	5.5 (4.5)	8.9 (6.2)
Human Chemo-resistant		
SKOV3TR	5.3 (2.5)	4.6 (1.5)
HeyA8MDR	12.2 (10.4)	7.7 (7.0)
A2780cp20	0.8 (0.5)	0.9 (0.6)
Murine Control		
M0505	0.6 (0.6)	0.6 (0.6)
Syngeneic Transplantable Murine		
STOSE	0.3 (0.28)	0.3 (0.28)
ID8	2.4 (3.0)	1.4 (1.6)
1g10	0.6 (0.6)	0.6 (0.6)
Transgenic Spontaneous Murine		
MISIIR	10.9 (3.1)	15.8 (4.9)

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Demographics, tumor characteristics, and survival differ between females and males with leiomyosarcoma

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Objectives: Leiomyosarcomas (LMS) are a rare and heterogeneous malignancy. Recently, positive randomized clinical trials have identified active agents in recurrent LMS. Herein, we identify gender differences in patients diagnosed with LMS.

Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried for demographic information, tumor history, and survival data points for patients with LMS from 2004 to 2012. χ^2 and analysis of variance tests were used for univariate analyses.

Results: A total of 5,190 women and 2,570 men with LMS were identified. The median age of diagnosis for men and women were 64 and 57, respectively ($P \leq .001$). For patients with reported stage, women were most commonly diagnosed at stage IV (30.4%), then stage III (28.7%), stage I (22.4%), and stage II (18.5%), whereas men were most frequently diagnosed at stage I (27.9%), then stage IV (27.3%), stage III (24.2%), and stage II (20.6%) ($P = .0014$). The most common primary sites for women were reproductive organs, soft tissue (defined as the heart, connective tissue, and fibrous tissue), and retroperitoneum. The most common primary sites in men were soft tissue, extremities, and retroperitoneum ($P \leq .0001$). Women most commonly had tumors between 5.1 and 10 cm, whereas men most commonly had tumors less than 5 cm. Men had an overall increased 5-year survival compared with women (71.7% vs 51.2%; $P \leq .001$). Men diagnosed with stage I disease had a higher 5-year survival compared with women (91.9% vs 80.4%; $P = .005$). When stratified by primary site, compared with women, men had higher 5-year survival with LMS of reproductive organs (76.7% vs 45.6%; $P \leq .001$) and soft tissue (71.5% vs 58.9%; $P \leq .001$). Women had higher 5-year survival with LMS of the thoracic cavity (45.7% vs 31.2%; $P = .005$). When stratified by tumor size at diagnosis, men had increased 5-year survival for tumors of 5 cm or smaller (89.8% vs 75.0%; $P \leq .001$).

Conclusions: Women with LMS were younger, had larger tumors, more advanced stages, and shorter 5-year survival than men. Gender differences in the randomized trials of pazopanib, trabectedin, and eribulin should be discussed in the context of these findings.

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Correlates and implications of failure to receive surgical treatment for epithelial ovarian cancer

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Objectives: To identify the prevalence, characteristics, and outcomes of patients who do not receive surgical treatment for epithelial ovarian cancer (EOC).

Methods: The National Cancer Data Base, capturing approximately 80% of incident cancers, was queried for cases of EOC between 1998 and 2012. Receipt of surgical treatment, reasons for failure to receive treatment, and survival data, along with clinicopathologic and process-based factors (e.g., treating hospital location and volume) were collected. Logistic regression and Cox proportional hazards models were used for analysis.

Results: A total of 140,030 cases met inclusion criteria, and 6,723 (4.8%) of patients did not undergo surgery. Of these, 4,075 (60.6%) received radiation, hormone therapy, or chemotherapy. The remainder received no treatment. Only 13.5% of cases without surgery were explicitly attributed to patient comorbidity, death, or refusal. Higher stage, older age, no/Medicare/Medicaid insurance, increased comorbidity, and low hospital volume were all significantly associated with decreased likelihood of undergoing surgery. No association was found between patient race or geographic region and lack of surgical treatment. After controlling for clinical, demographic, and process-based variables, receipt of surgical treatment conferred a significant survival advantage. Median survival for patients receiving surgical treatment was 61 months; median survival for all other patients was 7 months ($P < .001$).

Conclusions: One in 20 EOC patients failed to receive surgical treatment for reasons potentially unrelated to significant comorbidity, patient refusal, or death. These patients are at a significant survival disadvantage. This deviation from the standard of care may reflect a disparity in access to gynecologic oncology subspecialists. There is a critical need to decrease the prevalence and effects of such disparities.

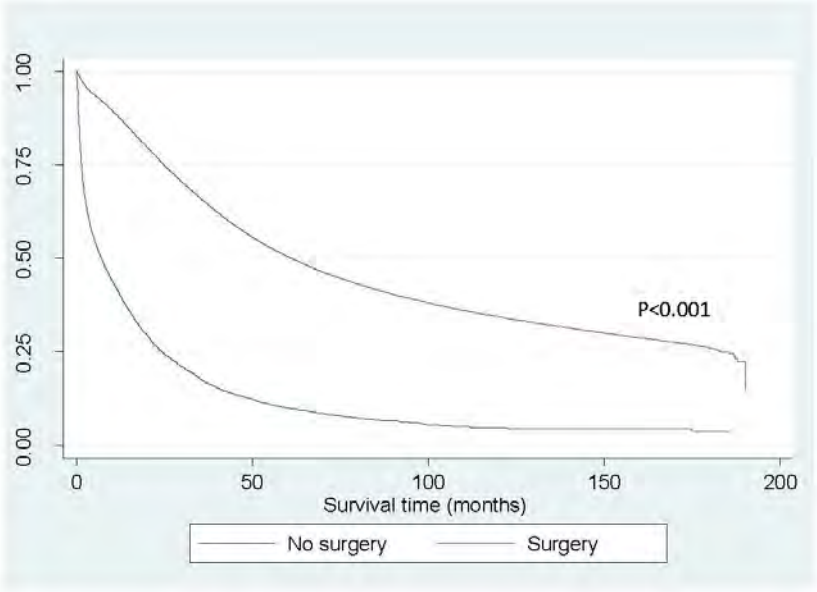

Fig. 1
Epitheial Ovarian Cancer Survival.

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Personalized surgical therapy for advanced ovarian cancer: R0 resection after neoadjuvant chemotherapy is associated with decreased event-free survival compared with primary cytoreductive surgery

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Objectives: To determine differences in survival among patients who undergo complete gross resection (R0) after primary cytoreductive surgery (PDS) compared with interval cytoreductive surgery (IDS).

Methods: Standard practice at our institution is to have all patients with advanced ovarian cancer (OC) undergo a triage algorithm to determine those who should receive PDS versus neoadjuvant chemotherapy (NACT) followed by IDS. Using a previously described algorithm, preoperatively defined parameters are analyzed using laparoscopy (LS) to determine who should be offered PDS. Patient outcomes were tracked prospectively. The Fisher exact test and Wilcoxon rank sum test were used to compare medians among patients with PDS versus IDS. Event-free survival (EFS) was defined as months from the date of diagnosis to the date of first recurrence, progressive disease, or death. Prognostic factors associated with EFS were evaluated with Cox proportional hazards regression.

Results: Between April 2013 and September 2015, 206 patients with suspected advanced OC presented to our center. Of these, 119 were offered LS; 88% had serous histology; 132 (64%) patients had stage III disease; and 74 (36%) had stage IV disease, with more patients in the NACT group having stage IV disease (10% vs 51%, $P < .001$). Rates of R0 resection were similar between the PDS and IDS groups (87% [n = 65] vs 83% [n = 85], $P = .521$). Compared with patients who underwent PDS, those who had IDS had higher pretreatment CA-125 levels (675 vs 247, $P < .001$) and platelet counts (379 vs 303 × 10^9/L, $P < .001$). EFS was longer in the PDS group (20.8 months) compared with the IDS group (13.8 months, $P = .002$). Factors associated with decreased EFS on multivariate analysis include Charlson Comorbidity Index >3 (HR 2.20, 95% CI 1.30–3.72, $P = .003$), pretreatment CA-125 higher than 73 (HR 3.02, 95% CI 1.16–7.85, $P = .032$), pretreatment platelet counts greater than 306 × 10^9/L (HR 1.70, 95% CI 1.02–2.82, $P = .041$), and administration of NACT (HR 1.84, 95% CI 1.11–3.04, $P = .019$). Stage as a surrogate marker for tumor burden was not associated with EFS.

Conclusions: Despite high rates of R0 cytoreduction at the time of IDS, patients undergoing NACT have decreased EFS than those undergoing PDS. Predicting those patients likely to achieve R0 resection in the upfront setting is important for maximizing patient outcomes.

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Venous thromboembolism after minimally invasive surgery for gynecologic malignancy: A NSQIP database analysis

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Objectives: To determine the overall incidence of venous thromboembolism (VTE) in patients undergoing minimally invasive surgery (MIS) for cervical and endometrial cancer

Methods: We inspected the National Surgical Quality Improvement Program (NSQIP) participant use files from 2007 to 2013 for subjects undergoing minimally invasive surgery (CPT codes 58500–58599) for endometrial and cervical cancers (ICD-9 codes 179, 180, 182). The primary outcome measured was diagnosis of VTE within 30 days of surgery. Features available in the database consistent with the American College of Obstetricians and Gynecologists (ACOG) recommendations for 30-day postsurgical thromboprophylaxis were evaluated and included active cancer diagnosis and body mass index (BMI) greater than or equal to 30 kg/m^2. The American Society of Clinical Oncology (ASCO) recommendations for 30-day postsurgical thromboprophylaxis were also evaluated, and included active cancer diagnosis and age greater than 60 years. Variables were compared using a χ^2 test with a nominal value of $P < .05$ as a test for significance.

Results: We identified 6,918 subjects who underwent MIS for gynecologic malignancy. Of these, 91% had endometrial cancer and 9% had cervical cancer. We identified 50 VTEs within 30 days of surgery, for a rate of 0.72%. The rate of VTE in was 0.24% normal-weight subjects and 0.97% in in obese subjects. The rate of VTE was 0.28% in subjects younger than 60 years and 1.04% in those aged 60 years and older. We analyzed high-risk features available in the dataset as recommended by ASCO and the relative risk of VTE increased 4-fold (RR 4.04, 95% CI 1.25–12.97). We analyzed high-risk features available in the

dataset as recommended by ACOG and the relative risk increased by more than 3-fold (RR 3.71, 95% CI 1.7–7.9). We combined ACOG and ASCO high-risk features available in the dataset and the relative risk increased 3-fold (RR 3.6, 95% CI 2.01–6.46).

Conclusions: The overall incidence of VTE within 30 days of minimally invasive surgery for endometrial and cervical cancer is low. The existing 30-day risk prediction models proposed by ACOG and ASCO are able to predict a statistically significant increased risk of VTE in patients undergoing minimally invasive surgery for cervical and endometrial cancer in this large national dataset.

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Has robotic hysterectomy increased the need for gynecologic oncologists?

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Objectives: Using a robotic platform for a hysterectomy is thought to increase access to minimally invasive surgery for patients because of its intuitive motion and improved optics. Although a greater percentage of patients are receiving robotic surgery, many of these patients are being referred to gynecologic oncologists. We sought to identify the characteristics and number of patients operated on by gynecologic oncologists for benign indications.

Methods: Patients who underwent a robotic hysterectomy at a large academic institution between January 2010 and April 2015 were identified. Data collected included demographic information, hysterectomy indication, complications, and surgical findings. The Student *t* test and Fisher exact test were used to compare patient characteristics.

Results: During the study period, 468 hysterectomies were identified, 363 (77.7%) were for benign indications. Gynecologists performed 287 (79%) of these benign hysterectomies. Medical comorbidities identified in this population included obesity (43.5%), hypertension (32.5%), diabetes (13.4%), and previous abdominal surgery (20.8%). Patients referred to gynecologic oncologists for benign indications were more likely to have prior abdominal surgery (26 vs 62, P = .04), uteri larger than 500 g (40 vs 110 g, P = .03), and body mass index greater than 30 (33 vs 86, P = .04). In the benign surgeon cohort, gynecologic oncologists were called for an intraoperative consultation in 33 cases (11.5%). The most common reasons for intraoperative consultations were adhesive disease (45.7%) and large uteri (21.9%). Interestingly, gynecologic oncologists were more likely to convert to an open procedure (11 vs 14, P = .01).

Conclusions: In a large academic setting, gynecologic oncologists perform 45.7% of all hysterectomies, including 30% of all benign hysterectomies. This trend will likely tax the limited resources of gynecologic oncologists. Additional fellowship training spots will be necessary to meet this demand.

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Correlation of endometrial biopsy and hysterectomy gene expression profiles in patients with endometrial cancer

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Objectives: The typical route to diagnosis for endometrial cancer (EC) is endometrial biopsy, which can yield prognostic information such as tumor grade and histology. The gene expression profile (GEP) of endometrial biopsy specimens may provide additional prognostic information, but its correlation with surgical staging and patient outcomes has yet to be explored. A molecular test that could be performed on preoperative endometrial biopsy specimens and identify patients who would benefit from or could be spared lymphadenectomy, would greatly affect surgical management decision-making and possibly reduce surgical morbidity. Thus, our goals were to (1) determine the correlation between GEPs of biopsy and hysterectomy specimens, (2) examine the relationship between GEPs of ECs and body mass index (BMI), and (3) correlate the GEPs of ECs with clinical factors.

Methods: Subjects were recruited from the Gynecology Oncology Clinic at University of North Carolina. Endometrial biopsy and hysterectomy specimens were examined by a pathologist to confirm cancer diagnosis. RNA was extracted from the specimens and analyzed using Agilent arrays. Clinical data were abstracted from the medical record. Statistical analysis was performed with the bioconductor package *LIMMA* in *R*.

Results: Tissue samples adequate for GEP were available in 108 subjects. Of these, 77% had tumors of endometrioid histology and 22% had serous tumors. Median age was 63 years (range, 29–89 years). Most were Caucasian (77%). Median BMI was 33.7 (range, 17.9–60). The majority had stage 1 disease (75%); grade was evenly distributed (34% grade 1, 33% grade 2, 31% grade 3). Most had endometrioid tumors (77%) and underwent lymphadenectomy (85%); a minority had positive lymph nodes (14%). Fifteen paired specimens were tested for correlation between biopsy and hysterectomy data; mean correlation coefficient was 0.85. In the endometrioid tumors, cyclin D1 expression was negatively associated with BMI. The GEPs of ECs were associated with histology (endometrioid vs serous) and stage (early vs late), but not with grade, progression-free survival, or overall survival.

Conclusions: The GEP of an endometrial biopsy correlates to the GEP of the hysterectomy specimen. The GEPs of ECs were associated with histology and stage but not grade or survival. This lack of association is likely because of the small sample size; however, recruitment remains ongoing.

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Are ovarian cancer debulking models reliable: Variance and predictability are dependent on institutional optimal debulking rates

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Objectives: We sought to evaluate the performance of ovarian cancer debulking models when applied to variable institutional optimal debulking rates (ODR), and the stability of positive predictive value (PPV) and negative predictive value (NPV) for each model. We hypothesized that the predictability of each model may differ based on institutional ODR which varied from 20% to 80%.

Methods: We performed a PubMed search to identify all published ovarian cancer prediction models for optimal debulking. ODR, sensitivity, specificity, PPV, and NPV of each model were extracted. Assuming fixed sensitivity and specificity, we calculated the PPV and NPV for each individual model while iteratively applying various published debulking rates using the following definitions: (1) PPV = (Sensitivity × ODR) / [(Sensitivity × ODR) + ({1 – Specificity} × {1 – ODR})] and (2) NPV = [Specificity × (1 – ODR)] / [(1 – Sensitivity) × ODR) + (Specificity × {1 – ODR})].

Results: Ten prediction models met study criteria. The median number of patients included in these models was 77 (range, 28–195). The median ODR was 63% (range, 36%–92%). Upon iteratively applying various ODRs to each model, we found that the PPV of these models significantly increased ($P < .001$) with increasing ODR, whereas the NPV decreased significantly ($P < .001$) (Figures 1 and 2). This was seen across all models, in which PPV increased and NPV decreased with higher ODR. Furthermore, the variance in predictability of PPV and NPV improved (decreased) when higher baseline ODRs were applied ($P = .037$) (Figures 1 and 2).

Conclusions: Ovarian cancer prediction models for optimal debulking are inherently dependent on baseline ODRs from which the models are developed. We demonstrated that when higher ODRs are applied, the PPV and NPV for each model is increased and decreased, respectively, with significant decrease in intermodel variation, no matter which model we tested, suggesting a lower impact of model differences. Although we seek to identify preoperative assessment tools to aid in ovarian cancer treatment decisions, we must consider that the applicability of a prediction model for optimal ovarian cancer debulking is dependent on the ODR from which it was derived and the debulking rate at the institution to which it is applied.

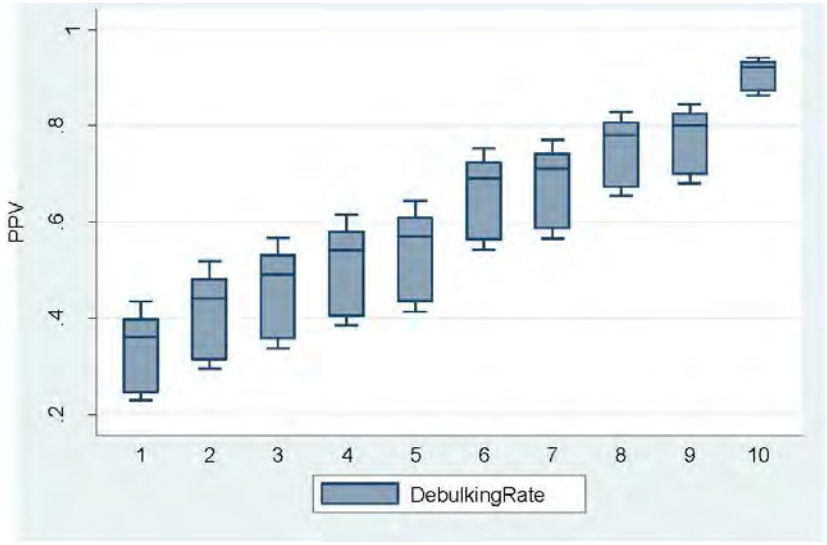

Fig. 1
Positive Predictive Value.

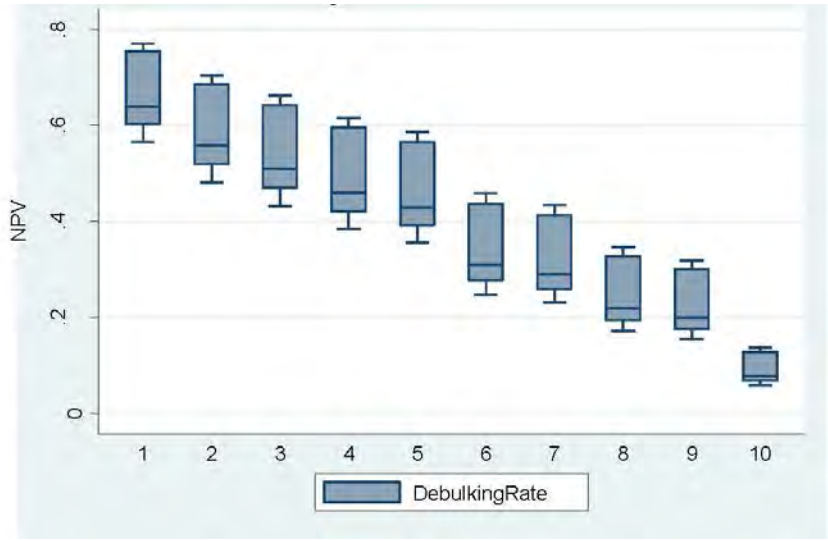

Fig. 2.
Negative Predictive Value.

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Outcomes among women diagnosed with cervical cancer at the time of hysterectomy

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Objectives: To describe the outcomes among women diagnosed with cervical cancer at the time of hysterectomy for a diagnosis other than invasive cervical cancer.

Methods: We conducted a retrospective cohort study of patients treated for cervical cancer at 2 academic urban hospitals between 1999 and 2013. Patients whose initial pathological diagnosis of cervical cancer was based on a hysterectomy specimen were identified. Demographic, pathologic, and treatment variables were abstracted from the medical record. Outcomes of interest included disease status at last follow-up, receipt of additional surgery, and adjuvant radiotherapy.

Results: We identified 1,119 women who received treatment for cervical cancer, among whom 57 (5%) were diagnosed after incidental hysterectomy. Indications for hysterectomy included cervical dysplasia (42%), concern for other gynecologic malignancy (39%), and benign gynecologic disease or vaginal bleeding (16%). Of patients diagnosed at the time of hysterectomy, 36% had microscopic disease, 36% had gross disease confined to the cervix and smaller than 4 cm, 22% had locally advanced disease with tumors greater than 4 cm, and 5% had distant metastases. Forty-two patients (74%) received additional treatment after hysterectomy, including 8 (14%) who had additional surgery only, 30 (52%) who underwent radiotherapy only, and 4 (7%) who received additional surgery and radiotherapy. At last follow-up, 44 patients (77%) were alive and free of disease, 4 patients (7%) were living with disease, and 8 patients (14%) were deceased. Patients who underwent incidental hysterectomy were more likely to undergo adjuvant radiation therapy than patients who had hysterectomy after the diagnosis of invasive cancer (52% vs 17%, $P < .001$). A multivariable Cox proportional model incorporating stage demonstrated that survival estimates of this population were not different from those of the entire cohort who underwent primary surgery (HR 1.01, 95% CI 0.51–2.0).

Conclusions: Overall survival was not statistically different for women who underwent incidental hysterectomy, though a greater proportion of these women underwent adjuvant radiotherapy compared with the remainder of the cohort that underwent primary surgery.

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Endometrial carcinoma as the presenting malignancy in an 18-year-old patient with Li-Fraumeni syndrome

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Objectives: We describe a patient with a germline *TP53* mutation who presented with an endometrial adenocarcinoma as a teenager and who was also found to have a colonic carcinoma. We will review the clinical history, the surgical pathology findings, and the molecular analyses undertaken to identify her mutation.

Methods: The patient presented with stage IV disease and underwent tumor debulking followed by chemotherapy. Her initial pathology showed high-grade endometrioid adenocarcinoma with retained mismatch repair protein expression and strongly positive p53 expression. DNA from the tumor was assessed for somatic mutations in a panel of 409 cancer-related genes by next-generation sequencing technology, using DNA isolated from a benign lymph node as the germline reference. A colonoscopy, done as part of her workup, revealed a carcinoma that was also removed and evaluated.

Results: A single nucleotide substitution in the *TP53* gene, encoding an R273H missense mutation, was identified in the endometrial adenocarcinoma as well as the patient's germline DNA. The frequencies of the *TP53* R273H mutation in DNA sequencing reads obtained from germline DNA and tumor DNA were compatible with a heterozygous germline mutation that had undergone loss of heterozygosity in the tumor. Four novel somatic mutations were also identified in the uterine tumor in *PTEN*, *TSC2, ITGB2,* and *TAF1L,* the latter 3 variants at lower allele frequencies. The patient's colonic tumor showed strong positivity for p53, as did the endometrial carcinoma. A detailed family history did not suggest a familial syndrome, but rather a de novo mutation.

Conclusions: Endometrial cancer is exceedingly rare in young people, especially teenagers, unless associated with hyperestrogenism or Lynch syndrome, neither of which can explain this patient's profile. Endometrial carcinoma is an unusual tumor in families with TP53 germline mutation and to date has not been reported as the sentinel carcinoma. Our patient is unusual also in that this appears to be not a familial case but a de novo mutation; genetic counseling did not reveal a family history. She is currently in the process of being considered for a novel targeted therapy which we hope will offer promising results.

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Pedigree analysis of uterine papillary serous carcinoma patients

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Objectives: To evaluate a uterine papillary serous carcinoma (UPSC) population for occurrence of a first-degree relative with a *BRCA* or Lynch syndrome (LS)–associated cancer.

Methods: We performed a retrospective analysis of women with all stages of UPSC diagnosed from 2007 to 2015. Reported pedigrees were analyzed, and any genetic counseling offered or testing obtained was noted. Demographic data were analyzed and compared. SPSS software was used for analysis. A χ^2 analysis was used for all discrete variables and a *t* test was used for continuous variables.

Results: A total of 58 patients with stage IA to IVB were identified for analysis. Of these, 35 (60.3%) had a first-degree relative with cancer of any origin. Twenty-three (39.7%) had first-degree relatives with LS or *BRCA*-associated cancers, including breast, colorectal, uterine, ovarian, pancreatic, gastric, and renal. Ten patients (16%) had first-degree relatives with breast cancer, 5 (8%) with colorectal, 4 (6.3%) with uterine, 2 (3.2%) with ovarian, 2 (3.2%) with pancreatic, 2 (3.2%) with gastric and 1 (1.7%) with renal. Of the 58 subjects, it was documented that 7 (11%) were offered genetic counseling. One patient received *BRCA* testing, which was negative, and one received microsatellite instability/immunohistochemistry testing for LS, which was negative. Although there was no significant association between a positive pedigree and age, race, body mass index, stage of disease or recurrence, there was a higher percentage of African American women with a positive pedigree (52% vs 40%). Disease recurrence in those with a positive pedigree was 30% compared with 26% in those with a negative pedigree. There was no significant difference in age between the 2 groups; median age of positive pedigree patients was 70.0 years and that of negative pedigree patients was 69.3 years.

Conclusions: Our data demonstrated a high proportion (39.7%) of UPSC patients with at least 1 first-degree relative with a *BRCA* or LS-associated cancer. This observation suggests that UPSC patients could be appropriately referred to genetic counseling with increased vigilance. Because the median age of both groups was almost identical, it is possible that age at diagnosis should not factor into referral for genetic testing for UPSC. Further studies would be beneficial in assessing the relationship between a positive pedigree and risk of recurrence.

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Does perceived stress correlate with cardiovascular stress when teaching gynecologic oncology staging procedures to fellowship trainees?

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Objectives: To determine if perceived stress correlates with cardiovascular (CV) parameters when teaching gynecologic oncology staging procedures to fellowship trainees.

Methods: After obtaining institutional review board approval, we performed a prospective, single-institution study evaluating CV parameters while teaching open, robotic, and laparoscopic (LS) endometrial cancer staging procedures to gynecologic oncology fellows. Open interval cytoreduction for ovarian cancer was allowed for the open method. Two gynecologic oncology faculty surgeons performed 4 cases each (open, LS, robotic) with fellows. Each surgeon completed a validated State-Trait Anxiety Index (STAI) instrument to evaluate perceived level of stress. Each surgeon underwent noninvasive cardiac monitoring (ICON) and BP assessment at baseline and throughout each surgery at set time intervals. Pearson correlation was used to assess the relationship between the STAI and CV parameters.

Results: Two surgeons performed 24 surgical procedures with fellow trainees (8 open, 8 LS, 8 robotic) with cardiovascular monitoring. One robotic case was excluded because of poor data collection. The median change in surgeon heart rate was greater for open than for LS (16.7 vs 13.7 beats/min, $P = .05$), open versus robotic (16.7 vs 2.7 beats/min, $P < .0001$), and LS vs robotic (13.7 vs 2.9 beats/min, $P < .0001$). Change in left ventricular ejection time (LVET) was greater for open versus robotic (–30 vs 3.3 msec, $P < .0001$) and LS versus robotic (–18.7 vs 3.3 msec, $P = .001$). There was a significant negative correlation between perceived stress preoperatively and actual change in CV parameters in open procedures including SV ($P < .0001$), CO

($P < .0001$), and LVET ($P = .004$); however, a positive correlation was seen with systolic blood pressure ($P = .01$). There was a significant negative correlation between perceived stress postoperatively and actual change in CV parameters in open surgery: SV ($P < .0001$), CO ($P < .0001$), LVET ($P < .0001$); LS: SV ($P = .004$), CO ($P = .0007$); and robotic procedures: SV ($P = .0004$), CO ($P < .0001$), however, a positive correlation with heart rate in LS procedures ($P = .015$).

Conclusions: Although more CV changes are associated with teaching open surgery, these changes did not correlate with surgeon-perceived level of stress before and after surgery. Surgeon-perceived postoperative stress did not correlate with changes in CV parameters for LS and robotic procedures.

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Targeting ovarian cancer by folic acid conjugated nanoceria

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Objectives: Nanoceria (NCe) have recently emerged in biochemical science because of their excellent antioxidant and free radical scavenger properties. Previously we demonstrated that NCe halted ovarian tumor growth in vivo. Folate receptor-α is shown to be overexpressed in ovarian malignancies. To enable NCe to specifically target ovarian cancer cells, we conjugated nanoceria to folic acid (NCe-FA). Our aim was to investigate the preclinical efficacy of NCe-FA alone and in combination with cisplatin.

Methods: Ovarian cancer cell lines A2780 and C200 were treated with NCe or FA-NCe. Cell viability was assessed using MTT and colony-forming units (CFU). In vivo studies were carried out in A2780-generated mouse xenografts treated with 0.1 mg/kg NCe, 0.1 mg/kg NCe-FA, and 4 mg/kg cisplatin in biweekly intraperitoneal injections. Tumor weights and burden scores were determined. H&E, immunohistochemistry, and toxicity assays were used to evaluate treatment effects.

Results: NCe-FA inhibited in vitro cell proliferation as shown by MTT ($P < .01$) and CFU ($P < .001$). Mice treated with FA-NCe had significantly less excised tumors and lower tumor burden score compared with controls and NCe ($P < .05$ to $.001$). NCe-FA also augmented the tumoricidal and apoptotic effect of cisplatin in vivo, and cells treated with cisplatin and NCe-FA exhibited the highest degree of oxidative stress. Immunohistochemistry revealed less tumor proliferation (Ki-67) and angiogenesis (CD31) in the NCe-FA–containing treatment arms. Liver and kidney function tests from treated mice showed no treatment toxicities.

Conclusions: FA-NCe treatment resulted in efficient inhibition of ovarian tumor growth both in vitro and in vivo and potentiated cisplatin's cytotoxic effect. Thus, NCe-FA should be further evaluated as potential therapeutic agents in ovarian cancer.

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High-grade serous carcinoma of ovary and fallopian tube after the new protocol of assignment of primary site: An analysis of incidence, demographics, and clinical features

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Objectives: In 2007, the protocol for Sectioning and Extensively Examining the FIMbriated End (SEE-FIM) of the fallopian tube was introduced for the assignment of primary site of high-grade serous pelvic carcinomas implicating the fallopian tube as the primary origin. We propose a large, population-based study to assess trends of incidence and compare demographic and clinical features of high-grade serous ovarian carcinoma (HGSC-O) and tubal carcinoma (HGSC-T).

Methods: Data were collected from the Surveillance, Epidemiology, and End Results (SEER) program spanning the years 1990 to 2012. Age-adjusted ovarian and tubal cancer incidence and annual percent changes (APCs) were obtained using SEER stat

software. Data were analyzed with the Mann Whitney and χ^2 tests for nonparametric variables using SPSS software. $P < .05$ was considered statistically significant.

Results: Age-adjusted incidence of HGSC-O increased from 1.69 per 100,000 during 1990 to 2007 to 1.91 per 100,000 during 2008 to 2012. However, the overall APC decreased from 2.17% to 0.27%, respectively. The HGSC-T age-adjusted incidence rate increased from 0.06 per 100,000 during 1990 to 2007 to 0.24 per 100,000 during 2008 to 2012, with an increase in the overall APC from 10.3% to 19.8%, respectively. After the implementation of the new protocol, women diagnosed with HGSC-T were older than women with HGSC-O (64.45 vs 63.0 years, $P < .001$) and presented more often with less advanced disease (62.9 vs 84.03%, $P < .001$). There was no difference in age before 2008. After 2008, there was also a significant increase in the number of nonwhite women diagnosed with HGSC-O (13.8% vs 12.0%, $P = .004$).

Conclusions: With the implementation of the new protocol for assignment of primary tumor, the incidence of HGSC-T has increased significantly. Women with HGSC-T are older than women with HGSC-0 and present at earlier stages of disease. HGSC-T is more common than historically reported and clinically distinct from HGSC-O. Shedding light on the differences between the 2 cancers will lead to novel strategies for prevention and treatment.

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Racial disparity in emergency department diagnosis of gynecologic malignancies

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Objectives: Up to 25% of patients with all malignancies are diagnosed in the emergency department. Our study aimed to define the prevalence of emergency department diagnoses, associated risk factors, and outcomes to improve cancer care and delivery for women with gynecologic malignancies.

Methods: After obtaining institutional review board approval, we retrospectively evaluated 250 records identified from the Gynecologic Oncology Tumor Registry. Data including place of diagnosis, patient demographics, insurance status, disease stage, grade, and treatment were recorded. Univariable analysis was performed using STATA software.

Results: Of 224 evaluable records, 52 (23%) women with gynecologic malignancies were diagnosed in the emergency department. Black race (46% vs 29%), higher Charlson Comorbidity Index, and past or current tobacco use were all more prevalent in those patients diagnosed with malignancy in the emergency department ($P \leq .05$). These patients were additionally more likely to have advanced-stage disease (stage III/IV) at diagnosis (50% vs 25%, $P < .001$) and less likely to have a surgical procedure (53.9% vs 84.3%, $P < .001$) compared with patients diagnosed in the office. Additionally, more ovary/primary peritoneal/fallopian tube cancers were diagnosed in the emergency department ($P = .05$). There were no differences in age, insurance, drug or alcohol use, family cancer history, or death within 6 months of disease.

Conclusions: In this population, black race and ovarian cancer were associated with diagnosis in the emergency department. Diagnosis in the emergency department was also associated with stage 4, metastatic disease. Cancer care and delivery research aimed at locale of diagnosis may provide insight into ethnic/racial groups at risk for late-stage diagnosis and targets for health care literacy and access interventions.

Table 1

Univariable comparison of risk factors associated with Emergency Department diagnosis of gynecologic malignancies.

Variable	Diagnosed in Office (N=172)	Diagnosed in ED (N=52)	P-value
Age (years)	62.0 (12.8)	61.2 (14.5)	0.70
Race/Ethnicity			0.05
White	28 (16.3)	7 (13.5)	
African American	50 (29.1)	24 (46.2)	
Hispanic	44 (25.6)	15 (28.9)	

Asian	26 (15.1)	2 (3.9)	
Unknown (declined or other)	24 (13.9)	4 (7.7)	
Insurance			0.19
Public (Medicaid/Medicare)	114 (66.3)	34 (65.4)	
Private	54 (31.4)	14 (26.9)	
Unknown	4 (2.3)	4 (7.7)	
Disease Site			0.05
Uterine	98 (57.0)	21 (40.4)	
Ovary/FT/PPC	24 (13.9)	14 (26.9)	
Cervix/vulva/vagina	49 (28.5)	16 (30.8)	
Other/unknown	1 (0.6)	1 (1.9)	
Stage			<0.001
I	110 (65.9)	22 (42.3)	
II	16 (9.6)	3 (5.8)	
III	28 (16.8)	10 (19.2)	
IV	13 (7.8)	16 (30.8)	
Unstaged	0 (0.0)	1 (1.9)	
Stage (dichotomous)			<0.001
I/II	126 (75.5)	25 (48.1)	
III/IV	41 (24.6)	26 (50.0)	
Unstaged	0 (0.0)	1 (1.9)	
Grade			0.06
1	74 (44.3)	15 (28.9)	
2	23 (20.4)	10 (19.2)	
3	53 (31.7)	22 (42.3)	
Not appropriate/no grade given	4 (2.4)	5 (9.6)	
Borderline	2 (1.2)	0 (0.0)	
Surgery			<0.001
No	27 (15.7)	24 (46.2)	
Yes	145 (84.3)	28 (53.9)	
Charlson Comorbidity Index	0 [0-4]	0 [0-6]	0.05*
Tobacco Use (past or present)	33 (19.8)	17 (32.7)	0.05
Alcohol Use	6 (3.6)	4 (7.7)	0.25
Drug Use (past or present)	4 (2.4)	4 (7.7)	0.09
Family History of Cancer			0.34
No	84 (50.3)	30 (57.7)	
Gynecologic Cancer	12 (7.2)	1 (1.9)	
Non-gynecologic Cancer	71 (42.5)	21 (40.4)	
Death within 1 month	0 (0.0)	1 (1.9)	0.24
Death within 6 months	2 (4.9)	2 (1.6)	0.25

*Wilcoxon rank sum

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Rate and predictors of predischarge versus postdischarge venous thromboembolism after open surgery for gynecologic malignancy

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Objectives: To report the rates of venous thromboembolism (VTE) within 30 days of surgery for gynecologic cancer and detail the rates and predictors of VTE before (PreDC) and after (PostDC) discharge from the hospital.

Methods: The American College of Surgeons National Surgical Quality Improvement Program database was used to identify and extract data on women who underwent a major cancer surgery for ovarian (OC), endometrial (EC), or cervical cancer (CC) from 2005 to 2011. VTE was defined as deep vein thrombosis (DVT) requiring therapy and pulmonary embolism (PE) within 30 days of surgery. Statistical analyses for categorical and continuous covariates were assessed using the χ^2 and Student *t*test, respectively, and regression models were used to identify risk factors for VTE.

Results: Within 30 days of laparotomy for gynecologic cancer, 101 (2.3%) of 4,369 patients were diagnosed with a VTE. Slightly more VTEs were diagnosed PreDC (1.3%) than PostDC (1.0%) at a median of 3 and 13.5 days after surgery, respectively. Patients with VTE had higher 30-day mortality than those with no VTE (8% vs 1.4%, $P < .001$). Univariate predictors of PreDC VTE included OC ($P = .009$), neoadjuvant chemotherapy ($P = .01$), higher American Society of Anesthesiology class ($P = .016$), preoperative renal failure ($P = .0002$), hypoalbuminemia ($P < .001$), and leukocytosis ($P = .014$). None of the previous predictors were associated with PostDC VTE. Preoperative weight loss was associated with PostDC VTE ($P = .004$) but not PreDC VTE rates. Both preDC VTE and postDC VTE were predicted by ascites ($P < .001$ and $P = .01$), operative time more than 3 hours ($P = .006$ and $P = .05$), and the performance of a bowel resection ($P = .004$ and $P = .017$). On multivariate analysis, predictors of PreDC VTE were ascites ($P = .004$), neoadjuvant chemotherapy ($P = .037$), renal failure ($P = .009$), operative time >3 hours ($P = .037$); predictors of PostDC VTE were weight loss ($P = .05$) and lymphadenectomy ($P = .020$). In multivariable analysis adjusting for other confounders, VTE within 30 days was a significant predictor of higher 30-day morality (OR 4.1, 95% 1.6–9.5, $P = .002$).

Conclusions: The rate of VTE within 30 days of laparotomy for gynecologic cancer surgery is 2.3%. Distinct risk factors for VTE are present in the periods before and after discharge from the hospital. VTE within 30 days was associated with significantly higher risk of 30-day mortality, even after adjusting for other confounders.

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Utilization of vaginal hysterectomy with curative intent for patients with endometrial cancer: Outcomes and cost of care compared with the robotic approach

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Objectives: Although 30% to 40% of patients with endometrial cancer are at negligible risk of lymphatic spread and may be treated safely with hysterectomy alone, the use of vaginal hysterectomy (VH) with curative intent has been poorly studied. Our objective was to compare outcomes and cost for patients undergoing VH or robotic hysterectomy (RH), with and without lymphadenectomy (LND).

Methods: Patients undergoing planned VH or RH for endometrial cancer between January 2007 and November 2012 were identified. Patients with stage IV disease, synchronous cancer, or those treated with palliative intent were excluded. During surgery, patients were objectively triaged to LND as per institutional protocol based on frozen section. Thirty-day costs were set based on the Medicare cost-to-charge ratio for each year and inflated to 2012 values. Outcomes were compared between VH and RH groups matched 1:1 on propensity scores (PS).

Results: A total of 153 patients underwent planned VH; 60 (39%) had concurrent LND (49 laparoscopic, 4 robotic, 7 open including failed VH), and 93 (61%) met low-risk criteria and did not require LND. RH was performed in 398 patients; 225 (56%) had concurrent LND (208 robotic, 17 open) and 173 (44%) did not. Among all patients without LND, 50 PS-matched

pairs were identified. There was no significant difference in complications, length of stay (LOS), or 30-day readmission rates. However, for patients undergoing RH, the median operative time was 1.3 hours longer ($P < .001$) and median overall cost was significantly higher ($12,190 vs $9,140, $P < .001$) compared with VH. Five-year progression-free survival was similar (94% for VH; 93% for RH). Among all patients requiring LND, 42 PS-matched pairs were identified. There was no significant difference in complications, LOS, or 30-day readmission. Median operative time was 4.8 hours in each group when pelvic and para-aortic LND was performed, and 12 minutes longer in the VH group for pelvic LND alone (3.7 vs. 3.5 hours, $P = 0.03$). A nonsignificant trend toward reduced median overall cost was observed in the VH group when LND was required ($17,102 vs $16,210, $P = .08$).

Conclusions: VH with or without laparoscopic LND for endometrial cancer results in similar surgical and oncologic outcomes and lower costs compared with RH and should be considered an option for appropriate patients.

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Predicting big problems: Simple measurements and surgical challenge in endometrial cancer

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Objectives: Anticipation of operative difficulty can assist the surgeon in preoperative decision making in the management of endometrial cancer patients. Simple radiologic linear measurements of visceral fat may allow for better anticipation of surgical difficulty than body mass index (BMI) alone or a surgeon's clinical assessment.

Methods: We prospectively enrolled 80 patients with newly diagnosed endometrial cancer in the study. Each patient had routine preoperative imaging (magnetic resonance imaging or computed tomography). Radiologic linear measurements of the following were obtained: anterior-to-posterior skin edge distance (A), anterior skin to anterior edge of L5 distance (B), anterior peritoneum to anterior edge of L5 distance (C), and posterior edge of L5 to posterior skin distance (D). The surgeon completed pre- and postoperative 9-point Likert scale questionnaires rating the preoperative anticipated perception of surgical difficulty (prePOD) and postoperative actual perception of difficulty (postPOD) of the surgery. The primary objective was to assess associations between linear measurements of visceral obesity and postPOD, and to determine if they improve upon BMI alone in predicting surgical difficulty.

Results: Seventy-nine patients completed the questionnaires, underwent preoperative imaging, and had surgery. One patient was excluded because she did not undergo surgery. Mean BMI was 38 kg/m^2 (range, 19–59 kg/m^2). Lymphadenectomy was performed in 39 cases. Surgeons' prePOD predicted postPOD in 27% of cases. In 30% of cases, a difference of 2 or more points was seen in prePOD and postPOD. Univariate analysis showed that all 4 linear measurements, BMI, weight, and prePOD were associated with increased postPOD ($P < .05$). PrePOD, B, and C were more predictive of postPOD than BMI. Among lymphadenectomy patients, A, B, and C were more predictive of postPOD than BMI. Multivariate analysis demonstrated that BMI, C, and D were independently associated with increased postPOD ($P < .05$). The combination of C with BMI was most predictive of increased postPOD. Cutoff values were found associated with significantly increased postPOD.

Conclusions: Simple linear measurements of visceral obesity can be obtained from routine preoperative imaging. Such measurements improve upon BMI alone in anticipating operative difficulty. These linear measurements can assist critical preoperative decision making and potentially avoid surgical morbidity in this challenging patient population.

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Disparity in survival between White and Asian patients with uterine serous carcinoma: Changes in clinical characteristics, pattern of care, and outcome over time from 1988 to 2011

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Objectives: Our study uses the Surveillance, Epidemiology, and End Result (SEER) database to determine if outcome disparities between white and Asian patients with uterine serous carcinoma (USC) have changed over time.

Methods: Women with USC were identified using the SEER database from 1988 to 2011 (n = 8,230), and grouped into 2 cohorts: white and Asian patients. Years of the study were divided into 3 periods (1988–1997, 1998–2004, and 2005–2011). Overall survival (OS) was estimated. Kaplan-Meier survival curves and Cox regression models were used.

Results: Asians were younger but no difference was noted in stage distribution, marital status, cancer-directed surgery, extent of lymphadenectomy, and radiation therapy over the 2 time periods compared with whites. In multivariable analysis, after adjusting for age, race, marital status, stage, cancer-directed surgery, extent of lymphadenectomy, adjuvant radiation, and geographic location, Asian patients were 29% less likely to die than were whites (HR 0.71, 95% CI 0.53–0.96, *P* = .023) in the period 1988–1997. However, this difference disappeared in the periods 1999 to 2004 (HR 1.13, 95% CI 0.89–1.44, *P* = .30) and 2005 to 2011 (HR 1.1, 95% CI 0.86–1.34, *P* = .55). In multivariable analysis, the survival for white patients with USC significantly improved over the 3 time periods (*P* = .004 and <.0002 for 1998–2004 and 2005–2011, respectively). On the other hand, no difference in outcome was seen in Asian patients with USC during the 3 periods (*P* = .09 and *P* = .32 for 1998–2004 and 2005–2011, respectively).

Conclusions: The survival difference between Asian and white patients with USC disappeared over time. White but not Asian patients with USC had improved outcome over time.

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The value of FDG-PET/CT in node-negative endometrial cancer on MRI

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Objectives: To evaluate the diagnostic performance of preoperative fluorodeoxyglucose positron emission tomography–computed tomography (FDG-PET/CT) in predicting lymph node status in node-negative endometrial cancer on preoperative magnetic resonance imaging (MRI).

Methods: Patients with endometrial cancer who underwent both preoperative MRI and FDG-PET/CT and then underwent hysterectomy and lymphadenectomy were included. MRI and FDG-PET/CT images were independently reviewed by 2 radiologists and 2 nuclear medicine physicians blinded to the clinical and pathologic information and the results of FDG-PET/CT or MRI. Lymph nodes smaller than 1 cm in short axis diameter were defined as negative lymph nodes on MRI. Lymph nodes were divided into 8 lymph node stations in each patient. The diagnostic performance of PET-CT in predicting lymph node metastasis was calculated in a patient-by-patient analysis and lymph node station-by-station analysis.

Results: A total of 362 patients did not have lymph node metastasis on preoperative MRI. All patients underwent pelvic lymph node dissection, and 118 patients underwent para-aortic lymph node dissection. A total of 10,238 lymph nodes were retrieved from 2,099 lymph node stations. Twenty-seven patients had lymph node metastasis on pathologic examination. PET-CT diagnosed only 5 patients (18.5%) with lymph node metastasis. The sensitivity of FDG-PET/CT was 18.5% in patient-by-patient analysis. Lymph node metastasis was found in 49 lymph node stations on pathologic examination. PET-CT diagnosed only 8 lymph node stations (16.3%) with lymph node metastasis. The sensitivity of FDG-PET/CT was 16.3% in lymph node station-by-station analysis. The median diameter of false-negative metastatic lymph nodes was 6 mm (range, 1–22 mm) in long axis and 3 mm (range, 1–11 mm) in short axis.

Conclusions: This study indicates the low value of preoperative FDG-PET/CT in predicting lymph node metastasis in node-negative endometrial cancer on preoperative MRI.

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Adjuvant chemotherapy beneficial for select early-stage, low-grade serous ovarian cancer patients

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Objectives: Low-grade serous ovarian cancer (LGSC) is a rare subtype of ovarian serous carcinoma accounting for only 6% of all serous ovarian carcinoma. These tumors are considered to be relatively chemoresistant because of their tumor biology, making the role of adjuvant chemotherapy in early stage LGSC unclear. Herein, we sought to identify any chemotherapy benefit in overall survival among women with early-stage LGSC.

Methods: The National Cancer Data Base was queried for all patients diagnosed from 1998 to 2012 with stage IA–IC LGSC. Only patients with nodal dissection were included for analysis. X^2 test, logistic regression analysis, and log-rank test were used to analyze chemotherapy utilization and survival.

Results: Of the 2,260 patients identified as having stage I LGSC, 1,481 had nodal dissection and were included for analysis. Chemotherapy was used in 15%, 21%, and 60% for stage IA, IB, and 1C, respectively. Age, insurance type (uninsured, private, Medicare/Medicaid), and stage were all associated with increased likelihood of receiving chemotherapy. Only age, Charlson-Deyo Comorbidity index, and insurance type were statistically significantly associated with survival on univariate and multivariable analysis. The 5-year overall survival (OS) for stage IA, IB, and IC without chemotherapy are 92%, 84%, and 88%, respectively. The 5-year OS for stage IA, IB, and IC with chemotherapy are 96%, 95%, and 94% respectively. A statistically significant difference in survival was seen in patients with stage IC receiving chemotherapy (*P* =.009).

Conclusions: This is the largest dataset to date to look at the usefulness of adjuvant chemotherapy in stage I LGSC. Age, comorbidities, and type of insurance were associated with survival in this cohort, but the substages of stage I LGSC were not. However, adjuvant chemotherapy does confer a survival benefit in patients with stage IC LGSC. Although typically considered relatively chemoresistant with an overall good prognosis, adjuvant chemotherapy demonstrates a survival benefit of 6.8% and should be considered in these patients.

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Minimally invasive radical hysterectomy for cervical cancer reduces morbidity with similar outcomes compared with laparotomy

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Objectives: Limited randomized trials have shown whether patient outcomes in cervical cancer are equivalent after radical hysterectomy (RH) via minimally invasive (MI) or traditional laparotomy (XL) approach. The aim of this study was to assess patient outcomes of women with cervical cancer undergoing upfront RH at 2 large academic institutions to determine if mode of surgery affects patient outcomes.

Methods: Women undergoing upfront RH between 2000 and 2013 at 2 academic institutions were identified. Patient charts were retrospectively reviewed, and relevant demographic and clinical variables were extracted. *T* test, Fisher exact tests, and Kaplan-Meier analyses were performed.

Results: From 2000 to 2013, 383 women met eligibility requirements. Of these, 101 underwent an MI (traditional laparoscopy, laparoendoscopic single site, or robotic) approach, and 282 underwent an XL. Overall survival (median not reached, *P* = .29) was not different between the groups. Recurrence was rare and equivalent between groups, with 5.0% of patients undergoing MI surgery recurring versus 6.4% of women in the XL group (*P* = .86). Pelvic lymph nodes were dissected in 98% and 97% of patients, respectively (*P* = 1.0) and were found to be positive in 10.9% and 8.5% of patients (*P* = .55). The mean number of pelvic lymph nodes retrieved was higher in the MI group (19.4 vs 16.0, *P* < .001). There was no difference in the rate of postoperative chemotherapy (*P* = .23) or radiation therapy (*P* = .20). Surgical margins were positive in 5.0% and 4.6% of specimens (*P* = .54). Though there was no difference in the overall rate of complications (17.2% and 18.7%, *P* = .87), laparotomy was associated with a higher mean estimated blood loss (75cc vs 226cc, *P* < .001) and a higher rate of perioperative blood transfusion (3.4% vs 30.8%, *P* < .001). Perioperative hospital stay was shorter in the MI group (1.9 days vs 4.7 days, *P* < .001).

Conclusions: RH using an MI procedure does not compromise patient outcomes, including overall survival, rate of recurrence, or the frequency of pelvic lymph node dissection or positivity. Morbidity was decreased in the MI group, including decreased estimated blood loss, fewer blood transfusions, and shorter hospital stay.

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The end-of-life costs for patients with advanced ovarian cancer

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Objectives: To describe the Medicare payments at the end of life for patients with advanced ovarian cancer in a population-based cohort, and assess factors responsible for variation in payments.

Methods: Using the linked Surveillance, Epidemiology and End Results (SEER)–Medicare database, we identified a cohort of women aged 65 years and older with stage III/IV epithelial ovarian cancer diagnosed between 1995 and 2007. We defined the end of life as the last 90 days before death. Patients who died within 90 days of diagnosis were excluded from the analysis. Total medical costs were estimated from overall Medicare payments, and adjusted for geography and for inflation to the 2009 US dollar. A log-linear regression was performed to assess factors associated with variability in cost.

Results: Of the 5,509 patients with stage III/IV ovarian cancer identified from 1995 to 2007, 78.9% died of ovarian cancer. In the 90 days before death, 65.2% of patients had an inpatient admission, 53.7% received chemotherapy, 19.3% had a palliative procedure, and 62.5% had hospice services. In the last 30 days of life, 43.2% patients had an inpatient admission and 21.2% patients received chemotherapy. The mean total payment per patient in the last 90 days of life was $24,073 (range, 0–$484,119) over the study period. The mean cost of inpatient admissions was $14,529 (range, 0–$483,932). On a multivariate analysis, costs at the end of life did not vary based on length of patient survival (*P* = .7718). Older age (>80 years) was associated with decreased costs at the end of life compared with patients aged 65 to 69 years. Compared with a diagnosis in 1995 to 1998, mean costs at the end of life were increased in later years of diagnosis. Other factors associated with significantly increased costs in the last 90 days of life were medical comorbidity, hospice services, chemotherapy, and any inpatient admission. Any inpatient admission was associated with a 5-fold increase in mean costs at the end of life.

Conclusions: The financial burden of caring for ovarian cancer patients is substantial. Understanding the causes of variation in cost associated with the care of advanced ovarian cancer patients may aid in the identification of areas where additional clinical resources can be used to lower overall costs.

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Evolution of surgical complexity in ovarian cancer: Experience from a developing tertiary referral center in Eastern India

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Objectives: Complete cytoreduction (R0) improves survival in advanced ovarian cancer compared with optimal cytoreduction (<1-cm residual disease). At our institution, we changed our practices since January 2015. The aim of this study is to compare the trend change in SCS (Aletti score) since adopting R0 resection strategy for primary debulking surgery (PDS) and interval debulking surgery (IDS).

Methods: Retrospective observational study. SCS was calculated for PDS and IDS at 6 monthly treatment periods P1 to P7 (with P1 being January–June 2012, and P7 being January–June 2015) from operation records in the hospital electronic database. Data for P8 (July–December 2015) will be updated.

Results: A total of 169 cases were evaluated: 56 PDS and 113 IDS cases. Mean ages were 49.1 and 53.6 years, respectively. PDS showed an increasing trend from P1 (4/21 [20%]) to P6 (10/32 [30%]) and P7 (20/35 [60%]). Major resection procedures for PDS and IDS were as follows: diaphragm (30.3% vs 13.2%), pelvic peritoneum (41% vs 18.5%), rectosigmoidectomy-anastomosis (19.6% vs 16.8%), splenectomy (14.2% vs 7.0%), small bowel (8.9% vs 3.5%), total colectomy (5.35% vs 0), lesser sac tumor (14.2% vs 2.6%), porta hepatis tumor (8.9% vs 0), distal pancreatectomy (5.35% vs 0), and cholecystectomy (14.2 % vs 7.9%). There was an increasing trend (from P1 to P7) for the mean SCS both for PDS (4.0 to 9.9) and IDS (5.0 to 7.9) (Table 1). Low SCS in PDS before 2015 may reflect selection bias, because most patients were at low stage of the disease. Optimal cytoreduction rate was 90% in both the PDS and IDS groups (P1–P7). Complete R0 in IDS improved from 60% in P1 to 80% in P7.

Conclusions: The surgical complexity increases with R0 and PDS. Detailed prospective recording of morbidity and survival has been instituted with regular audit of practice and outcome. This should be mandatory and include health economic analysis in a developing country so as to overcome the barriers of changing practice.

Table 1
SCS Scores in IDS and PDS.

Periods	IDS SCS Mean	PDS SCS Mean
P1 (Jan-Jun 2012)	**5.05**	**4**
P2 (Jul- Dec 2012)	**4.09**	**3.5**
P3 (Jan-Jun 2013)	**5.31**	**4**
P4 (Jul- Dec 2013)	**4.6**	**3.5**
P5 (Jan-Jun 2014)	**6.88**	**4**
P6 (Jul- Dec 2014)	**6.13**	**5.6**
P7 (Jan-Jun 2015)	**7.86**	**9.85**

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456 - Poster
Association analysis of oxidative stress–related genes and endometrial cancer in The Cancer Genome Atlas
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Objectives: The effect of genetic variation as it relates to oxidative stress (OS) in the context of endometrial cancer (EC) is unclear. We previously identified several OS-related genes and single nucleotide polymorphisms (SNPs) associated with EC development, stage, and grade. Our aim was to validate the significant genes as well as perform an association analysis of known OS-related genes within The Cancer Genome Atlas (TCGA).

Methods: Genotyping was performed on 79 patients (58 cancer, 21 no cancer) at 48 known SNPs using Fluidigm 192.24 Dynamic Array integrated fluid circuits (Fluidigm, San Francisco, CA). Linear regression analysis was used to assess SNP-EC incidence, grade, and stage associations while controlling for patient characteristics, which were determined by a chart review. In the TCGA population, genotypes of the selected genes were extracted from the Affymetrix Genome Wide Human SNP Array 6.0 performed in EC patients. The annotation file was cross-referenced to identify SNPs located within OS-associated genes, and the association analysis was performed with the 'SNPassoc' R package using 5 different genetic models.

Results: 15 genes associated with OS were identified. *TP53* was associated with EC incidence, *SIRT1* was associated with advanced-stage disease, and 3 SNPs located within *FOXO3* were associated with increased grade. All but 1 gene, *SIRT7*, were represented in the TCGA database, and 254 SNPs were identified in the selected genes. *TP53*, *SIRT1*, *SIRT6*, and *CAMK4* were associated with EC risk ($P < .05$); *CAMK4*, *FOXO1*, *FOXO3*, *SIRT2*, *SIRT3*, *SIRT4*, *SIRT5*, *SOD2*, and *SOD3* were associated with grade ($P < .05$); and *CAMK4*, *FOXO1*, *FOXO3*, *SIRT2*, *SOD2*, *SOD3*, and *TP53* were associated with stage ($P < .05$) in the different genetic models of inheritance patterns.

Conclusions: Several OS-related genes are significantly associated with EC risk, stage, and grade both in an independent model and within TCGA. Reactive oxygen species and the OS pathway should be further studied because it relates to the pathophysiology of EC.

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Capitalizing on synthetic lethality in homologous recombination-deficient high-grade serous ovarian cancers with a novel ATR inhibitor

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Objectives: Approximately 50% of high-grade serous ovarian cancers (HGSOCs) have defects in genes involved in homologous recombination repair (HR). Targeting the ATR/CHK1 axis is a strategy for HR-deficient HGSOCs capitalizing on synthetic lethality. A new ATR inhibitor (ATRi), ATRN119, will be evaluated in ovarian cancer cells and in a novel *BRCA2*mutant patient-derived xenograft (PDX) model.

Methods: ATR and PARP inhibitors were evaluated in vitro and in vivo. *BRCA*-mutant (PEO1, JHOS4) and wildtype (PEO4) ovarian cancer lines were used for MTT and immunoblot studies. Using a *BRCA2*-deficient patient-derived xenograft (PDX) model (8945delAA), the tumor was expanded via orthotopic transplantation onto the fallopian tube/ovary into 5- to 8-week female mice. Mice were randomized into 3 groups: untreated, ATRIN 60 mg/kg twice daily, and ATRIN 100 mg/kg/ twice daily. Once tumor volumes reached 70 to 100 mm^3, treatment was initiated and tumor volume was followed by ultrasound.

Results: ATRIN119 was more effective in targeting ATR by decreasing pATR and downstream pCHK at lower concentrations than other ATRi, with no effect on MTOR or ATM showing selectivity. ATRIN119 decreased cell viability and induced DNA damage by an increase in pH2AX in ovarian cancer cells. ATRi with ATRIN119 had similar antiproliferative effects to PARPi in *BRCA*-mutant ovarian cancer cells. ATRIN119 had antitumor effects with minimal toxicity using a novel *BRCA2*-mutant patient-derived xenograft (PDX) model supporting a possible synthetic lethality mechanism.

Conclusions: Strategies to optimize approaches capitalizing on synthetic lethality in HR-deficient ovarian cancers are needed. ATR inhibition with ATRIN119 is a viable therapeutic option and further preclinical work is ongoing to optimize bioavailability and to identify the maximum tolerated dose.

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TGF/Wnt signaling: A metastasis signature for poor-prognosis ovarian cancer

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Objectives: TGF/Wnt pathway expression has been associated with the presence of upper abdominal metastatic epithelial ovarian cancer (EOC). TGF-β and Wnt signaling are known modulators of epithelial-mesenchymal-transition (EMT), which promotes metastasis. We sought to determine if a signature based on TGF/Wnt pathway expression can predict metastatic potential in vitro, and created cell line models to investigate the mechanisms of TGF/Wnt signaling in promoting prometastatic behaviors such as proliferation, migration, and invasion.

Methods: A 182-gene principal component analysis-based TGF/Wnt "metastasis signature" was developed and tested for association with clinical outcomes in a publicly available clinicogenomic dataset (n = 218, GSE9891). This expression signature was used to select 11 EOC cell lines with high versus low TGF/Wnt signature scores, and therefore differential predicted metastatic potential. Cell lines were evaluated for TGF/Wnt signaling and EMT by Western blot. Basement membrane invasion and wound healing assays were used to evaluate cell migration and invasive potential in the presence and absence of TGF-β stimulation as well as pharmacologic inhibition of TGF and/or Wnt signaling.

Results: Our metastasis signature was significantly associated with suboptimal surgical cytoreduction ($P = .005$) and overall survival ($P = .009$). Baseline Western blots comparing cell lines by signature-predicted metastatic potential (high vs low TGF/Wnt signaling mRNA pathway expression) confirmed differential expression of TGF/Wnt signaling proteins Wnt3a, Wnt5a, Beta Catenin, as well as differential expression of EMT markers including Snail and E-cadherin. Cell lines with greater predicted metastatic potential migrated more readily and showed a higher degree of invasion in surrounding basement membranes. TGF-β stimulation and coculture with TGF-β and Wnt pathway inhibitors did not measurably alter invasive behavior.

Conclusions: A TGF/Wnt–based gene expression signature identifies a more aggressive ovarian cancer phenotype, characterized by EMT and increased invasive potential. Although we were not able to identify therapeutic targets within the TGF/Wnt pathway, TGF/Wnt expression may be a biomarker of unresectable disease in patients with advanced ovarian cancer.

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459 - Poster
Obesity and race as risk factors in triple-negative breast cancer
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Objectives: To determine if obesity is a risk factor for triple-negative breast cancer (TNBC) and if there are racial differences in body mass index (BMI in kg/m^2) in different breast cancer subsets, including TNBC and estrogen receptor–positive (ER+) breast cancers.

Methods: We performed a single-institution retrospective study of women diagnosed with breast cancer between January 2010 and August 2013. Race, BMI, immunohistochemistry testing, and age at diagnosis were abstracted from the patient records. We sought to determine if obesity is a risk factor for triple-negative breast cancer and if there are racial differences in BMIs for different breast cancer subsets.

Results: In our cohort of 230 women, women with TNBC had a similar mean BMI as those who were ER+ (30.89 vs 31.02; $P = .880$). African American (AA) women with TNBC had a mean BMI of 34.2 compared with AA ER+ women who had a mean BMI of 31.2 ($P < .02$). Caucasian women with TNBC had a mean BMI of 27.4 compared with ER+ women with a mean BMI of 30.7 ($P < .008$). AA women with TNBC had a significantly higher mean BMI than Caucasian women (34.4 vs 27.4; $P < .0001$). There was no difference in BMI between AA and Caucasian women who were ER+ (31.3 vs 30.7; $P = .635$). A post hoc Tukey test showed that AA women with TNBC had a higher premenopausal BMI, which was statistically significant compared with postmenopausal AA women (6.050, 95% CI 1.985–10.12, $P < .05$). This was not true for Caucasian women with TNBC (–2.015, 95% CI –6.3 to 2.280).

Conclusions: In women with TNBC, AA women had significantly higher BMIs than Caucasian women, but this is not the case for those with ER+ cancers. BMI for Caucasian women with TNBC is significantly lower than for Caucasian women with ER+ breast cancer. The mean BMI for premenopausal AA women was significantly higher than postmenopausal AA women with TNBC but this was not true for Caucasian women.

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Outcomes of pelvic exenteration: Does size matter?
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Objectives: Pelvic exenteration is often the only curative option for locally advanced or recurrent pelvic malignancies. However, this major surgical procedure is associated with high morbidity and mortality rates. Currently the data on the impact of tumor size on outcomes of patients undergoing a pelvic exenteration are limited. In this study, we sought to determine the effect of tumor size on perioperative outcomes and survival in patients undergoing pelvic exenteration at 2 institutions.

Methods: A retrospective chart review was performed of women who underwent pelvic exenteration at the Ohio State University Wexner Medical Center (OSUWMC) and University of Colorado (UCO) from 2000 to 2015. Patient demographics, complications, and outcomes were recorded. Statistical analysis was performed using the χ^2, Student *t* test, logistic regression, and nonparametric tests as appropriate, as well as the log-rank test and Cox proportional hazards for survival analysis.

Results: One hundred fifty-one women underwent pelvic exenteration. Gynecologic Oncology, Surgical Oncology, and Urology performed 83, 29, and 31 exenterations, respectively. Information on pathologic tumor size was available in 143 women, and greatest dimension of tumors ranged from 0 to 25.5 cm. Sixteen patients had no residual tumor on final pathology. Not surprisingly, larger tumors were more likely to undergo total pelvic exenteration (OR 1.14, 95% CI 1.03–1.27 for 1-cm increase in size). Average OR time, estimated blood loss, intraoperative blood transfusion, postoperative complications, length of stay (LOS) in the intensive care unit, overall hospital LOS, 30-day mortality, and reoperation were not different among those with tumors larger than 4 cm than those with less than 4 cm or no residual tumor. Larger tumors were more likely to recur (65% vs 42% and 20%, $P = .016$) and have positive margins (OR 1.11, 95% CI 1.02–1.22). Tumor size was inversely related to overall survival (HR 1.05; 95% CI 1.00–1.10). However, when positive margins and exenteration type were controlled, tumor size was no longer associated with decreased overall survival (HR 1.02, 95% CI 0.97–1.07).

Conclusions: Increased tumor size is not independently associated with worse overall perioperative morbidity. Larger tumors are, however, associated with worse survival, which is explained by the need for more extensive operations and higher rate of positive margins. Patients should be counseled regarding the risks of this major operation.

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Impact of residents and fellows on postoperative outcomes in gynecologic cancer patients: An analysis of the ACS-NSQIP database

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Objectives: To determine the impact of postgraduate years (PGY) of trainee experience on postoperative outcomes in gynecologic cancer patients.

Methods: We evaluated the National Surgical Quality Improvement Program (NSQIP) participant use files from 2006 to 2013 for patients undergoing elective surgery for gynecologic cancers (ICD-9 codes 179–184). Trainees were categorized as junior (PGY 1–2), senior (PGY 3–4), or fellow (PGY 5–8). Surgical length was characterized as long or short with a 4-hour cutoff. Postoperative outcomes including surgical site infection and sepsis, return to the operating room (ROR), and death were recorded. Postoperative outcomes were compared using logistic regression. $P < .05$ was used as a threshold of significance.

Results: Of 5,330 elective surgeries for gynecologic cancer with complete data, 4,097 (76.9%) involved trainees. Most trainees (57.9%) were senior residents. Compared with surgeries in which no trainee was involved, the complication risk was increased in surgeries performed with senior residents (RR 1.89, 95% CI 1.55–2.31) and fellows (RR 2.73, 95% CI 2.21–3.39). The odds of a long surgery were higher across all trainee levels (RR 4.60 for junior residents [95% CI 3.33–6.34]; 4.30 for senior residents [95% CI 3.32–5.56]; and 6.95 for fellows [95% CI 5.32–9.07]). More surgical site infections were seen in cases involving senior residents (RR 1.86, 95% CI 1.31–2.64) or fellows (RR 2.02, 95% CI 1.38–2.95). Sepsis was more common with any level of trainee involvement. Surgeries with fellows involved also had more common ROR (RR 2.11, 95% CI 1.23–3.61). Despite increased risk of complications, trainee involvement at any level was not associated with a risk of death after surgery. After adjusting for length of surgery and extent of disease, the risk of infectious complications was attenuated and ROR was no longer significant.

Conclusions: Trainee involvement in surgery increases the length of surgery, as well as the risk of postoperative complications. Much of the risk of complications is attributable to longer operative times and more widespread disease with trainee involvement. Despite the increased operative time and surgical risks, continued surgical education of trainees is imperative to maintain an educated workforce.

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Neoadjuvant chemotherapy in advanced-stage epithelial ovarian, fallopian tube, and primary peritoneal carcinoma: Do number of cycles matter?

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Objectives: There has been a growing body of literature supporting the use of neoadjuvant chemotherapy (NACT) in advanced-stage epithelial ovarian cancer (EOC); however, there are no data to inform the optimal number of cycles before interval debulking surgery (IDS). The objective of this study was to determine if the number of cycles of NACT has an impact on clinical outcomes in advanced EOC.

Methods: Institutional review board approval was obtained. From January 2007 to December 2014, patients treated with either primary debulking surgery (PDS) or NACT followed by IDS were included. Patient charts were abstracted for demographic information, treatment characteristics, and patient outcomes. Statistical tests were performed with the Fisher exact, Pearson χ^2, and simple linear regression using STATA version 14. $P = .05$ was considered statistically significant.

Results: A total of 239 patients were identified, 141 in the PDS group and 98 in the NACT group. We compared patients who received ≤3 cycles of NACT before IDS with those who had ≥4 cycles. In the ≤3-cycles cohort, 77.2% achieved R0 status compared with 61.8% in the ≥4-cycles cohort. There was no difference in the rate of optimal debulking between groups ($P = .18$). When comparing both NACT cohorts with the PDS group, the number of cycles was associated with debulking status. The PDS group had a 40.4% R0 rate, which was significantly lower than that in the ≤3-cycles cohort ($P = .006$) and the ≥4-cycles cohort ($P < .001$). The median progression-free interval (PFI) was not different between the 2 NACT cohorts. The median PFI in the ≤3-cycles group was 13.4 months and in the ≥4-cycles group was 7.7 months ($P = .993$). Complete pathologic response was achieved in 3 patients (3.1%), who received 4, 5, and 6 of cycles of NACT, respectively, and 16 patients (16.7%) had microscopic disease of 5 mm or less. The pathologic response was a predictor of PFI, with a median PFI of 34.4 months in the complete pathologic response group, 11.1 in the group with 5 mm or less disease versus 7.3 in the group with more than 5 mm disease ($P = .0002$).

Conclusions: The number of cycles of NACT before IDS did not affect optimal debulking rates or PFI after primary treatment, but resulted in a higher R0 resection rate than PDS. Additionally, pathologic response rates may be a surrogate marker for survival. Prospective study is warranted to better evaluate prognosticators for outcomes in patients treated with NACT.

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Radiation therapy is not a risk factor for sexual dysfunction in women with gynecologic cancers

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Objectives: Sexual health is an important component of quality of life. The evidence as to whether radiation therapy for gynecologic cancers has an impact on sexual health is inconsistent. Vaginal brachytherapy, an underused treatment modality, is thought to have less adverse effects than pelvic external beam radiation therapy (EBRT). This study examines the associations of pelvic EBRT and vaginal brachytherapy with sexual dysfunction.

Methods: A cross-sectional study of women with gynecologic cancers, which used validated instruments to assess sexual dysfunction, found that 41% of women reported decreased sexual function after treatment. A subanalysis examined sexual dysfunction after radiation treatment with pelvic EBRT or vaginal brachytherapy. Sexual dysfunction was measured by change in the Female Sexual Function Index (FSFI) score from before treatment to that after treatment, with significant decline defined as a 5.8-point decrease using a Reliable Change Index Statistic (RCIS). The Pearson X^2 and independent *t* tests were used.

Results: A total of 171 women completed the survey; 35% (n = 60) had radiation treatment, of whom, 73% (n = 44) received pelvic EBRT and 27% (n = 16) received vaginal brachytherapy alone. Women with radiation treatment had similar sexual dysfunction rates as women who did not receive radiation (47% vs 38%). Women who received brachytherapy treatment also had similar sexual dysfunction as women with no radiation (37.5% vs 37.8%). Women undergoing EBRT had similar sexual dysfunction rates as those with brachytherapy and no radiation (50% vs 38% vs 38%, respectively). Women experiencing

sexual dysfunction after radiation treatment were more likely to be younger than 50 years (50% vs 16%; OR 5.4, 95% CI 1.6–18.1). Radiation total dose, location, body mass index, and primary vs recurrent disease status were not predictors for sexual dysfunction in women with radiation therapy.

Conclusions: Treatment with pelvic EBRT or vaginal brachytherapy does not appear to decrease sexual function. Providers should counsel women similarly regarding the risks associated with EBRT and vaginal brachytherapy. A larger study should examine brachytherapy as it becomes a more accepted treatment modality.

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The impact of hyperglycemic intensity on postoperative outcomes for a gynecologic oncology service: A cohort study

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Objectives: To determine the impact of hyperglycemic level and intensity on postoperative outcomes.

Methods: Patients were prospectively entered into a surgical database and postoperative glucose levels were retrospectively retrieved from the medical record. Using hospital-wide surgical outcomes, low-intensity (group 1) and high-intensity (group 2) hyperglycemic thresholds were defined. Group 1 had maximum glucose from 170 to 220 mg/dL, with less than 50% of glucose values between those limits. Group 2 hyperglycemia was defined as 50% or more glucose values above 230 mg/dL, 25% or more values above 240 mg/dL, or any value above 300 mg/dL. Infectious complications were defined as any surgical site infection, pneumonia, urinary tract infection, or sepsis. Noninfectious complications included return to the operating room and venous thromboembolic event. Death within 30 days of surgery was analyzed separately. Postoperative outcomes were compared using the χ^2 test of independence. Mantel-Haenszel adjustments were used. $P < .05$ was considered significant.

Results: We identified 619 patients with complete data who underwent elective surgery with the gynecologic oncology service. Group 1 had 180 patients and group 2 had 26 patients. Group 1 was primarily nondiabetic (59.3%), and group 2 was mostly diabetic patients (68.4%). The rate of infectious complications was 216.7 per 1,000 surgeries among those with group 1 hyperglycemia, 230.8 per 1,000 surgeries among those with group 2 hyperglycemia, and 127.2 per 1,000 surgeries among those with no hyperglycemia. There are increased risks of infectious complications for both group 1 (RR 1.70, 95% CI 1.10–2.64) and group 2 (RR 1.81, 95% CI 0.83–3.96), though group 2 had small patient numbers. The risks of noninfectious complications were significantly elevated for both group 1 (RR 3.80, 95% CI 1.54–9.37) and group 2 (RR 5.84, 95% CI 1.76–19.38). Death was also significantly more common in group 1, but not in group 2. Controlling for diabetes failed to remove significant associations.

Conclusions: Postoperative hyperglycemia is associated with adverse outcomes in gynecologic patients. There are different risks to patients based on hyperglycemic intensity. Continued efforts should be made to control glucose levels in the postoperative period.

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Ovarian cancer patients treated with intraperitoneal/intravenous chemotherapy do not experience increased toxicity at recurrence

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Objectives: Ovarian, fallopian tube, and primary peritoneal cancer (OVCA) patients who receive initial intraperitoneal/intravenous (IP/IV) chemotherapy have greater toxicity than those who receive IV treatment. We investigated whether IP/IV patients also experienced increased toxicity at recurrence compared with those who received IV therapy alone.

Methods: We identified OVCA patients (2005–2015) using our institution's Ovarian Cancer Database and pharmacy records. Eligible patients had complete chemotherapy records for initial treatment and subsequent recurrences. We compared chemotherapy dosages, toxicity, and outcome for IP/IV and IV patients using appropriate statistical tests.

Results: A convenience sample of 67 patients followed for a median of 33.7 months (standard deviation, 29.5) had sufficient chemotherapy data: IV paclitaxel and carboplatin every 21 days (n = 41) and IP/IV chemotherapy (n = 26; 11 IV paclitaxel, IP carboplatin, IP paclitaxel; 11 IV paclitaxel, IP carboplatin; 4 IV paclitaxel, IP cisplatin, IP paclitaxel). IP/IV patients had significantly more dose delays (50% vs 22%, *P* = .017), at least grade 3 neutropenia (62% vs 24%, *P* = .024), thrombocytopenia (19% vs 2%, *P* = .029), or metabolic disturbances (27% vs 2%, *P* = .002) compared with IV patients. At recurrence, both patient groups received a mean of 6 chemotherapy cycles (range, 1–21). Dose delay at recurrence was more common in patients who received initial IP/IV treatment (7% vs 38%, *P* = .003); chemotherapy toxicities were similar for second-line chemotherapy. Both groups received a mean of 3 subsequent chemotherapy regimens (range, 2–7).

Conclusions: OVCA patients treated with IP/IV chemotherapy are more likely to experience initial chemotherapy toxicity; however, they are able to receive a similar number of subsequent chemotherapy regimens and do not experience increased toxicity or dose delay with second-line chemotherapy.

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Gene expression profiling of 389 endometrioid endometrial carcinomas reveals 4 distinct molecular subtypes

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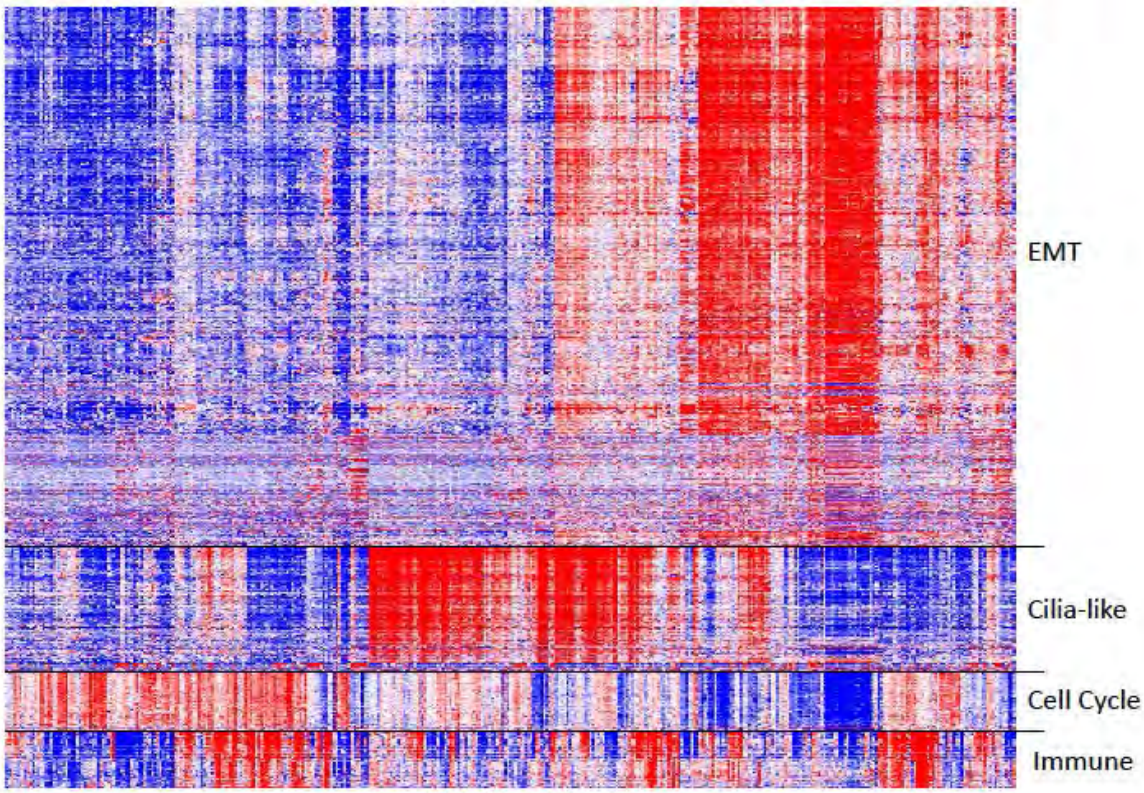
Objectives: Molecular subtyping of gene expression data led to the development of the US Food and Drug Administration–approved breast cancer risk stratification tool, PAM50, and has the potential to enhance efforts to both identify new targeted therapies and personalize treatment regimens based on individual tumor biology profiles for many cancers. We describe the use of coexpression analysis and principal component analysis (PCA) to identify core molecular subtypes of endometrioid endometrial cancer, and examine associations with pathologic characteristics and clinical outcomes.

Methods: We analyzed gene expression for 389 endometrioid endometrial adenocarcinomas collected from the Moffitt Total Cancer Care Consortium (TCC). Sample collection data, pathology reports, and patient medical records were reviewed to confirm that all included samples were collected from primary endometrioid endometrial carcinomas. Coexpression analysis was used to find molecular subtypes based on clustering of genes with high degree of coexpression. The predominant, unifying biology describing each gene cluster was determined using both the PANTHER classification system as well as correlation of known gene-signatures to identify cellular processes associated with signatures derived from each cluster. Tumor samples were labeled according to relative enrichment for each molecular subtype using PCA modeling.

Results: PCA modeling of gene expression in endometrioid endometrial cancer samples yielded 4 unique gene clusters associated with 4 distinct molecular subtypes. Cluster 1 included genes for both extracellular matrix and cell-cell junction gene sets, in addition to pathways such as transforming growth factor beta traditionally associated with epithelial-mesenchymal transition. Cluster 2 included genes related to cilia formation and motility. Cluster 3 included cell cycle–related genes. We identified 2 distinct subclasses of cluster 4—immunoreactive endometrioid carcinomas, B-cell activated and T-cell activated. Sample molecular subtypes were evaluated for correlation with clinical pathologic variables including age, grade, stage, depth of invasion, lymphovascular space invasion, and recurrence.

Conclusions: We present molecular profiling of a large, well-curated dataset of endometrioid endometrial carcinomas.



Footnote: Genes on vertical axis, 389 samples on horizontal axis.

Fig. 1
Heat Map of 4 Molecular Subtypes of Endometrioid Endometrial Carcinomas.

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Epigenetic regulation of FOXA2 in endometrial cancer
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Objectives: *FOXA2* is a pioneer transcription factor that plays an important role in normal development and in adult tissues. The Cancer Genome Atlas project identified *FOXA2* as a "significantly mutated gene" in endometrial cancer, with the majority of mutations being loss-of-function defects. Epigenetic silencing of genes associated with methylation of CpG-rich promoter regions is seen in cancers. We sought to analyze the *FOXA2* promoter region for methylation and to determine the relationship between methylation and mRNA and protein expression.

Methods: DNA from 26 primary endometrioid tumors (both wild-type and *FOXA2* mutant), cell lines (A549, HepG2, RL952, AN3CA), and 9 matched normal blood samples were evaluated using combined-bisulfite restriction analysis (COBRA). Four CpG islands were identified in the 3000-base pair 5' to the transcription start site (TSS) using *EMBOSS Cpgblot*, and COBRA assays were devised. FOXA2 protein and mRNA levels were assessed using Western blot (WB) analysis and quantitative reverse transcriptase–polymerase chain reaction (PCR), respectively.

Results: COBRA analysis for the A549, HepG2, RL952, and AN3CA cell lines revealed a checkerboard pattern of methylation as shown in Table 1. *FOXA2*-expressing lines were largely unmethylated, whereas nonexpressers had more methylation. Island 2 methylation was present in all primary tissue samples and cell lines were tested. Island 1 (most distal to the TSS) showed variable levels of methylation. Blood leukocytes (*FOXA2* nonexpressing) on the other hand were methylated at island 1 in 8 of 9 specimens studied. One-third (9/26) of primary tumors had methylation in island 1. Real-time qPCR shows higher mRNA

expression in mutant tumors than wild-type tumors with relative normalized expression (RNE) values of 3.73 to 0.93 (*P* = .015). Transcript levels were lower in primary tumors with promoter methylation with an average 40% reduction relative to wild-type. In a sampling of wild-type *FOXA2* tumors with protein available, 14 of 15 had expression on WB.

Conclusions: Our data show a component of epigenetic regulation in the CG-rich promoter region of *FOXA2*. This complex 'on/off' pattern of methylation is seen in both primary tumors and expressing cell lines. A clear difference was seen in the methylation of *FOXA2* nonexpressing blood DNA and expressing primary tumor DNA. Further analysis is ongoing to determine true sequencing of CpG islands to assess full methylation status.

Table 1
CpG Island Methylation Grid.

	CpG Island 1	CpG Island 2	CpG Island 3	CpG Island 4
*A549	○	●	○	○
*HepG2	○	●	○	○
**RL952	●	●	●	○
**AN3CA	●	●	○	●

**FOXA2 expressor*
***FOXA2 non-expressor*

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Patient reported clinical outcomes and personal perspectives after risk reducing surgery
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Objectives: Risk-reducing bilateral salpingo-oophorectomy (RRBSO) is recommended for women at increased risk for gynecologic cancers because of a genetic mutation. This procedure is recommended of premenopausal women, which may lead to long-term physical and emotional symptoms. We sought to evaluate the patients' perspective on psychological and physical changes after RRBSO.

Methods: Institutional review board approval was obtained and institutional databases were used to identify patients with a genetic mutation. Eligible patients were unaffected with gynecologic cancer and had undergone RRBSO between 2004 and 2014. Patients were contacted either in clinic or by mail and asked to fill out the questionnaire.

Results: Ninety-one questionnaires were sent, and 42 patients (46%) returned questionnaires. Seventeen patients (40%) were *BRCA1* positive, 21 patients (50%) were *BRCA2* positive, and 4 patients (10%) had Lynch syndrome. The median age was 47 years. Thirty-five (83%) patients felt they were provided with information about expected menopausal symptoms. Twenty-seven patients (61%) reported being informed about possible changes in sexual function. Forty patients answered questions specifically about vasomotor symptoms. Of this group, 19 patients (48%) reported increase in hot flashes, and 23 patients (58%) reported an increase in vaginal dryness. Twenty-five patients (63%) reported worsening sleep and 14 patients (35%) reported an increase in depression. Twenty-six women (62%) were premenopausal before surgery, of whom 15 (58%) reported using a form of hormone therapy after surgery to treat bothersome vasomotor symptoms. Six patients (15%) reported an increase in anxiety, and most patients (93%) reported that their RRBSO relieved their worry about developing cancer. Overall, 41 patients (98%) were content with their decision to undergo risk-reducing surgery.

Conclusions: Most patients who underwent risk-reducing surgery reported no regret and a sense of relief. However, patients did report bothersome clinical symptoms related to surgical menopause as well as worsening anxiety and depression. Our study identified areas for improvement in counseling patients before RRBSO, as well as areas in which to focus treatment after surgery.

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Increasing genetic counseling referral rates after ovarian cancer diagnosis: Improving the quality of ovarian cancer care

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Objectives: Despite guidelines from the National Comprehensive Cancer Network (NCCN) in 2007 and Society of Gynecologic Oncology (SGO) in 2014 recommending universal genetic counseling referral for women with epithelial ovarian cancer (EOC), current rates are 14.5% to 32.3%. We aimed to increase our rate of genetic counseling referral using a toolkit based on the results of a practice gap analysis.

Methods: All new EOC patients evaluated at a single academic tertiary referral cancer center from July 1, 2013, to December 31, 2013, were retrospectively identified, and a chart and electronic order review was performed. Clinicopathologic factors and whether genetic referral, counseling, and testing were completed were abstracted. A practice gap analysis was performed to identify points of intervention, and a multipronged toolkit (Table 1) was built with the goal of increasing genetic referral rates to 75%. The toolkit was implemented in April 2015. Data from new EOC patients evaluated from May 1, 2015, to June 30, 2015, was abstracted to determine postintervention referral rates. This was a quality improvement project involving a multidisciplinary team from oncology, genetics, and nursing.

Results: The preintervention EOC cohort included 83 women with a primary presentation of EOC, with a mean age of 61.8 years at diagnosis. Sixty percent had stage III or IV disease, and serous histology was present in 59%. The postintervention EOC cohort included 23 women with primary EOC presentation, with a mean age of 60.6 years. Stage III or IV disease was present in 82.6%, and 60.9% had serous histology. Forty-one percent (34/83) of women in the preintervention cohort were referred for genetic counseling. After toolkit implementation, the referral rate increased to 91.3% (21/23; $P < .05$, with the Fisher exact test). In the preintervention cohort, 76.5% referred completed genetic counseling, and, of those, 77.0% underwent genetic testing. In the postintervention cohort, to date, 34.8% have completed genetic counseling, and 75% of them have undergone genetic testing thus far.

Conclusions: Implementation of a multipronged toolkit designed to improve adherence to NCCN and SGO guidelines resulted in a significant increase in the genetic counseling referral rate among women with newly diagnosed EOC. Continued maintenance of this practice change is under way.

Table 1

A multipronged, low cost toolkit to increase the genetic counseling referral rate in women with epithelial ovarian cancer.

Toolkit components	Description
Patient education	-Hereditary breast and ovarian cancer risk factor checklist at initial consult -Plain language summary of NCCN guidelines in each EOC hospital dismissal summary -Family history worksheet at hospital dismissal
Staff education	-Education sessions for providers, specialty specific and multi-disciplinary -Genetics referral recommendation template generated for residents/fellows/PAs to use in dismissal summary
Outside primary provider education	-Letter with NCCN guidelines and genetics referral recommendation to referring provider
Appointment coordination	-Coordination of outpatient genetics consult and 6 week post-operative appointment

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Implementation of an enhanced recovery after gynecologic oncology surgery pathway: Improving compliance with key elements of preoperative care

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Objectives: To describe a process change and evaluate compliance with the use of preventive analgesia and deep vein thromboembolic (DVT) prophylaxis in an enhanced recovery pathway (ERP).

Methods: The ERP at MD Anderson Cancer Center was initiated in the Department of Gynecologic Oncology in November 2014. We used the following medications for preventive analgesia: pregabalin (neuropathic pain), celecoxib (nonsteroidal anti-inflammatory), and tramadol (mu-opioid receptor, synthetic opioid). To ensure compliance, an order set was developed to include these medications in all patients undergoing gynecologic surgery provided there were no contraindications. All patients were also written in the order set to receive subcutaneous heparin 5,000 units subcutaneously administered on arrival to the holding area. The order set is completed at the time of surgical posting by a member of the gynecologic oncology team and verified by a staff anesthesiologist before surgery. Medications are administered on arrival in the preoperative holding area by the nursing staff. Training on the new order set was provided before ERP rollout in November 2014 to members of the gynecologic oncology team as well as to the nurses in the preoperative holding area. To improve adherence to the process change, a repeat training was performed for the clinic staff 6 weeks after implementation.

Results: A total of 153 patients were included in the analysis. We estimated the percentage of patients receiving preemptive analgesia components with exact 95% confidence intervals. Since the implementation of our program and the availability of the order set, our compliance for preemptive analgesia and subcutaneous heparin orders in the surgical posting period has been 95% for the first 153 patients (145/153). All patients (153/153) had the order set complete by the time they arrived in holding; anesthesiologists verify the presence of the order set before midnight of the day of surgery. Individual components of the order set were administered to patients if there were no contraindications to administration. This resulted in 95.4% receiving heparin, 90.9% receiving celecoxib, 92.2% receiving pregabalin, and 94.1% receiving tramadol.

Conclusions: Creation of specific order sets can be helpful to improve compliance with ERP. However, as with any new process change, audits of process flow can identify areas for improvement.

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Neoadjuvant chemotherapy and robot-assisted interval cytoreduction in patients with advanced ovarian cancer

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Objectives: To review our preliminary experience with robot-assisted interval cytoreduction after neoadjuvant chemotherapy in the management of ovarian cancer.

Methods: A retrospective chart review was completed on 25 patients who received neoadjuvant chemotherapy with subsequent robot-assisted interval cytoreduction for the treatment of ovarian cancer from 2011 to 2015. Data collected included demographic information, procedures performed, chemotherapy duration and type, operative times, estimated blood loss, hospitalization data, intra- and postoperative complications, and reported disease reoccurrence. Summary statistics were calculated using SPSS statistical software.

Results: The study included 25 patients with a mean age of 62 years and a mean body mass index of 29.24 kg/m^2. Patients initially presented with the following disease symptoms: abdominal ascites (92%), pleural effusion (20%), and deep vein thromboembolism (8%). Patients reviewed received an average of 3.8 cycles of carboplatin/paclitaxel neoadjuvant chemotherapy before undergoing a robot-assisted interval cytoreduction. The mean operative time was 159 minutes, with a mean estimated blood loss of 107 mL. Five (20%) of 25 cases were converted to open procedures because of limited visibility or completion of an Omentectomy. No intraoperative complications were reported and 3 postoperative complications, including 1 case each of the following: crepitus from insufflation, ileus, and chest-tube placement for persistent pleural effusion. Of 25 patients, 17 (68%) underwent a complete cytoreduction, 5 (20%) underwent an optimal cytoreduction, and 3 (12%) underwent a suboptimal cytoreduction. The average hospitalization was 1.79 days and 20 patients (80%) patients received an average of 2.89 cycles of adjuvant chemotherapy after surgery. Seven cases of disease recurrence were recorded.

Conclusions: Robotic surgery after neoadjuvant chemotherapy is not only feasible, but may be preferable to primary cytoreductive surgery in select patients. Larger controlled studies are necessary to further explore this topic.

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Vaginal cuff underdosing is observed across different surgical approaches

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Objectives: Vaginal failures occur after cylinder-based vaginal brachytherapy (VB) for endometrial cancer. It is unknown whether they occur because of inadequate radiation coverage, and whether surgical techniques contribute to restriction of full insertion of the vaginal cylinder. We hypothesized that underdosing occurs in a contemporary cohort of patients undergoing VB, and sought to determine if there were correlations between underdosing and surgical technique.

Methods: Thirty-two patients with endometrial cancer who underwent VB were retrospectively analyzed. Eighty-one T2-weighted magnetic resonance images were evaluated to assess for vaginal cuff (VC) underdosing. The VC was contoured and the volume of VC receiving specified doses was calculated for each patient. The following surgical parameters were obtained from the medical record: surgeon, surgical approach (robotic vs nonrobotic laparoscopic vs open hysterectomy), use of endostitch device, cuff closure method (figure of 8 vs not).

Results: More than two-thirds of patients (68.8%) had VC areas that did not touch the vaginal cylinder. Half of patients (50%) had at least 1 mL of VC that received less than 50% of the intended prescription dose and two-thirds (68.8%) had at least 1 mL of VC that received less than 75% of the prescription dose. For a 7-Gy prescription, the mean minimum dose to the VC was 2.4 Gy or 34% of the intended prescription dose. Underdosing was seen in all surgical approaches, including 1 case with a vaginal closure, and across all surgeons. In some cases, what appeared to be suture material was seen obstructing the vaginal cylinder from being inserted fully to the top of the VC.

Conclusions: In our study, half of our patients had VC areas that received only 50% of the intended dose, signifying significant underdosing. It is unknown whether this will lead to increased rates of vaginal failure, or whether it suggests that some patients are being exposed to excessive doses and toxicity to compensate for anatomic changes across the population. We observed likely suture material blocking the cylinder, but did not identify any clear correlations between surgical approach or surgeon and underdosing. Further investigation is needed to determine whether specific surgical techniques contribute to underdosing.

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Evaluation of resource utilization using time-derived activity-based costing results in more effective processes and cost reduction

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Objectives: Current changes in health care economics have led to a focus on value-based health care. Time-derived activity-based costing (TDABC) is a systematic method to assess personnel utilization and the associated cost in the delivery of medical care. Based on baseline process maps and cost estimates in our outpatient center, cancer surveillance visits (CSVs) were identified as inefficient, lengthy, and high cost. The purpose of this study was to determine if reallocation of personnel was feasible, and if it resulted in lower cost and better value care.

Methods: In 2014, a multidisciplinary team developed process maps for each visit type in the outpatient center. Maps included each step of clinical care from registration to checkout and the personnel associated with that care. Total personnel costs were based on the estimated time spent with each patient and the average salary of the care provider. In September 2014, we instituted an advanced practice provider (APP) independent practice initiative in which CSVs were done by either faculty or APP, no longer both. Billing codes were used to determine the percentage of CSVs seen by APPs only. Patient and staff satisfaction were assessed before and after implementation with validated measures.

Results: At baseline, the estimated patient time and personnel cost for a CSV was 98 minutes and $380.79. The estimated patient time and personnel cost for a CSV with an APP only was 53 minutes and $132.60, resulting in a potential savings of $249 per CSV. Before September 2014, less than 21% were seen by APPs only. After implementation of the initiative, the number of APP-only visits increased each quarter (Q) to 27% in Q1, 38% in Q2, 40% in Q3, and 41% in Q4. The estimated cost

savings based on 4,000 CSVs per year was $354,000. Patient satisfaction remained the same (Press-Ganey). APP and physician engagement/satisfaction increased by 30% (Gallup Employee Survey).

Conclusions: Evaluation of our outpatient clinic using TDABC allowed us to identify low-efficiency, high-cost processes. After implementation of a new process, patient wait times and personnel costs were significantly reduced, resulting in better value care and improved provider satisfaction.

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The good, the bad, and the ugly: Estrogen metabolites and endometrial cancer risk

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Objectives: Obesity is a known risk factor for endometrial cancer (EMCA); however, not all obese women are affected with disease. Biologically, obesity is a surrogate for endogenous estrogen exposure. The exact mechanisms by which endogenous estrogens affect carcinogenesis remain unclear. The metabolism of endogenous estrogen is known to result in carcinogenic and chemoprotective byproducts. We sought to identify a phenotype of estrogen metabolism among EMCA patients that may better predict cancer risk than obesity.

Methods: Urine samples from EMCA patients and benign controls were collected. Fifteen estrogen metabolites (EM) in urine samples were liberated by enzymatic digestion with glucuronidase and sulphatases and concentrated by solid-phase extraction. Known concentrations of standard EMs and samples were dansylated and subjected to liquid chromatography–mass spectrometry analysis using Acquity UPLC and Q-Tof Premier system for separation of molecules at ultra–high pressure for the analysis and quantification. Records were reviewed for clinicopathologic data. Uni- and multivariate logistic regression were used to evaluate the association between EMs and EMCA.

Results: A total of 105 specimen were collected, 90 EMCA cases and 15 benign controls. Median age of the groups was 63 years. Median body mass index (BMI) of the groups was 33 versus 32.3. Sixty-five percent of cases had endometrioid histology. Increased urinary concentrations of estradiol (E2) and 16-hydroxylase metabolite 16-epiestriol were found to be protective of EMCA development (OR 0.570, $P = .039$ vs 0.986, $P = .009$). BMI alone was not independently associated with the presence of EMCA, but the protective association of urinary excretion of E2 and 16-epiestriol remained significant on multivariate analysis, independent of age, race, or BMI. Race did not significantly correlate with disease, but the protective association of E2 was stronger in Caucasian patients (OR 0.564, $P = .0392$).

Conclusions: Obesity is an epidemiologic surrogate for an undefined mechanism of estrogen-induced carcinogenesis. Our data support the hypothesis that particular estrogen metabolites and metabolic pathways may protect against EMCA. Further investigation of the "estrogen metabolome" may allow for the development of a "protective" versus "putative" phenotype that can stratify patients at highest risk for EMCA.

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Resident physicians' contribution to human papillomavirus vaccine uptake: Are residents offering the vaccine to eligible patients?

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Objectives: The goal of the study was to determine if resident physicians are vaccinating eligible patients with the human papillomavirus (HPV) vaccine. A comparison of the primary care specialties in the United States was undertaken to compare utilization of the vaccine, education during training, and foundation of knowledge. Family medicine, internal medicine, pediatrics, and obstetrics and gynecology were compared.

Methods: A 37-point electronic survey was generated using the online software. Program coordinators were asked to share the web link to the survey with their residents. The survey was conducted from August to November 2014.

Results: The survey was completed by 1,549 resident physicians, including 413 pediatric residents, 167 obstetrics and gynecology residents, 579 family medicine residents, and 355 internal medicine residents. For all specialties, 58.9% reported that they always counsel patients to receive the vaccine. Pediatrics residents were the group with the highest number of respondents always recommending the vaccine (82.2%). With regard to education about the HPV vaccine, 63.6% reported receiving it as medical students, but only 39.9% reported receiving formal lectures as residents. A total of 58.5% of residents reported "always" counseling patients to receive the HPV vaccine. This accounted for a wide distribution among specialties. Of the pediatric residents, 82.2% responded that they "always" offer the vaccine, whereas obstetrics and gynecology, family medicine, and internal medicine residents were at 38.6%, 63.5%, and 28%, respectively. When stratifying a response to education received in residency, it was seen that education in residency directly increased rates of "always" offering the HPV vaccine.

Conclusions: Residents have a unique opportunity to capture a subset of patients who may not otherwise have an opportunity to receive the HPV vaccine. As expected, pediatric residents are providing the most HPV vaccines to patients and internal medicine residents the least. Education about the HPV vaccine in resident curriculum is critical to improve the uptake of the HPV vaccine in the United States.

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The increasing use of neoadjuvant chemotherapy for the treatment of epithelial ovarian carcinoma in the United States: A study of practice patterns

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Objectives: In 2010, a randomized controlled trial was published, which showed similar survival outcomes when epithelial ovarian cancer (EOC) was treated with neoadjuvant chemotherapy (NACT) versus primary debulking surgery. Which treatment should be the standard of care has been controversial since the publication of this trial. At present, the use of NACT is still considered to be controversial. We sought to investigate if the use of NACT has changed in the United States since the publication of this trial.

Methods: The National Cancer Data Base was queried for all stage III–IV EOC patients from 1998 to 2012. Chemotherapy sequencing was obtained and validated by comparing days to surgery and chemotherapy along with a dedicated treatment-sequencing field. Univariate analysis was done with the χ^2 test. Independent associations were assessed using binary logistic regression modeling.

Results: A total of 108,007 patients were found to have stage III–IV EOC. Of these patients, 75% had consistent chemotherapy-sequencing data, which were used for analysis. On multivariable analysis, factors associated with increased use of NACT included facilities located in Western states ($P = .001$), higher tumor grade ($P < .001$), increasing comorbidity score ($P < .001$), and older age ($P < .001$). Only Caucasian ethnicity was associated with decreased use of NACT ($P < .001$). The proportion of patients older than 70 years with high comorbidity scores or with stage IV disease has not changed during the study period. NACT use before 2010 was found in 11.9% of patients compared with 23.3% in the 2 years after 2010 ($P < .0001$, OR 2.26, CI 2.15–2.37). NACT use has steadily increased from 2011 to 2012, with utilization rates of 21.5% and 25.3%, respectively.

Conclusions: The use of NACT has increased significantly after the publication of the randomized controlled trial on NACT, even without changes in the patient population. This seemingly rapid adoption of NACT warrants further evaluation, both to validate results and to address concerns regarding overall survival outcomes reported in the 2010 randomized control trial.

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Developing combinatorial approaches for durable cancer treatment

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Objectives: Considerable effort has been extended in testing vaccine platforms in clinical trials. However, the combination of vaccines with traditional modalities like chemotherapy remains largely untested. We show that by monitoring chemotherapy-induced hematopoietic reconstitution kinetics, we were able to time vaccine administration after chemotherapy to optimize its combinatorial efficacy in a murine model.

Methods: BL6 mice were given paclitaxel (TAX), and blood samples drawn and analyzed to monitor for lymphopenia and reconstitution thereof. After establishing the nadir, we administered tumor subcutaneously (EG6 thymoma over the right hindquarter for ease of measurement and fast growth) and devised a treatment strategy of TAX with or without MIS-OVA vaccine, administered at different points along the cycle of lymphocyte nadir and reconstitution. Therefore, the mice were given MIS-OVA, and naïve OT-1 cells were adoptively transferred to provide a means to monitor for T-cell activation and proliferation. They were then split into 3 groups and given the vaccine on day 0, day 7 (during nadir), or day 14 (during reconstitution). The mice were observed for treatment response measurable with tumor size. After establishing the optimal timing, we tested MIS alone versus TAX alone versus MIS + TAX administered at time 0 to tumor-bearing mice to accurately conclude that the effect of tumor shrinkage was because of the vaccination/timing in concert with the TAX, and not any one factor alone.

Results: Flow cytometric analysis of splenic and lymphatic tissue demonstrated significant activation and memory responses. Much higher expansion and activation was noted in the day 0 and day 14 groups, particularly in the day 0 group, with 569,174 activated OT-1 cells recovered versus less than 200,000 from groups B and C mice when analyzing the spleen. Similar effect was noted in the lymph nodes, with 138,825 cells elicited on day 0, 13,964 cells on day 7, and 106,584 total OT-1 cells on day 14. Furthermore, 4 of 5 mice given MIS + TAX were NED 21 days after TAX administration, whereas the other populations had multiple deaths and heavy tumor burden.

Conclusions: The keystone to tumor-specific immunologic treatment will be establishing benchmarks such as vaccination schedules in concert with current adjuvant chemotherapy. Given the strong evidence of memory and activation in group A, and the ease of clinical application, a phase I human clinical trial is both feasible and easy to implement in current clinical models.

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Effects of an olaparib and metformin combination on the AMPK and DNA-damage pathways in ovarian cancer

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Objectives: We previously reported that the combination of olaparib and metformin significantly inhibits the growth of ovarian cancer cell lines carrying the *BRCA1* wild-type allele in vitro and in vivo. Our aim in this study was to identify the mechanism behind the combination's synergistic inhibition of cell growth. We investigated the effect of the 2 drugs on the AMPK and DNA-damage pathways.

Methods: The effect of olaparib and metformin on PARP activation was assayed using a fluorometric activity kit. Two ovarian cancer cell lines, A2780 and SKOV3, were used to determine the effect of the drugs on phospho(p)-AMPK, pACC, and pH2AX with Western blot analysis. Immunohistochemical (IHC) staining of tumor tissues from A2780 and SKOV3 xenografts in nude mice was performed for pACC, H2AX, and SIRT1. ATP and NAD+/NADH levels were estimated with their respective activity kits.

Results: The combination of olaparib and metformin significantly inhibited the growth of *BRCA1* wild-type ovarian cancer cells in vitro ($P < .01$) and in vivo ($P < .01$). Treatment with olaparib induced activation of AMPK pathway in a dose-dependent manner as evidenced by increased pACC, a 33% increase in ATP levels, and a 41% increase in the NAD+/NADH ratio. Olaparib enhanced metformin-induced activation of AMPK in both cell lines, as reflected on the Western blot. This activation of AMPK was also confirmed in xenografts from mice treated with the drug combination. An increase in SIRT1 mRNA expression further supported activation of AMPK in response to olaparib treatment. Olaparib showed a dose-dependent ability to inhibit PARP activity, whereas metformin had no effect. Furthermore, increased pH2AX was detected with Western blot in response to olaparib but not metformin in both cell lines. Paradoxically, IHC revealed decreased pH2AX staining in mice treated with the combination compared with olaparib alone.

Conclusions: The combination of olaparib and metformin acted synergistically to activate the AMPK pathway. Metformin did not have any effect on PARP activity. Differences in pH2AX staining between treatments in the animal model raise the question of whether metformin may alter olaparib-induced DNA damage. This is a subject of ongoing investigation.

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Robotic simulation: Setting benchmarks for the new user and implementation of a trainee curriculum

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Objectives: There is growing emphasis on learning outside of the operating room; however, it is unclear how effective surgical simulation is to a new learner. The goal of this study was to validate scores generated by a robotic simulator by comparing new users with those who have robotic experience. We then sought to determine how many attempts it would take for trainees to accomplish "experienced" status.

Methods: The faculty and trainees at a single institution were asked to participate in a blinded robotic simulator study. For phase 1, each participant completed a total of 9 modules 3 times each. Users were divided into 2 groups based on the prior number of robotic cases performed as primary surgeon: beginner (0–50) and experienced (>50). Comparison was made to determine if the simulator scores accurately reflected surgeon experience. The median scores from phase 1 for the experienced group were defined as the benchmark scores. In phase 2, trainees who did not meet the benchmark score on a specific module were asked to repeat that module until they reached the benchmark score twice and were considered proficient.

Results: Twenty-four surgeons participated in phase 1: 18 beginners and 6 experienced. For all modules, the experienced surgeon received: energy switching 1 (87.5 vs 92.5, $P = .002$) and suture sponge 2 (75.0 vs 87.3, $P = .011$). Thirteen trainees participated in phase 2. In 8 of 9 modules, more than 75% of trainees met proficiency in a median of 3 to 6 attempts, based on the module. The range of attempts was broad. For example, for suture sponge 2, among the 9 (69%) who passed, the number of attempts required to achieve proficiency ranged from 2 to 17. The other 30% were unable to achieve proficiency over multiple attempts.

Conclusions: Scores on the robotic simulator accurately reflected surgeon experience. With repetition, most trainees were able to reach the benchmarks set by the experienced users. Further study is needed to determine the impact of surgical simulation on true intraoperative experience.

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Effect of perioperative blood transfusion on quality of life, progression-free and overall survival in primary treatment of advanced epithelial ovarian cancer: An EORTC ancillary study

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Objectives: To investigate the impact of perioperative blood transfusion on progression-free survival (PFS), overall survival (OS), and quality of life (QOL) in patients with advanced ovarian cancer.

Methods: We performed an ancillary analysis of the European Organization for Research and Treatment of Cancer (EORTC) 55971 trial in which patients were randomized to primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS). Patients included in the per-protocol analysis were stratified by receipt of a perioperative blood transfusion. Demographics, preoperative, and intraoperative variables were compared between transfusion and nontransfusion cohorts. The primary endpoint was OS. Secondary endpoints included PFS and QOL. Clinical significance was defined as a change of 10 points on the EORTC QLQ-C30.

Results: Of the 612 patients included in our analysis, 52.8% received a perioperative blood transfusion. The transfusion cohort was more likely to have had better WHO performance status, undergone PDS, and received more aggressive surgery. There was no difference in PFS in the transfusion versus nontransfusion groups (median 12.6 vs 13.57 months; *P* = .96). There was also no difference in OS in the transfusion versus nontransfusion groups (median 35.2 vs 34.0 months; *P* = .97). Grade 3 and 4 infections were more common in the transfusion cohort than in the nontransfusion cohort (n = 25 [8.0%] vs 4 [1.6%]; *P* = .001). There were no clinically significant differences in QOL between the 2 cohorts at baseline and after transfusion. At the first post-transfusion QOL assessment (third cycle of chemotherapy for PDS and sixth cycle of chemotherapy for IDS), both groups demonstrated QOL improvements and decreased symptom burden for dyspnea and fatigue. Although differences between the transfusion and nontransfusion cohorts were significant over time, the magnitude of change did not differ between the groups.

Conclusions: Perioperative blood transfusions are not associated with changes in PFS or OS in advanced-stage ovarian cancer. However, transfusions are associated with increased perioperative infections with minimal impact on QOL. Given these findings, judicious use of perioperative blood transfusions is warranted.

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18F-FDG PET/CT in the assessment of metabolic response to chemoradiation therapy in locally advanced cervical cancer

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Objectives: To investigate if a ratio of pretreatment and posttreatment standard uptake values (SUVs) measured with fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) has prognostic value in patients with locally advanced cervical cancer treated with primary chemoradiation therapy.

Methods: Two hundred fifty-one cases of locally advanced cervical cancer (FIGO stage IB2–IVA) treated with concurrent chemoradiation therapy were reviewed. 18F-FDG PET/CT parameters including SUVmax and SUVmean were evaluated before treatment and 6 weeks after the end of the treatment. Metabolic response was evaluated with European Organization for Research and Treatment of Cancer guidelines (EORTC), and compared with radiologic response measured with Response Evaluation Criteria in Solid Tumours (RECIST).

Results: Of the patients who received chemoradiation therapy, 195 showed metabolic and radiologic response (69% decrease in SUVmax, 48% decrease in SUVmean). The correlation between radiologic response and metabolic response was significant either with SUVmax or SUVmean (*r* = .25, *P* = .0009; *r* = .15, *P* = .0457, respectively). Kaplan-Meier survival analysis revealed significant differences in the overall and progression-free survival probabilities between the responder and nonresponder groups, based on the EORTC criteria (both *P* < .001), whereas no significant difference was found when this was based on RECIST criteria (*P* = .058, *P* = .088, respectively).

Conclusions: 18F-FDG PET/CT parameters are good prognostic markers of cervical cancer in patients who received concurrent chemoradiation therapy.

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Cervical cancer care in rural America: The impact of distance on outcomes and the role of nonspecialized radiation centers

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Objectives: Locally advanced cervical cancer rates are high in rural Virginia. Patients often travel long distances to be evaluated in a tertiary care center, and may choose to be treated at a local facility. This study sought to characterize the influence of distance from a tertiary care facility on outcomes in cervical cancer patients, and to evaluate the impact of receiving care locally at a nonspecialized center.

Methods: Eligible patients included those with cervical cancer at all stages who were referred to a single tertiary care facility for consultation between 2003 and 2012. Shortest travel routes from patients' homes to the facility were determined with an online mapping website. Socioeconomic, demographic, and clinical data were collected.

Results: A total of 281 patients met the criteria for inclusion. Of these, 70% received chemoradiation as part of their primary therapy, and all patients received the brachytherapy portion of treatment at the tertiary institution. The majority of patients (61%) lived more than 50 miles away from the tertiary care center (15% of patients lived <30 miles away; 20%, 30–50 miles away; 44%, 50–100 miles; and 21%, >100 miles). Race, insurance type, and employment status did not vary by distance from the tertiary care center, nor did nodal status at diagnosis. Twenty-six percent of patients had a recurrence or never achieved a complete response; distance was not a predictor of recurrence. Twenty-nine percent of patients divided their therapy, receiving chemotherapy plus external beam radiotherapy (EBRT) at a local facility and brachytherapy at the tertiary center. The average distance to the tertiary center did not differ between those who divided their care and those who traveled for EBRT. The recurrence rate for patients who received all chemoradiation therapy at the tertiary care center was 9%, compared with 31% among those who divided their care across centers ($P = .04$).

Conclusions: Despite similarities in socioeconomic characteristics, nodal status at presentation, and distance from the tertiary care center, cervical cancer patients who divided their care and received chemotherapy and EBRT at a local, nonspecialized center had higher recurrence rates. This suggests improved oncologic outcomes when radiation care for cervical cancer is centralized, and supports the development of services to facilitate patients' ability to receive all care at a single specialized center regardless of distance from their home.

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CommunityRx: Connecting health care to self-care for women with breast and gynecologic cancer on Chicago's South Side

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Objectives: To describe patterns of comorbidity and referrals to community-based self-care resources for women with breast or gynecologic cancer.

Methods: CommunityRx, a program developed with a US Centers for Medicare & Medicaid Services Health Care Innovation Award (1C1CMS330997-01-00), employed local youth to conduct an annual census of all businesses and organizations (www.mapscorps.org). These data fed an e-prescribing system, HealtheRx, which was integrated with electronic medical records to generate personalized referrals to community-based resources. Breast and gynecologic cancer ontologies generated referrals for physical activity, nutrition resources (classes, fresh food), and mental health services nearest to patients' homes. A HealtheRx was generated at every visit for women with breast and gynecologic cancer from the 16–ZIP code demonstration area (58% of households at less than 200% of the federal poverty level) presenting at 1 of 33 health care sites. This analysis uses data from 5 health care sites (4 ambulatory clinics and 1 emergency department).

Results: Between July 2014 and May 2015, 2,318 HealtheRxs were generated for 1,021 women (ages 20–102 years) with a history of breast (69%) or gynecologic (13% cervical, 6% ovarian, 3% uterine, 9% other) cancer. In addition to cancer, 87% of patients also received self-care referrals for 2 or more comorbidities, most commonly hypertension (77%), back pain (51%), and diabetes (35%) (Table 1). The availability of self-care resources by patient home ZIP code was: 0 to 4.2 fitness classes per patient (mean 0.9); 0.2 to 13.0 nutrition resources per patient (mean 2.0), and 0 to 11.5 mental health sites per patient (mean 2.3). For 81% of HealtheRxs generated, all listed referrals were located in the patient's home ZIP code.

Conclusions: CommunityRx connected patients to local self-care resources for cancer and chronic disease management goals. Self-care resources can be found in high-poverty communities, though resource availability varied widely by ZIP code in this urban area.

Table 1
The HealtheRx generated referrals for cancer survivors that connected them to resources for their cancer type and for any comorbidities listed in the electronic medical record. This table shows the prevalence of comorbidities among women with cancer by cancer type.

Comorbidities	% of all cancer in study (n=1021)	% of women with breast CA (n=708)	% of women with ovarian CA (n=63)	% of women with cervical CA (n=131)	% of women with uterine CA (n=27)
Hypertension	77	79	65	65	89
Back pain	51	50	49	44	70
Diabetes	35	36	38	29	63
Hyperlipidemia	34	35	32	29	37
Mental Health	23	23	30	24	26
Obesity	22	20	27	24	11
Anemia	21	19	30	27	30
Asthma	18	17	25	18	15
Depression	14	14	16	13	11
Substance abuse	9	8	8	13	11
COPD	7	8	5	8	7
Smoking	7	6	5	10	11

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Pharmacological focal adhesion kinase (FAK) inhibition suppresses cisplatin-resistant human ovarian carcinoma growth
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Objectives: FAK is a cytoplasmic protein tyrosine kinase promoting ovarian cancer tumor growth and metastasis. Phase I and II clinical trials are testing small molecule inhibitors to FAK in different cancers. Determination of cancer cell susceptibility to FAK inhibition is an important yet undefined parameter. We test the hypothesis that elevated FAK activity contributes to the growth of aggressive cisplatin (CP)–resistant ovarian cancer.

Methods: Growth of paired CP-sensitive (A2780 and OVCAR10) and CP-resistant (A2780-CP and OVCAR10-CP) human ovarian cells was evaluated in adherent, nonadherent, and methylcellulose spheroid culture in the presence or absence of 100 nM concentration of FAK inhibitor (FAKi). Quantification of cancer stemlike cells (CSCs) and cell cycle analyses was performed using flow cytometry for aldehyde dehydrogenase (ALDH) activity and propidium iodide DNA staining, respectively. Cell apoptosis was evaluated with Annexin-V and (7-aminoactinomycin D) 7-AAD staining. Changes in cellular protein expression were determined with quantitative immunoblotting. Intraperitoneal tumor growth in mice was evaluated for combined inhibitory effects of CP and FAKi administration.

Results: FAK tyrosine phosphorylation and CSC protein markers were elevated in CP-resistant cells, which was reversed by FAKi addition. On immunoblotting, the levels of the transcription factor OCT4, ALDH, and the cell surface protein N-cadherin were increased in CP-resistant cells. FAKi addition selectively prevented CP-resistant cell growth as spheroids. The combination of FAKi with CP exhibited a combined effect on the CP-resistant cells, with significant decreases in spheroid and tumor growth compared with either agent alone. When comparing the percentage of CSCs with flow cytometry, FAKi addition dramatically reduced the ALDH-positive cell population in both parental and CP-resistant cells. This was associated with a G1 cell cycle growth phase arrest, decreased cyclin D protein expression, but not increased cell apoptosis.

Conclusions: CSCs are implicated in the molecular mechanisms of cisplatin-resistance, and we find that FAK inhibition prevents CP-resistant CSC growth. Because FAKi therapy is well tolerated with limited adverse events, our results support further testing of FAKi in either primary or recurrent settings of CP-resistant ovarian cancer.

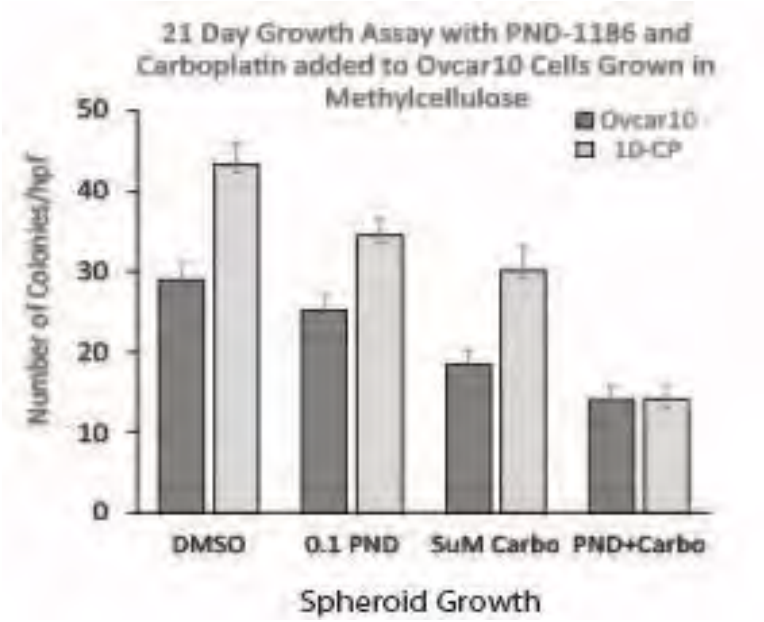

Fig. 1
21-Day Growth Assay with PND-1186 and Carboplatin Added to Ovcar10 Cells Grown in Methylcellulose.

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Should ovarian preservation be considered for women younger than 60 years with endometrial carcinoma?
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Objectives: To investigate whether the age at diagnosis for patients with endometrioid adenocarcinoma (EC) has decreased over time.

Methods: Using the 18 registries of the Surveillance, Epidemiology and End Results (SEER) database, the frequency with which women were diagnosed with endometrioid adenocarcinoma of the uterus was evaluated from 1980 to 2010. Patients were stratified by age, stage, and year of diagnosis. A user-defined variable was created to separate women, based on age, into less than 60 years and 60 years or older. The annual proportion of women less than 60 years of age was calculated and evaluated using a regression line model. The proportions were separated by decade and the means were compared using one-way analysis of variance.

Results: The SEER database included 42,352 women younger than 60 years and 53,027 women of age 60 years or older who were diagnosed with EC from 1980 to 2012. Currently, the proportion of women diagnosed who are younger than 60 years is 0.4399 (44%), compared with 0.5601 (56%) among those aged 60 years or older. This proportion has continued to rise steadily since 1980, at which time only 20% of women diagnosed were younger than 60 years. Since then, the risk of being

diagnosed before age 60 years has increased significantly with each decade ($P < .0001$). Over the duration of the study period, regardless of age, the incidence of adnexal metastasis did not change ($P = .982$).

Conclusions: As demonstrated in this study, the proportion of women diagnosed with EC who are younger than 60 years has risen significantly over time. Though standard of care dictates bilateral oophorectomy, there is no consensus on the practice of ovarian preservation in these young women. This has become increasingly important, given the decreasing age at diagnosis, worsening obesity pandemic, and the known cardiovascular benefits conferred by ovarian retention, particularly in this young population. Our finding of a stable proportion of adnexal metastases in both age groups over time makes it essential to consider all associated risks and benefits. Reconsideration of the current standard of care may be appropriate as the number of these young patients with endometrial carcinoma continues to rise.

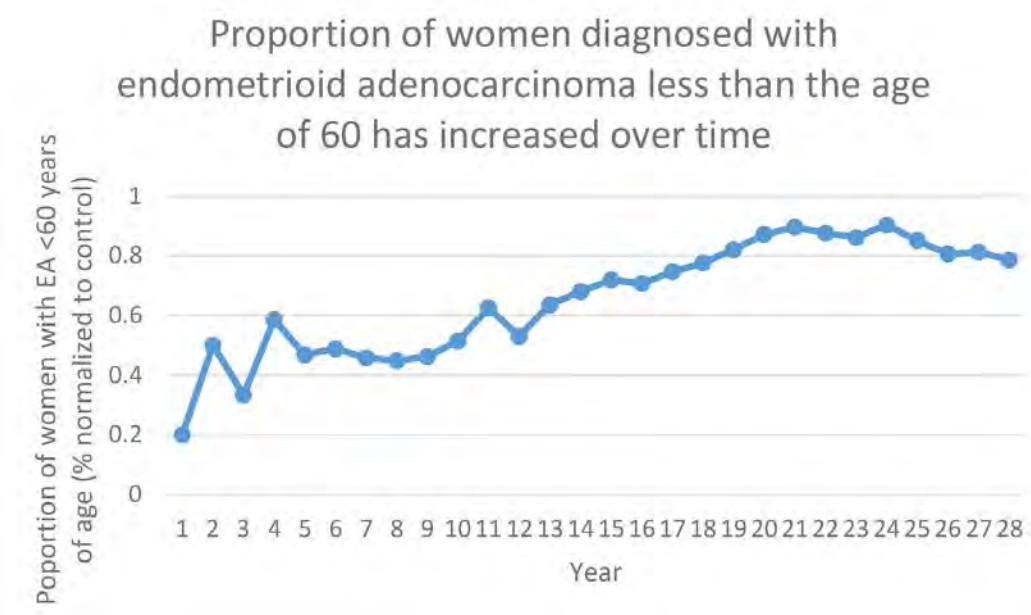

Fig. 1
Proportion of women diagnosed with endometroid adenocarcinoma less than the age of 60 has increased over time.

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486 - Poster
Malignant Brenner tumor of the ovary: A population-based study
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Objectives: Only 1% of Brenner tumors are diagnosed as malignant (MBT), making these rare tumors difficult to study and the literature sparse. This study aims to be the first population-based investigation of demographic and survival outcome data in patients with this rare tumor.

Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried from 1973 to 2012 to perform a retrospective analysis of women diagnosed with MBT of the ovary. Survival rates were determined using SEERStat and the Kaplan-Meier method, and 95% confidence intervals were calculated. Survival rates were then determined by age, race, stage, laterality, disease spread, and treatment type.

Results: A total of 200 women in the SEER database were diagnosed with MBT of the ovary between 1972 and 2012. Of these, 164 (82%) were white, 21 (10.5%) were black, 3 (1.5%) were American Indian/Alaskan Native, and 12 (6%) were Asian/Pacific Islander. Thirty women (15%) were diagnosed before age 50 years and 170 (85%) were diagnosed at age 50 years or later. Patients with MBT ranged in age from 30 years to more than 85 years, most commonly being diagnosed between the ages of 65 and 69 years. Fourteen women (30%) were diagnosed after age 85 years. The 5-year survival rate of

the entire cohort was 55.6% (95% CI 48.1–62.4). When determined by race, 5-year survival rates were found to be lower in African American women (36.2%; 95% CI 20.4–54.0) and highest among Whites at 58.3% (95% CI 50.9–66.4). Comparison by age showed 5-year survival improved in those younger than 50 years (75.3%) compared with those 50 years or older (57.3%). Women were most commonly diagnosed with stage I disease (42%), having a 5-year survival of 87.2% (95% CI 57.5–96.7). Survival of patients with stage IV disease at 5 years was 27.7%. Bilateral tumors were found in 33 women (16.5%), having a lower 5-year survival rate of 37.2% (95% CI 20.4–54.0). Survival rates were also found to decrease with distant disease ($P <$ .0001) and improve with surgical treatment ($P <$ .007).

Conclusions: MBT remains a rare disease about which we know little. Factors associated with better survival include age less than 50 years, white race, lower stage, unilateral and localized tumor, and surgical treatment. This study provides the first population-based description of this neoplasm in the literature. It is our hope that characterizing the demographic and epidemiologic factors of this cohort will provide some insight into the behavior of these rare tumors and improve patient outcome.

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487 - Poster

The evaluation of combined chemotherapy plus radiation therapy in an elderly advanced-stage endometrial cancer cohort

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Objectives: Optimal adjuvant therapy for advanced endometrial cancer has not been well defined. Chemotherapy is commonly administered as single-modality treatment at stages III and IV to avoid toxicities associated with radiation therapy. Yet there remain proponents of combined chemotherapy plus tumor-directed radiation therapy in advanced-stage disease to reduce both local and distant recurrence risk. Data showing improved outcome with combined-modality treatment are limited. We therefore sought to evaluate the effect of chemotherapy plus radiation therapy in an advanced endometrial cancer cohort.

Methods: We selected a cohort of stage III and IV endometrial cancer patients previously identified as part of a retrospective study using the Surveillance, Epidemiology and End Results (SEER) registries and Medicare claims files. Data were included on 2,987 patients who were diagnosed with endometrial cancer between 2007 and 2009 and who received a hysterectomy. Only patients with stage III and IV disease who received chemotherapy were included. Cox proportional hazards regression models were used to determine the impact of radiation therapy on overall survival.

Results: We identified 233 stage III and IV endometrial cancer patients who underwent primary surgical resection followed by adjuvant chemotherapy. Radiation therapy was administered to 63 patients (27%). The mean survival for radiation patients was 32.7 months versus 26.3 months for nonradiation patients (P = .003). In multivariate analysis, after adjusting for age, stage, grade, diabetes, obesity, hypertension, Charlson score, and hysterectomy type, radiation therapy was not independently associated with improved overall survival (HR 0.54, 95% CI 0.21–1.02, P = .06).

Conclusions: In this select cohort of advanced-stage endometrial cancer patients, overall survival appears improved in patients who received both chemotherapy and radiation therapy. Although there is a trend toward improved survival with radiation therapy, it does not reach statistical significance on multivariate analysis. These findings should be further evaluated in a larger cohort.

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Alkyl–lysophosphatidic acid and ovarian cancer cell growth inhibition

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Objectives: Lysophosphatidic acid (LPA) is a family of bioactive phosphoglycerides that are abundant in the malignant ascites of women with advanced epithelial ovarian cancer. Ester-linked acyl-LPA is the dominant species of LPA in malignant ascites, and is well documented to promote ovarian cancer cell proliferation, survival, and invasion. Alkyl-LPA, which has an ether linkage between the fatty acid chain and glycerol, is a minor species of LPA that is present in malignant ascites of women with

advanced EOC. Our objective was to characterize the novel finding of ovarian cancer cell growth inhibition with exposure to Alkyl-LPA and to determine the mechanism of action of that growth inhibition.

Methods: A series of in vitro experiments were performed with multiple established ovarian cancer cell lines. CyQUANT cell proliferation assays, cell cycle analysis with flow cytometry, Western blot analysis of components of the apoptotic cascade, and LIVE/DEAD assays were performed on cells exposed to 10 μM and 100 μM Alkyl-LPA for 24 and 48 hours. A pilot xenograft mouse experiment was performed. Nude mice were injected with SKOV3ip1Luc cells and then given daily intraperitoneal injections with 200 μL of 100 μM Alkyl-LPA or Acyl-LPA in BSA for 6 weeks.

Results: ID8ip2, IGROV, OVAR8, and SKOV3ip1 cell lines demonstrated dramatic growth inhibition with in vitro exposure to 10 μM and 100 μM alkyl-LPA. Cell cycle analysis of OVCAR8 and SKOV3ip1 cells exposed to alkyl-LPA demonstrated a significant increase in the sub-G1 cell population as well as a significant increase in red fluorescence with exposure to ethidium in the LIVE/DEAD assay, another indicator of cell death. Poly ADP ribose polymerase (PARP) cleavage was also noted, indicating apoptosis as a possible mechanism of cell death. Preliminary evidence from the mouse experiment indicated a trend toward less tumor burden with Alkyl-LPA exposure; however, this was not statistically significant.

Conclusions: Lipid metabolism is altered in malignant cells. The production of ether-linked lipids was previously associated with more aggressive cell behavior. Our data demonstrate that exposure to Alkyl-LPA induces cell death in a subset of ovarian cancer cells in vitro. Elucidating pathways responsible for Alkyl-LPA–induced ovarian cancer cell death may lead to the identification of potential therapeutic targets.

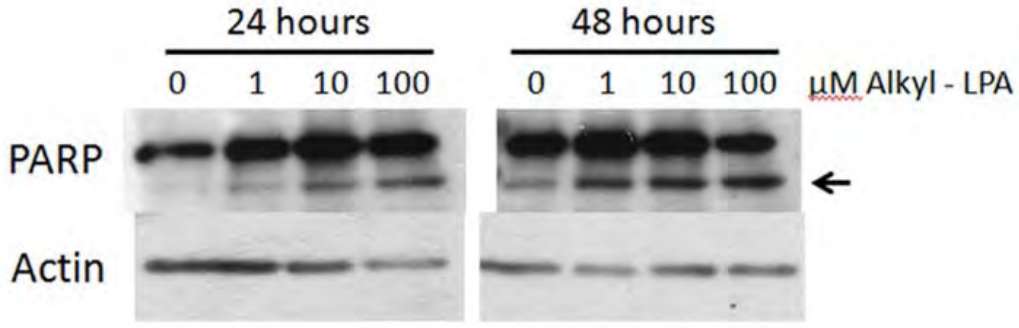

Fig. 1
OVCAR8 Cells Exposed to Alkyl-LPA.

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489 - Poster
Positive predictors of inherited cancer susceptibility among women with ovarian and endometrial cancer
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Objectives: This study assessed potential factors influencing the likelihood of a positive result in ovarian and/or endometrial cancer patients undergoing hereditary cancer multigene panel testing (MGPT).

Methods: A total of 4,511 ovarian and/or endometrial cancer patients (3,043 with ovarian, 1,227 with endometrial, and 241 with both) were identified from a cohort of more than 41,000 individuals undergoing MGPT at 1 clinical diagnostic laboratory. Rates of pathogenic and likely pathogenic alterations (mutations) were calculated and comparisons were made using the Fisher exact test, based on the available clinical and demographic information from test requisition forms.

Results: Among ovarian and endometrial cancer patients, 13.2% and 12.2%, respectively, harbored a mutation in 1 or more of the genes analyzed, as listed in Table 1. Mutation rates were higher among non-Caucasians (15.0%) than Caucasians (12.6%), but the difference was not significant ($P = .1$). Among mixed-ethnicity women, 20.3% carried a mutation ($P = 0.007$ vs Caucasians). Other ethnicities were examined and not found to significantly influence the likelihood of a mutation. Women diagnosed with either ovarian or endometrial cancer before age 50 years were not significantly more likely to have positive results than women diagnosed at age 50 years or later ($P = .3$ for ovarian cancer, $P = .08$ for endometrial cancer). Women

diagnosed between ages 40 and 59 years had the highest rate of mutation (16.3%). More than one-third of women tested (n = 1,593) had more than 1 primary cancer, including 5.3% with both ovarian and endometrial cancer. Among probands with both ovarian and endometrial cancer, mutation rates were lower (10.8%) than those with only 1 cancer (11.8%), though this difference was not significant ($P = .3$). Mutations were significantly more common (15.7%, $P = .03$) among those with other combinations of multiple primaries, and mutation rates were highest (19.1%, $P = .0001$) among probands with 3 or more primary cancers.

Conclusions: Among ovarian and endometrial cancer patients referred for MGPT, positive results were more prevalent among women of mixed ethnicity, those diagnosed in their 40s and 50s, and those with additional primary cancers, suggesting that the likelihood of positive results may be influenced by ethnicity, age at diagnosis, and the presence of multiple cancers.

Table 1
Genes Tested and Positive Results Identified.

	% of Individuals Tested with Pathogenic or Likely Pathogenic Alteration		
Gene	**Ovarian Cancer**	**Endometrial Cancer**	**Ovarian & Endometrial Cancer**
BRCA1	4.22	1.19	0.91
BRCA2	2.69	1.11	0.46
CHEK2	1.89	2.43	2.45
MSH6	0.91	3.27	3.91
BRIP1	1.17	0.40	0.62
MSH2	0.40	2.16	1.74
RAD51C	1.09	0.00	0.00
APC	0.53	0.96	0.00
ATM	0.62	1.06	1.23
PALB2	0.54	0.93	0.61
PMS2	0.34	0.96	0.43
RAD51D	0.59	0.00	0.00
MLH1	0.10	1.12	0.00
PTEN	0.31	0.48	0.00
NBN	0.33	0.13	0.62
TP53	0.30	0.14	0.00
CDKN2A	0.00	0.48	0.00
RAD50	0.29	0.00	0.00
NF1	0.23	0.00	0.00
MUTYH*	0.08	0.44	0.00
MRE11A	0.13	0.13	0.00
SMAD4	0.27	0.00	0.00
BARD1	0.08	0.13	0.00
CDH1	0.00	0.09	0.00
EPCAM	0.03	0.00	0.00

*Carriers were not included.

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Comparison of treatment and survival between carcinosarcoma and serous epithelial ovarian cancer

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Objectives: Carcinosarcoma of the ovary is a rare histologic subtype of ovarian cancer. Most survival data are based on small cohort studies. We queried a large national database to compare outcomes in patients with ovarian carcinosarcoma with those in patients with serous epithelial ovarian cancer (sEOC).

Methods: The ovarian dataset of the National Cancer Data Base was queried for all patients with sEOC and carcinosarcoma. Low-grade sEOCs were excluded from the analysis. Overall survival was estimated with the Kaplan-Meier method, univariate comparisons were made with log-rank tests, and multivariable analysis was performed using Cox proportional hazards modeling. All tests were 2-tailed, with the significance threshold set at $P < .05$.

Results: A total of 97,133 patients met inclusion criteria, of whom, 2,861 (2.9%) were diagnosed with carcinosarcoma. The median age was 67 and 63 years for carcinosarcoma and sEOC, respectively ($P < .001$). Lymph node assessment was performed in 49% in both groups. Positive lymph nodes were found in 32% and 46% of the patients with carcinosarcoma and sEOC, respectively ($P < .0001$). Patients with carcinosarcoma and sEOC presented with advanced-stage disease 76% and 82% of the time, respectively. In carcinosarcoma, 85%, 9%, 4%, and 3% of patients were White, African-American, Hispanic, and Asian, respectively. In sEOC, 86%, 7%, 5%, and 3% were Caucasian, African-American, Hispanic, and Asian, respectively. Median survivals for patients with stage I, II, III, and IV carcinosarcoma were 72, 37, 19, and 12 months, respectively. Median survivals for patients with stage I, II, III, and IV sEOC were 170, 95, 40, and 24 months, respectively. Differences in survival rates were significant for every stage ($P < .0001$). Chemotherapy was used in 75% of patients with carcinosarcoma. Survival benefit was seen with chemotherapy at all stages except stage I ($P = .787$ for stage I, $P < .0001$ for stage II–IV). Stage, comorbidities, age, use of chemotherapy, and nodal positivity were all associated with survival on both univariate and multivariable analysis.

Conclusions: Carcinosarcoma of the ovary has an extremely poor prognosis. Median survival is at least 50% lower for all stages compared with sEOC. No survival benefit for chemotherapy was seen in stage I disease, but this may be limited by the small cohort size. Further evaluation is warranted in this group.

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Margin status of conization specimen obtained by see-and-treat strategy and 3-step strategy

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Objectives: To evaluate the margin status of conization specimens based on treatment strategy.

Methods: A retrospective review was performed for patients who underwent conization at a single institution from January 2003 to August 2012. The patients were divided into 2 groups depending on whether they had undergone a punch biopsy before conization or not (the "see-and-treat" group or the "3-step" group). The final histologic results of the 2 groups were compared.

Results: Of the 862 patients, 694 women were in the see-and-treat group (cervical intraepithelial neoplasia [CIN] grade 1, 159 [22.9%]; CIN 2, 87 [12.5%]; CIN 3, 207 [29.8%]; invasive carcinoma, 76 [10.9%]) and 168 women were in the 3-step group (CIN 1, 14 [8.3%]; CIN 2, 31 [18.4%]; CIN 3, 68 [40.4%]; invasive carcinoma, 33 [19.6]). There was no significant statistical difference in the rate of cone margin involvement between the see-and-treat and 3-step groups. However, cone margin involvement rate of patients with CIN 3 was higher in the see-and-treat group (26.5% in the see-and-treat group vs 11.7% in the 3-step group, $P = .012$).

Conclusions: Without inspection of cervical precancerous lesion, the patients with CIN 3 treated with the see-and-treat strategy are more likely to show positive cone margin involvement. Therefore, physicians should follow the 3-step strategy when treating patients with high-grade squamous intraepithelial lesion.

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The time interval of adjuvant radiation therapy is influenced by the primary surgical technique used in treatment of endometrial cancer

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Objectives: There is evidence that time intervals between diagnosis, surgery, and initiating adjuvant treatment in endometrial cancer (EC) influence patient outcomes. Further, we know that surgical techniques may influence recovery time and interval between surgery and adjuvant treatment. In this study, we sought to evaluate the impact of surgical techniques on the time interval for initiating radiation therapy (RT).

Methods: Between 2010 and 2012, we identified 84,008 patients in the National Cancer Data Base (NCDB) with stage I-III EC who underwent primary surgery and for whom the surgical technique was known. Among these, 16,066 patients received adjuvant RT and constitute the study cohort. The stage distribution was 56% stage I, 11.8% stage II, 21.8% stage III, and 10.4% stage unknown. The types of RT delivered were as follows: external beam (ERT) 27.6%, combined ERT and brachytherapy (BRT) 16.1%, BRT alone 55%, RT unknown 1.3%. For this study, the time interval between surgery and RT was defined as 1.5 months (1–45 days), 2 months (1–60 days); and 3 months (1–90 days).

Results: The frequency of surgical technique used was 39.6% robotic, 15.3% laparoscopy, and 45.2% open surgery. The number of patients undergoing any lymph node surgery (LNS) was 82.9%. LNS using robotic, laparoscopy, and open procedure was 87.2%, 78.3%, and 80.6%, respectively ($P < .0001$). We observed statistically significant differences in the comorbidity score with a score of 2 or higher in open cases (5.76) compared with (4.08) in robotic cases ($P < .0001$). The observations are summarized in Table 1. Patients in whom RT was initiated within 6 weeks were more likely to have had an open surgical procedure ($P < .0001$). However, at 2 months, the RT utilization was similar across all surgical techniques. At 3 months, more patients undergoing the robotic procedure had initiated adjuvant RT ($P < .0001$). The stage distribution was comparable across all 3 time intervals.

Conclusions: To the best of our knowledge, this is the first report in a large database to have studied the impact of surgical technique on the time interval for initiating adjuvant RT. Our follow-up study will report the impact of this time interval on clinical outcomes.

Table 1

	Adjuvant radiation therapy		
Surgery procedure	**<45 days (1.5 mo)**	**<60 days (2 mo)**	**<90 days (3 mo)**
Robotic	18.2%	42%	71%
Laparotomy	18.5%	46%	72%
Open	21.06%	42.5%	67.6%

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The Society of Gynecologic Oncology Clinical Outcomes Registry: A single-institution experience

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Objectives: The Society of Gynecologic Oncology (SGO) Quality and Outcomes Committee established the Clinical Outcomes Registry (COR) to collect data on the treatment of women with gynecologic cancers. The objective of this study was to query the registry to identify quality parameters in women diagnosed with uterine cancer at our institution. We also assessed the ability of the registry to create functional data reports for our institution.

Methods: All patients with newly diagnosed uterine cancer who underwent surgery between January 1, 2014, and December 31, 2015, were entered into the registry. Data were abstracted from the electronic medical records according to the COR operation and follow-up forms. Patient demographics, surgical approach, adjuvant therapy, and 6-month follow-up data were entered. Quality parameters included minimally invasive surgery (MIS), postoperative complications, and use of adjuvant therapy.

Results: After an initial query of the online database using the report wizard, an Excel file was created with all relevant data points. Several issues were discovered that limited interpretation of the data including a True/False data entry method. We created an institutional data sheet that was completed by the Advertek statistical team. Data entry was complete for each data element 75.0% to 99.6% of the time. We identified 248 patients with uterine cancer. The median age was 62.5 years, 67.7% of patients were white, and the median body mass index was 35.3 (range, 18.3–83.3). One hundred sixty-one patients (64.9%) were at stage I, and 42 patients (16.9%) were at stage III/IV disease. Endometrioid histology was seen in 151 patients (60.9%). One hundred fifty-six patients (62.9%) had a robotic hysterectomy, 62 (25.0%) had a laparotomy, and 15 (6.0%) had a laparoscopic hysterectomy. Seven cases were converted from MIS to laparotomy. One hundred thirty-six patients underwent a pelvic lymphadenectomy (LND) and 64 underwent a para-aortic LND. Seventy-nine patients received chemotherapy, with the majority receiving paclitaxel/carboplatin. Twenty patients received radiation therapy. Thirty-two patients had a 30-day postoperative complication; of these, 78.1% were grade 2. Four patients were admitted to the intensive care unit and 1 patient required a reoperation. Nine patients developed a wound infection and 2 patients had deep vein thromboembolism/pulmonary embolism. There was one mortality. At last follow-up, 93.4% patients were alive.

Conclusions: With some operational improvements, the SGO COR can be used by a single institution to monitor the quality of care provided to patients with uterine cancer. This initial query activity also highlights the importance of auditing the data by either SGO or the individual institutions, and accurate data entry can be improved with additional training. In the future, comparing individual physician or institutional data with national benchmarks may identify areas for quality improvement.

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494 - Poster

Obesity is a key prognostic factor in stage IIIC-IV ovarian cancer diagnosed prior to 65 years of age: A 10-year survival analysis

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Objectives: Approximately half of all women diagnosed with advanced ovarian cancer (AOC) are older than 65 years. According to the World Health Organization (WHO), age 65 years is the cutoff for distinguishing elderly individuals from younger people. The aim of our study was to analyze, in a 10-year retrospective series, the age-related differences in perioperative outcome of cytoreductive surgery for stage IIIC-IV ovarian cancer, identifying the clinicopathological factors associated with poor prognosis in those aged 65 years and older and those younger than 65 years.

Methods: One hundred and sixty-seven patients with primary epithelial AOC FIGO stage IIIC-IV underwent cytoreduction and platinum-based chemotherapy from 2005 to 2015 at Sapienza University of Rome. Patients aged 65 years and older and those younger than 65 years were compared regarding surgical outcome, clinicopathologic variables, and prognosis.

Results: Median age was 56 years (19–87 years); 50 patients (29.9%) were aged 65 years or older, whereas 117 patients (70.1%) were younger. Forty-two percent (21/50) in the elderly group and 39% (46/117) in the younger group received neoadjuvant chemotherapy followed by interval debulking surgery. No residual tumor was seen in 82% of elderly patients and in 82.9% of younger patients (P =1.00). No differences between the 2 groups were found in terms of mean operative time, mean number of blood units transfused, mean postoperative stay, and number of patients requiring intensive care unit stay. The perioperative complication rate was 16% in the elderly group and 10.2% in younger patients (P = .029). The 60-day postoperative mortality was 2% for the elderly group and 0.8% for younger patients (P = .079). The 10-year progression-free survival was 11.6% versus 15.2% (P = .84) and the 10-year overall survival (OS) was 16.9% versus 21.4% (P = .60) in elderly and younger patients, respectively. Multivariate analysis showed that age itself was not a prognostic factor for OS but in those younger than 65 years, obesity had an independent prognostic significance (HR 4.97, CI 95% 2.09–11.83), together with residual tumor, which was also confirmed to be an independent prognostic factor in elderly patients (HR 7.33, CI 95% 1.30–41.33).

Conclusions: Elderly patients with AOC showed a similar perioperative outcome compared with younger pts. In patients aged 65 years or older, residual tumor was the only variable affecting significantly survival, whereas in those younger than 65 years, obesity was also found to be an independent prognostic factor for OS.

Table 1
Univariate and Multivariate Analysis for OS in pts<65y.

OVERALL SURVIVAL				
	UNIVARIATE ANALYSIS		MULTIVARIATE ANALYSIS	
	HR (95%CI)	P	HR (95%CI)	P
PREOPERATIVE ALBUMIN (<3 VS > 3 g/dl)	1.01 (0.30-3.36)	0.97		
PREOPERATIVE HGB	0.99 (0.97-1.01)	0.34	0.99 (0.97-1.01)	0.56
BMI (≥30 vs <30)	**2.79 (1.32-5.89)**	**0.007**	**4.97 (2.09-11.83)**	**<0.001**
Type of first line treatment (NACT vs PDS)	1.96 (0.90-4.25)	0.90		
ASA Score (3 vs 1-2)	3.75 (0.5-28.09)	0.20	2.93 (0.36-23.59)	0.31
ECOG PS (2-3 vs 0-1)	2.16 (0.89-5.24)	0.90		
RT	**2.09 (1.37-3.17)**	**0.001**	**8.84 (2.88-27.17)**	**<0.001**
Peri-operative complications (yes vs no)	1.75 (0.72-4.23)	0.21	1.21 (0.46-3.15)	0.68
Histotype (serous vs others)	1.25 (0.48-3.25)	0.65		
Grading (3 vs 1-2)	1.74 (0.83-3.62)	0.14	1.32 (0.58-3.00)	0.51

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Feasibility and accuracy of 99mTc SPECT-MRI fusion for the selective assessment of sentinel nodes in cervical cancer patients with unsuspicious <10-mm lymph nodes

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Objectives: In early-stage cervical cancer, lymph nodes smaller than 10 mm on magnetic resonance imaging (MRI) are commonly considered unsuspicious and are not assessed further. To reduce the rate of missed metastases, we hypothesize that it may be beneficial to focus solely on sentinel lymph nodes (SLN), rather than indiscriminately reviewing all nodes. Here, we aim to explore the feasibility and accuracy of ^{99m}Tc single photon emission computed tomography (SPECT)-MRI fusion for the selective assessment of SLNs.

Methods: Stage IA1 to IIB1 cervical cancer patients were consecutively included when they presented at our tertiary referral center (2011–2015). Only patients with less than 10 mm short axis lymph nodes on MRI were included. All underwent an SLN procedure with preoperative SPECT-CT–based SLN mapping. By creating fused datasets of SPECT and the workup MRI (Fig. 1), SLNs could be identified on MRI with accurate correlation to the histology of each SLN. An experienced radiologist, blinded to histology, reviewed all SPECT-MRIs and scored morphologic SLN parameters on a standardized form. Multivariate regression and receiver operating curves (ROC) were used to analyze the parameters against the SLN status.

Results: In 75 women, 136 SLNs could be analyzed, of which 13 contained metastases (9.6%, 8 patients). Three parameters: short-axis diameter, long-axis diameter, and absence of sharp demarcation significantly predicted metastases with a diagnostic odds ratio (adjusted for MRI quality) of 1.42 (95% CI 1.01–1.99), 1.28 (95% CI 1.03–1.57), and 7.55 (95%CI: 1.09–

52.28), respectively. The area under the curve of the ROC combining these parameters was 0.75 (95% CI 0.56–0.93). Interestingly, gadolinium enhancement patterns, cortical thickness, round shape, or SLN size compared with the nearest non-SLN, showed no association with metastases (*P* 0.06–0.80).

Conclusions: In cervical cancer patients, selective SLN evaluation is feasible and can noninvasively diagnose metastases in nodes that by conventional evaluation would be considered unsuspicious.

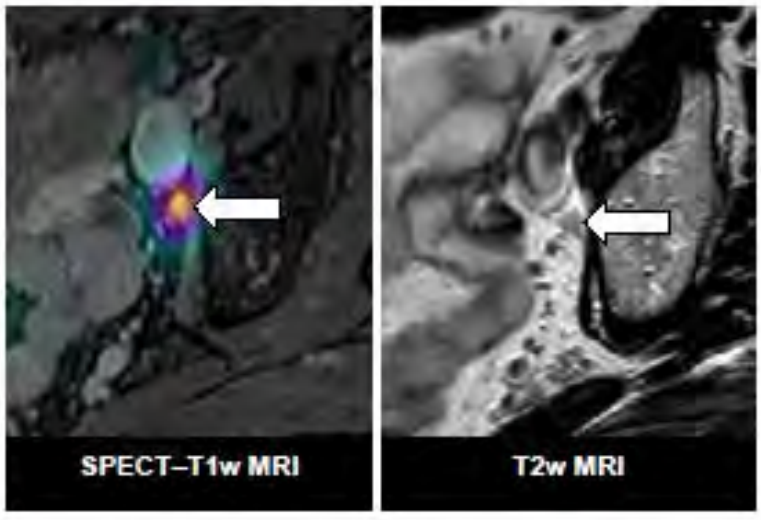

Fig. 1

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496 – Poster
Combining a symptom index, CA-125, and HE4 (triple screen) to detect ovarian cancer in women with a pelvic mass

Withdrawn at author's request

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497 - Poster
The first T2-weighted imaging of stage IB1–IIB cervical cancer by ultra–high field 7.0T MRI using an endorectal antenna: A prospective feasibility study
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Objectives: Magnetic resonance imaging (MRI), particularly T_2-weighted sequences, is increasingly used in the workup of cervical cancer. To improve image quality, we studied the feasibility of T_2-weighted cervical cancer imaging on an ultra–high field MRI system. Central to our approach is the use of an endorectal antenna which should boost the signal-to-noise ratio (SNR), thus allowing higher resolutions. Here, we will assess patient discomfort and quantify its SNR increase.

Methods: We conducted a prospective feasibility study on 18 stage IB1 to IIB histology-proven cervical cancer patients who had a routine 1.5T MRI in their workup. All underwent an additional 7.0T MRI, which included transversal, sagittal, and oblique T_2-weighted turbo spin echo sequences. Seven external transmit and receive dipole antennas were positioned around the pelvis, and combined with a single in-house built endorectal monopole antenna. Its signal receive optimum was placed 6 to 10 cm beyond the anodermal transition. Patients scored the level of discomfort related to the antenna from 0 (none whatsoever) to 10 (worst imaginable).

Results: Patients had a median age of 39.3 years (range, 25.3–66.5 years) and stage IB1 (n = 9), IB2 (n = 3), IIA (n = 1) or IIB (n = 5) cervical cancer. Discomfort of antenna placement and removal was low with a median score of 1 (range 0–5) and 0 (range 0–2), respectively. The endorectal antenna increased the SNR at the cervix by a mean factor of 1.8 and by 2.9 in a 30-mm radius from the antenna. No adverse events occurred related to the antenna. Although some artefacts remained, 7.0T MRI was found qualitatively superior to the clinical 1.5T MRI. In Figure 1, the corresponding oblique (perpendicular to the cervical canal) T_2-weighted slices of an exemplary stage IIB2 patient are shown.

Conclusions: We demonstrated the feasibility and qualitative increase of cervical cancer imaging with 7.0T MRI. The use of an endorectal antenna is well tolerated and enables optimal signal capture with a substantial increase in SNR.

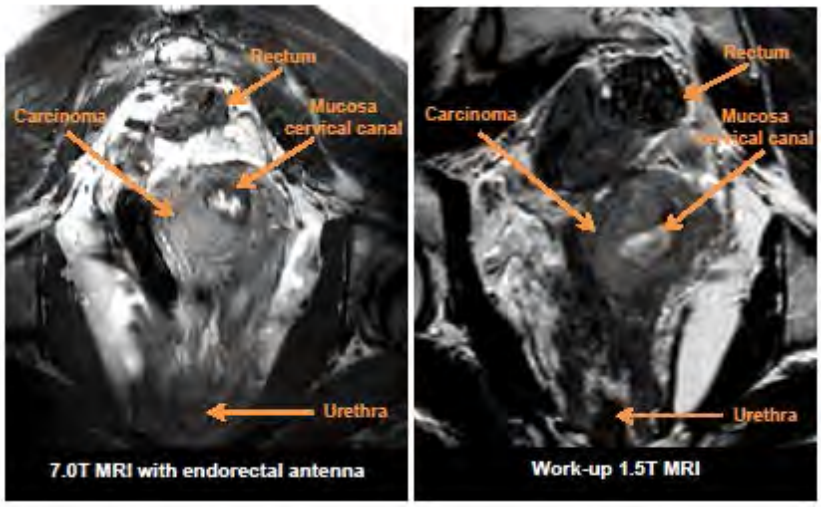

Fig. 1