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The Society of Gynecologic Oncology (SGO) proudly hosts its 46th Annual Meeting on Women’s Cancer® from March 28 to 31, 2015, in Chicago, home of the SGO.

On behalf of the Society, I sincerely appreciate those who have generously contributed their time in support of the scientific curriculum presented at this year’s meeting, the premier educational event for the subspecialty of gynecologic oncology that attracts more than 1800 gynecologic oncologists and health professionals from around the world.

This supplement to Gynecologic Oncology contains the abstracts selected for presentation at the 2015 Annual Meeting. We received 755 submissions for abstracts and 47 for surgical films. After careful discussion and deliberation, the Program Committee selected 39 for Scientific Plenary presentations, 12 for Focused Plenary presentations, 9 Surgical Forums, 99 for Featured Poster presentations, and 360 for Poster presentations. Much of the research addresses novel approaches to precision surgery, molecular drivers of gynecologic cancers, and global health issues.

This year’s abstracts were reviewed and selected by the 2015 Annual Meeting Program Committee, chaired by Nadeem Abu-Rustum, MD. Members of this year’s committee are:

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*In addition to the Program Committee, these members served on the Steering Committee to help guide synthesized education delivered to attendees.

I hope that, while reviewing the following abstracts included within this supplement, you are both educated and inspired. This body of scientific research embodies what the Society truly represents: an organization that embraces the highest quality of new research findings, innovative patient care models and advanced surgical techniques that continue to contribute toward SGO’s vision to eradicate women’s cancers.

Again, on behalf of the SGO, I thank the member volunteers whose dedicated time assisted in the Annual Meeting’s overall success.

Richard R. Barakat, MD
2014–2015 SGO President
Randomized phase II trial of maintenance autologous tumor cell vaccine (FANG™) following clinical complete response (cCR) in stage III/IV ovarian cancer: Preliminary results

J. Oha, M. Barvea,b, E.A. Grosenc, B.A. Finea, T.P. Heffernand, C.M. Matthewsa, C.A. Stringer, E.C. Koon, H.M. Goodman, E.L. Fleming, L.R. DeMars, M.S. Bergmanc, N. Senzerb,g, J. Nemunaitisa,b, g,h.
a Texas Oncology, P.A., Dallas, TX, USA, b Mary Crowley Cancer Research Centers, Dallas, TX, USA, c Cancer Care Northwest, Spokane, WA, USA, d North Texas Gynecologic Oncology, Dallas, TX, USA, e Florida Cancer Specialists, West Palm Beach, FL, USA, f Dartmouth Hitchcock Medical Center, Lebanon, NH, USA, g Gradalis, Inc., Dallas, TX, USA, h Medical City Dallas Hospital, Dallas, TX, USA

Objectives: Phase I evaluation of FANG vaccine (granulocyte macrophage colony-stimulating factor [GMCSF]/bi-shRNAi furin vector transfected autologous tumor cells) demonstrated safety; confirmed both GMCSF transgene expression and knockdown of furin and consequent transforming growth factor-b1 and b2 expression; showed T-cell activation per gamma interferon (IFN)–enzyme-linked immunospot assay (ELISPOT); and resulted in a longer-than-expected survival duration correlated with ELISPOT “turn on.” These findings justified phase II testing (Senzer et al. Mol Ther. 2012; Senzer et al. Vaccines and Vaccination. 2013). The majority of women with stage III/IV ovarian cancer who achieve cCR with standard of care (SOC) (the combination of debulking surgery and chemotherapy) relapse within 2 years. The objective of this trial was to determine regression-free survival difference in a 2:1 randomized phase II trial.

Methods: This 2:1 randomized phase II open-label trial of FANG used tumor harvested at the time of surgical debulking. Stage III/IV ovarian cancer patients achieving cCR following primary surgical debulking and chemotherapy were entered to undergo vaccine construction. Given the high recurrence rate and subsequent progression seen with frontline SOC treatment, we initiated a randomized phase II study of maintenance FANG vaccination following initial debulking/chemotherapy. Patients received $1.0 \times 10^7$ cells/intradermal injection once a month for up to 12 doses or were followed as per SOC, i.e., without maintenance therapy. Key endpoints included safety, immune response (RFS), and progression.

Results: Twenty-one evaluable (ELISPOT-negative following confirmed cCR) patients were randomized, 14 of whom had received at least 1 FANG injection and 7 of whom had been randomized to No FANG treatment. This trial design allowed for control group crossover at time of progression. No toxic effects were observed. A higher rate of IFN ELISPOT response was elicited in this prior chemotherapy-naive population in comparison to that achieved in phase I trial (92% vs. 50%). Mean and median RFS of the FANG and No FANG patients are shown in Fig. 1.

Conclusions: Based on safety, the high rate of T-cell activation in this population in correlation, and the marked delay in time to regression, randomization was discontinued and phase III testing involving 382 evaluable patients is being pursued.
2 – Scientific Plenary

Restoration of apoptosis in serous cancer stem cells sensitizes them to platinum therapy resulting in tumor eradication

D.M. Janzen, E. Tiorin, J.A. Salehi, J. Li, A. Soragni, D.S. Eisenberg, M. Pellegrini, S. Memarzadeh.

UCLA David Geffen School of Medicine, Los Angeles, CA, USA, University of California, Los Angeles, Los Angeles, CA, USA

Objectives: Relapse of disease in serous cancer patients despite normal examination findings and serum CA-125 values suggests that there is a platinum-resistant CA-125-negative tumor population. Using primary human serous carcinomas, we recently discovered that the CA-125-negative tumor cell population contains serous cancer stem cells (SCSC) that efficiently initiate tumors and undergo multi-lineage differentiation in vivo. Importantly, the CA-125-negative SCSC were carboplatin-resistant due to antiapoptotic signaling. Pathways involved in evasion of apoptosis in the SCSC included high expression of inhibitor of apoptosis proteins (IAPs) and inactivation of TP53. In this investigation, we evaluated whether therapy-resistant SCSC could be sensitized to carboplatin by restoration of apoptosis.

Methods: Two strategies were used to enhance apoptosis in serous tumors: 1) degradation of IAPs using the United States Food and Drug Administration-approved drug Birinapant and 2) restoration of TP53 function using a novel structure-based peptide (P53AI) that prevents TP53 aggregation. Mice harboring xenografts derived from either a primary human cancer cell line or control cell lines with known drug sensitivities were treated with the combination of carboplatin (50 mg/kg biw ×9) or P53AI (15 mg/kg ip qd ×28). For comparison, the efficacy of each drug was examined as a single agent.

Results: The combinatorial therapeutic approaches using either Birinapant or P53AI in conjunction with carboplatin were the only treatments capable of eliminating all serous tumors cells, including the SCSC (Fig. 1). Combination therapies were also the only treatments that provided durable response, evidenced by no relapse of tumor after cessation of treatment (Fig. 1). While tumors shrank in response to carboplatin, this therapy enriched for the SCSC, and tumors grew robustly after cessation of treatment. Under the conditions tested, neither Birinapant nor P53AI alone was able to eliminate tumors completely.

Conclusions: Our results demonstrate that complete eradication of serous cancers requires therapeutic targeting of the SCSC. This goal can be achieved simply by adding an additional therapy tailored to the patient’s tumor that can sensitize the SCSC to carboplatin.

3 – Scientific Plenary

A phase III randomized controlled clinical trial of carboplatin and paclitaxel alone or in combination with bevacizumab followed by bevacizumab and secondary cytoreductive surgery in platinum-sensitive, recurrent ovarian, peritoneal primary and fallopian tube cancer

Gynecologic Oncology Group 0213


The University of Texas MD Anderson Cancer Center, Houston, TX, USA, University of Buffalo, Buffalo, NY, USA, University of Cincinnati, Cincinnati, OH, USA, Memorial Sloan Kettering Cancer Center, New York, NY, USA, Johns Hopkins Kimmel Cancer Center, Baltimore, MD, USA, The University of Oklahoma, Oklahoma City, OK, USA, Sungkyunkwan University School of Medicine, Seoul, South Korea, Saitama Medical University International Medical Center, Hidako-Shi, Japan, UC Irvine Medical Center, Orange, CA, USA, The Ohio State University, James Cancer Hospital, Columbus, OH, USA

Objectives: Platinum-based doublets have become a standard of care for women with platinum-sensitive recurrent ovarian cancer. The roles of secondary surgery and addition of bevacizumab have yet to be defined as neither intervention has demonstrated an improvement in overall survival (OS) in a phase III trial. GOG0213 sought to examine both.

Methods: GOG0213 is a bifactorial, randomized, phase III trial with two primary objectives: (1) to examine the role of bevacizumab (15 mg/kg) in combination with paclitaxel (175 mg/m²) + carboplatin (AUC5) followed by bevacizumab maintenance and (2) to examine the role of secondary cytoreduction before initiation of chemotherapy. The primary endpoint for both objectives is overall survival (OS). Secondary endpoints include: safety/toxicity, allergy (HSR), progression-free survival (PFS), and intervention-dependent quality of life (Qol). Three strata were prospectively defined: participation on Objective 2, Platinum-free interval (6–12, >12 months) and prior bevacizumab treatment. Chemotherapy randomization for Objective 1 terminated on 8/29/11 and matured for OS (n = 214 events in the control arm) on 11/5/2014. Enrollment for Objective 2 is ongoing.

Results: Six hundred seventy four patients (n = 567, Objective 1; n = 107, Objectives 1 and 2) were randomized to CT (n = 374) or CTB (n = 374) and evaluable for OS. Equal representation in each treatment strata were prospectively de

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doi:10.1016/j.ygyno.2015.01.004

doi:10.1016/j.ygyno.2015.01.003
4 — Scientific Plenary

**Definition of a dynamic laparoscopic model for the prediction of incomplete cytoreduction in advanced epithelial ovarian cancer:**

**Proof of concept**

M. Petrillo, G. Vizzielli, F. Fanfani, V. Gallotta, F. Cosentino, V. Chiantera, G. Scambia, A. Fagotti, Catholic University of the Sacred Heart, Milan, Italy, St. Maria Hospital, University of Perugia, Terni, Italy

**Objectives:** To develop an updated laparoscopy-based model to predict incomplete cytoreduction (RT > 0) in advanced epithelial ovarian cancer (EOC) after the introduction of upper abdominal surgery (UAS).

**Methods:** The presence of omental cake, peritoneal extensive carcinomatosis, diaphragmatic confluent carcinomatosis, bowel infiltration, stomach and/or spleen and/or lesser omentum infiltration, and liver superficial metastasis were evaluated by staging laparoscopy (S-LS) in a consecutive series of 234 women with newly diagnosed AEOC undergoing laparoscopic PDS after S-LS. Parameters showing a specificity > 75%, positive predictive value (PPV) ≥ 50%, and negative predictive value (NPV) ≥ 50% received a 1-point score, with a point added when the accuracy was > 60% in predicting incomplete cytoreduction. A total predictive index value was tabulated for each patient by summing positive features. The overall discriminating performance of the LPS-PI was finally estimated by receiver operating characteristic curve analysis.

**Results:** PDS with no gross residual disease was achieved in 135 cases (57.5%). Among them, UAS was required in 72 cases (53.3%) for a total of 112 procedures, and approximately 25% of these patients received bowel resection, excluding rectosigmoid resection. We observed a very high overall agreement between S-LS and laparoscopic findings, which ranged from 74.7% for omental cake to 94.8% for stomach infiltration, and liver superficial metastasis were evaluated by staging laparoscopy (S-LS) in a consecutive series of 234 women with newly diagnosed AEOC undergoing laparoscopic PDS after S-LS. Parameters showing a specificity ≥ 75%, positive predictive value (PPV) ≥ 50%, and negative predictive value (NPV) ≥ 50% received a 1-point score, with a point added when the accuracy was ≥ 60% in predicting incomplete cytoreduction. A total predictive index value was tabulated for each patient by summing positive features. The overall discriminating performance of the LPS-PI was finally estimated by receiver operating characteristic curve analysis.

**Conclusions:** S-LS is an accurate tool in predicting complete PDS in women with AEOC. The updated LPS-PI showed improved discriminating performance, with a lower rate of inappropriate laparoscopic explorations at the established cut-off value of 10.

**doi:** 10.1016/j.ygyno.2015.01.006

5 — Scientific Plenary

**Correlation between surgeon’s assessment of residual disease and findings on postoperative pre-treatment computed tomography scan in women with advanced stage ovarian cancer reported to have undergone optimal cytoreduction:**

**An NRG Oncology/GOG study**

R.N. Eskander, J. Kauderer, K.S. Tewari, R.E. Bristow, R.A. Burger, UC Irvine Medical Center, Orange, CA, USA, Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, University of California, Irvine, Irvine, CA, USA, University of Pennsylvania, Philadelphia, PA, USA

**Objectives:** To assess the effectiveness of tumor microsatellite instability (MSI) and methylation analysis combined with immunohistochemistry (IHC) in predicting germline mutations in DNA mismatch repair (MMR) (Lynch syndrome [LS]) in endometrial cancer patients.

**Methods:** This is a post-trial ad hoc analysis of Gynecologic Oncology Group protocol 218, a phase III randomized clinical trial that evaluated the impact of bevacizumab in primary and maintenance therapy for patients with newly diagnosed advanced-stage ovarian cancer. All patients underwent imaging of the chest/abdomen/pelvis to establish a postsurgical baseline prior to the initiation of chemotherapy. Information collected on the surgical status form, pretreatment summary form, and surgical reporting form was used to compare surgeon’s operative assessment of RD to pretreatment imaging. Descriptive statistics were reported and proportional hazards regression (HR) was used to determine the impact of RD on progression free and overall survival.

**Results:** A total of 1718 patients were randomized and enrolled. Surgical outcome was described as optimal (RD ≤ 1 cm) in 639 patients. Twelve patients were excluded because they did not have a baseline CT scan, leaving 627 participants for analysis. The average interval from surgery to baseline scan was 26 days (range: 1–109 days). In 251 cases (40%), the postoperative scan was discordant with surgeon assessment, demonstrating RD > 1 cm in size, with 69.2% of patients having ≥ 2 target lesions (total of 719 target lesions reported). RD > 1 cm was most commonly identified in the right upper quadrant (28.4%), retroperitoneal lymph nodes (28.2%), and the left upper quadrant (10.7%). Patients with RD > 1 cm on pretreatment CT (discordant) exhibited a significantly greater risk of progression (HR 1.30; 95% CI 1.08–1.56; P = 0.0059). No difference in overall survival was noted (HR 0.99; 95% CI 0.80–1.23; P = ns).

**Conclusions:** Among patients reported to have undergone optimal cytoreduction, 40% were found to have lesions > 1 cm on postoperative CT imaging. Although postoperative inflammatory changes and/or rapid tumor regrowth could account for the observed discordance, the distribution of RD favoring the upper abdomen and retroperitoneum may indicate underestimation by the operating surgeon.

**doi:** 10.1016/j.ygyno.2015.01.007

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**Scientific Plenary II**

Saturday, March 28, 2015

Moderator: Noriaki Sakuragi, MD, Hokkaido University School of Medicine, Sapporo, Japan

Laura Jean Havrilesky, MD, Duke University Medical Center, Durham, NC, USA

6 — Scientific Plenary

**Clinical implications for MSI, MLH1 methylation analysis and IHC in Lynch screening for endometrial cancer patients:**

An analysis of 940 endometrioid endometrial cancer cases from the GOG 0210 study

C.C. Billingsley, D.E. Cohn, D.G. Mitchel, R. Broadus, N. Ramirez, H. Lankes, S. Ali, F.J. Backes, L.M. Landrum, P.J. Goodfellow, The Ohio State University, Columbus, OH, USA, Washington University School of Medicine, St. Louis, MO, USA, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Gynecologic Oncology Group Tissue Bank, Biopathology Center, Research Institute at Nationwide Children’s Hospital, Columbus, OH, USA, Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, Roswell Park Cancer Institute, Buffalo, NY, USA, The Ohio State University, James Cancer Hospital, Columbus, OH, USA, The University of Oklahoma, Oklahoma City, OK, USA

**Objectives:** To assess the effectiveness of tumor microsatellite instability (MSI) and methylation analysis combined with immunohistochemistry (IHC) in predicting germline mutations in DNA mismatch repair (MMR) (Lynch syndrome [LS]) in endometrial cancer patients.

**Methods:** This is a post-trial ad hoc analysis of Gynecologic Oncology Group protocol 218, a phase III randomized clinical trial that evaluated the impact of bevacizumab in primary and maintenance therapy for patients with newly diagnosed advanced-stage ovarian cancer. All patients underwent imaging of the chest/abdomen/pelvis to establish a postsurgical baseline prior to the initiation of chemotherapy. Information collected on the surgical status form, pretreatment summary form, and surgical reporting form was used to compare surgeon’s operative assessment of RD to pretreatment imaging. Descriptive statistics were reported and proportional hazards regression (HR) was used to determine the impact of RD on progression free and overall survival.

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**doi:** 10.1016/j.ygyno.2015.01.007

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cancer patients and to determine the relationship between tumor phenotype and family cancer history.

**Methods:** Tumors from women enrolled in Gynecologic Oncology Group (GOG) 0210 were evaluated for MMR protein expression by IHC in a CLIA-approved laboratory. MSI and MLH1 methylation were performed using multiplexed polymerase chain reaction and pyrosequencing. Family history data were abstracted from GOG 0210 questionnaires. Germline testing was performed for a subset of subjects (47) using ColoSeq in a CLIA-approved laboratory.

**Results:** Tumor MMR status was determined for 940 cases for which family cancer histories were provided. Molecular features consistent with defective DNA MMR were seen in 38% of tumors. Among those, MLH1 methylation and tumor MSI+ (consistent with epigenetic silencing of MLH1) were seen in 238 (66%) cases. The remaining 120 cases with MSI+ and/or an IHC defect (loss of MSH2, MSH6, PMS2, or MLH1) with no MLH1 methylation suggest mutation in one of the DNA MMR genes and increased risk for germline mutation. Based on the molecular typing, cases were assigned to one of three categories: MMR normal, sporadic MMR defect (methylation), or possible MMR mutation. Women with a tumor MMR defect but lacking MLH1 methylation were significantly younger and thinner than the rest of the population. (P = 0.015 and P = 0.001). ColoSeq revealed LS mutations in 20 of 47 “probable MMR mutation” cases investigated (42%), with a predicted overall 5% rate of LS in cases with MSI+ and/or an IHC defect and a 2.1% (20/940) rate of LS for the entire cohort. Notably, two of nine tumors with no IHC abnormality (MSI+, unmethylated) harbored germline mutations, one in PMS2 and one in MSH6.

**Conclusions:** MSI analysis coupled with MLH1 methylation studies should be considered as part of screening programs for LS. Screening that relies on IHC alone will fail to detect approximately 10% of LS cases. Family history alone does not reliably predict women at risk for LS. Our findings, combined with the increasing recognition of the importance of MLH1 methylation analysis as a triage for genetic testing, supports a combined IHC and DNA analysis approach to LS screening.

**doi:** 10.1016/j.ygyno.2015.01.008

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**7 — Scientific Plenary**

**The association of Medicaid coverage status at the time of cancer diagnosis in women with gynecologic malignancies: A population-based study**

**K.M. Doll**, E.L. Barber, K. Meng, E. Basch, P.A. Gehrig, W.R. Brewster, A.M. Meyer, A. University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, bUniversity of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

**Objectives:** Lack of health insurance is associated with poor health outcomes. Because of the income requirements for Medicaid, low-income patients only qualify for Medicaid after cancer diagnosis. It is unclear if postdiagnosis enrollment protects against poor health outcomes. We examined the timing of Medicaid enrollment in relation to gynecologic cancer diagnosis and its association with clinical outcomes.

**Methods:** The North Carolina Central Cancer Registry (NCCCR) was used to identify women diagnosed with a gynecologic cancer from 2003 to 2008. Data were linked to Medicaid enrollment files. Inclusion criteria were a gynecologic cancer diagnosis, exclusive enrollment in Medicaid, and age younger than 65 years. Timing of Medicaid enrollment was defined as “pre- and post-” or “only post-“ cancer diagnosis. Primary outcomes were stage at diagnosis and all-cause mortality, which were evaluated with multiple logistic regression, Cox proportional hazard models, and Kaplan Meier curves. Age, race, geography, disease stage, and disease site were covariates.

**Results:** Of 16,770 women diagnosed with gynecologic cancer, 650 met study criteria. Mean age was 47 years, 62% were White race, and 61% resided in metropolitan areas. Nearly half (46%) had early-stage disease. Disease site distributions were cervical (43%), uterine (31%), ovarian (20%), and vulvar/vaginal (6%). In logistic regression adjusting for all covariates, patients with postdiagnosis enrollment had an increased probability of advanced-stage disease (odds ratio [OR] 2.34, 95% CI 1.64–3.34). Women enrolled in Medicaid only after cancer diagnosis also had increased mortality compared to those with prior coverage (Fig. 1). This was driven by the disparate survival between enrollment groups within cervical and uterine cancers. When stratified by cancer site, later stage at diagnosis was the primary mediator of the mortality difference between enrollment groups for all disease sites.

**Conclusions:** Timing of Medicaid enrollment is associated with gynecologic cancer outcomes. Women enrolled only after diagnosis had later stage disease and increased mortality. Low-income populations who do not qualify for Medicaid until after cancer diagnosis may face disparate outcomes due to delayed access to care.

**doi:** 10.1016/j.ygyno.2015.01.009

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**8 — Scientific Plenary**

**A randomized double-blind phase III trial comparing vintafolide (EC145) and pegylated liposomal doxorubicin (PLD/Doxil®/Caelyx®) in combination versus PLD in participants with platinum-resistant ovarian cancer (PROCEED) (NCT01170650)**

**A.M. Oza**, I.B. Vergote, L.G. Gilbert, Lucy, P. Ghatage, A. Lisyankaya, S. Ghamande, S.K. Chambers, J.A. Arranz, D.M. Provencher, P. Bessette, A. Ammon, J. Symanowski, R.T. Benson, R.W. Naumann, R. Clark. aPrincess Margaret Hospital, Toronto, ON, Canada, bUniversity Hospital Leuven, Leuven, Belgium, cMcGill University, Montreal, QC, Canada, dTom Baker Cancer Centre, Calgary, AB, Canada, eSt. Petersburg City Oncology Hospital, Saint Petersburg, Russia, fGeorgia Regents University, Augusta, GA, USA, gUniversity of Arizona Cancer Center, Tucson, AZ, USA, hHospital General, Madrid, Spain, iCentre Hospitalier de l’Université de Montréal, Montreal, QC, Canada, jUniversity of Sherbrooke, Quebec, QC, Canada, kRambam Medical Center, Haifa, Israel, lLevine Cancer Institute, Charlotte, NC, USA, mMassachusetts General Hospital/Harvard University, Boston, MA, USA, nEndocyte, Inc., Dover, DE, USA

**Fig. 1. Mortality after gynecologic cancer diagnosis for women <65 by timing of medicaid enrollment, 2003–2008.**
Objectives: The folate receptor (FR) is overexpressed in many cancers, including platinum-resistant ovarian cancer (PROC), and is known to be a negative prognostic factor. Etfalolate, a folate conjugate, binds Tc-99m to detect FR+ lesions on single-photon emission computed tomography scans. Vintafolide, a folate–vinca conjugate, targets FR+ cancers. In the phase II PRECEDENT study, vintafolide + PLD improved progression-free survival (PFS) over PLD (HR 0.381; 95% CI, 0.172 to 0.845; P = 0.013) in FR(100%) PROC patients (pts) (all target lesions FR+). This result led to this randomized phase III PROCEED study.

Methods: PROCEED pts were randomized to a 28-day cycle of PLD 50 mg/m² + vintafolide 2.5 mg intravenously (IV) on days 1, 3, and 5 of weeks 1 and 3 (Arm A) or PLD 50 mg/m² IV on day 1 (Arm B). Eligibility criteria included PD within 6 months of first pt regimen (1FR) or PD during or within 6 months of second pt regimen (2FR), ≥ 1 FR+ target lesion, and ECOG PS 0–1. Randomization was initially 2:1 (Arm A:Arm B) but later amended to 1:1. The primary endpoint was progression-free survival (PFS) using protocol-defined progression criteria, with an initial futility threshold set to protect against a 30% increase in the PFS hazard ratio (HR) to 0.995, which was crossed after the planned interim analysis (IA) of 350 FR(100%) pts. The trial would cross the futility bound if PFS HR was >0.8.

Results: At the time of IA, 230 FR(100%) pts were randomized. Pts were well balanced between arms for age, PS, platinum failure status, and baseline CA-125 value. Median treatment cycles were 4 in Arm A and 2 in Arm B. Safety was analyzed in pts treated with ≥ 1 dose of therapy (Arm A, n = 136; Arm B, n = 82). The percent of grade 3–4 treatment emergent adverse events was higher in Arm A than Arm B: stomatitis (9% vs. 6%); sensory neuropathy (4% vs. 0%); and neutropenia/fibrile neutropenia (27%/0.7% vs. 10%/1.2%). The percent of grade 3–4 palmar-plantar syndrome was higher in Arm B (5% vs. 9%). Efficacy was analyzed in all randomized pts (Arm A, n = 143; Arm B, n = 87). The difference in PFS between arms in FR(100%) pts was not significant (HR = 0.976; 95% CI: 0.633–1.505; 1-sided stratified test; P = 0.4617). Response rates between arms were comparable (Arm A 23.1%; Arm B 22.9%). Seventy-five percent of pts were censored for OS.

Conclusions: In this phase III study, PLD + vintafolide was generally well tolerated, with no new safety issues. Because the interim results did not meet the futility threshold, the PROCEED trial stopped patient enrollment per Data Safety Monitoring Board recommendation.

doi:10.1016/j.ygyno.2015.01.010

10 — Scientific Plenary

Multicenter study comparing two approaches to nodal assessment in patients with low-risk endometrial carcinoma: Contemporary sentinel lymph node mapping versus historical selective systematic surgical staging


Objectives: To assess clinicopathologic outcomes for two nodal assessment approaches in patients with low-risk endometrial carcinoma.

Methods: Patients with endometrial cancer at two institutions were reviewed. The historical approach (2004–2008) at one institution was a complete pelvic and paraaortic lymphadenectomy to the renal veins in select cases deemed at risk for nodal metastasis (excluding patients with tumors ≤2 cm) [LND cohort]. At the other institution, a sentinel lymph node mapping algorithm was used per institutional protocol from 2006 to 2013 (SLN cohort). Low risk was defined as endometrioid adenocarcinoma with myometrial invasion ≤50%. Isolated tumor cells and micro- and macrometastases were all considered node-positive for this analysis.

Results: A total of 1135 cases were identified (642 in the SLN cohort; 493 in the LND cohort). Patients had similar tumor grade distributions. Pelvic nodes were removed in 93% of patients in the SLN cohort and 58% in the LND cohort (P < 0.001). Median number of pelvic nodes removed was 6 (interquartile range [IQR]: 3, 11) in the SLN group vs. 34 (IQR: 26, 45) in the LND group (P < 0.001). Metastasis to pelvic nodes was detected in 5.1% (SLN) vs. 2.6% (LND) of patients (P = 0.03) and to paraaortic nodes in 0.8% (SLN) vs. 1.0% (LND) (P = 0.75). The rate of stage IIC disease was 5.6% (SLN) vs. 2.8% (LND) (P = 0.02). Median follow-up was 2.1 years (SLN) vs. 3.5 years (LND) (P < 0.001). The SLN 3-year disease-specific survival was 94.9% (95% CI: 92.4, 97.5) vs. 96.8% (95% CI: 95.2, 98.5) with LND (P = 0.35). The SLN 3-year disease-specific survival was 100.0% vs. 98.8% (95% CI: 97.7, 99.3) with LND (P = 0.03). Only two isolated lymph node recurrences occurred within

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3 years of surgery in each group, with a 3-year nodal-free recurrence of 99.6% in both groups (P = 0.88).

Conclusions: Applying an SLN algorithm seemed to detect stage IIIIC disease as well or better than traditional LND, with no compromise in oncologic outcomes, supporting the use of this algorithm in low-risk endometrioid endometrial cancer cases. The benefit of SLN detection in ultra-low-risk patients with tumors ≤2 cm is uncertain, given the excellent outcomes with complete omission of lymph node assessment. The clinical significance of disease detected on ultra-staging and the role of adjuvant therapy in these cases is yet to be determined.

Methods: Patients diagnosed with endometrial cancer and surgically staged at two collaborating cancer centers were identified. The historical (2004–2008) approach at one institution was to perform a complete pelvic and paraaortic lymphadenectomy to the renal veins (LND cohort). At the second institution, a sentinel lymph node mapping algorithm and ultra-staging was performed according to institutional protocol from 2006 to 2013 (SLN cohort). We defined intermediate risk as endometrioid histology with ≥50% myometrial invasion and high risk as serous or clear cell carcinoma with any degree of myometrial invasion. Isolated tumor cells, micrometastases, and macrometastases were all considered as being node-positive for the purpose of this analysis.

Results: In total, we identified 210 patients in the LND cohort and 202 patients in the SLN cohort. Table 1 summarizes pertinent results. In the intermediate-risk group, stage IIIC disease was diagnosed in 30 (28.0%) patients in the LND cohort and in 29 (35.4%) SLN patients (P = 0.28). In the high-risk group, stage IIIC was diagnosed in 20 (19.4%) patients in the LND cohort and 29 (35.4%) SLN patients (P = 0.001). As a consequence, paraaortic lymph node metastases were detected more frequently in the LND cohort (P = 0.001).

Table 1 Comparison of lymph node data and stage IIIC disease between institutions performing comprehensive lymphadenectomy vs a SLN mapping algorithm.

<table>
<thead>
<tr>
<th></th>
<th>Intermediate-risk</th>
<th>High-risk</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>LND</td>
<td>SLN</td>
</tr>
<tr>
<td>Total patients, N</td>
<td>107</td>
<td>82</td>
</tr>
<tr>
<td>Number of patients with any LNs removed, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>101</td>
<td>81</td>
</tr>
<tr>
<td>(94.4)</td>
<td>(98.8)</td>
<td>(85.4)</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>96</td>
<td>28</td>
</tr>
<tr>
<td>(89.7)</td>
<td>(34.1)</td>
<td>(79.6)</td>
</tr>
<tr>
<td>Total number of LNs removed, median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>(27, 45)</td>
<td>(4, 14)</td>
<td>(26, 41)</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>(12, 23)</td>
<td>(2, 9)</td>
<td>(11, 23)</td>
</tr>
<tr>
<td>Number of patients with positive LNs, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>(23.4)</td>
<td>(32.9)</td>
<td>(19.4)</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>(18.7)</td>
<td>(3.7)</td>
<td>(12.6)</td>
</tr>
<tr>
<td>Stage IIIC disease, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>(28.0)</td>
<td>(35.4)</td>
<td>(19.4)</td>
</tr>
<tr>
<td>Paraaortic</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>(11.2)</td>
<td>(31.7)</td>
<td>(8.7)</td>
</tr>
<tr>
<td>IIIC2</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>(16.8)</td>
<td>(3.7)</td>
<td>(10.7)</td>
</tr>
</tbody>
</table>

Note: Number of patients with positive lymph node metastases exceeds that of patients with stage IIIC disease, as some of these patients had microscopic stage IV disease.

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11 – Scientific Plenary
Multicenter study assessing the detection of stage IIIC endometrial cancer in intermediate- and high-risk tumors between a contemporary sentinel node mapping versus historical comprehensive lymphadenectomy approach


Objectives: To determine if the sentinel lymph node mapping (SLN) algorithm compromises detection of nodal disease in patients with both endometrioid and intermediate- and high-risk endometrial carcinoma.
Abstracts / Gynecologic Oncology 137 (2015) 2–91

Scientific Plenary III
Saturday, March 28, 2015

Moderator: David M. O’Malley, MD, The Ohio State University, Columbus, OH, USA

Jeff Boyd, PhD, Fox Chase Cancer Center, Philadelphia, PA, USA

12 — Scientific Plenary
The genetic basis of ovarian cancer: Identifying hereditary ovarian cancer using a 25-gene panel
L.R. Langer1, B. Evans1, J. Saam2, R.J. Wenstrup3, 4US Oncology, Portland, OR, USA, 3Myriad Genetic Laboratories, Inc., Salt Lake City, UT, USA

Objectives: Ovarian cancer is recognized in different hereditary cancer syndromes, including hereditary breast and ovarian cancer (HBOC) caused by mutations in BRCA1 and BRCA2 and Lynch syndrome (LS) caused by mutations in MLH1, MSH2, MSH6, PMS2, and EPCAM. Recently, mutations in other genes have been identified as increasing ovarian cancer risk, including RAD51C, RAD51D, and BRIPI. This analysis describes the genetic testing results for patients with ovarian cancer tested with a 25-gene hereditary cancer panel.

Methods: We queried a laboratory database for patients affected with ovarian cancer and tested with a 25-gene panel of hereditary cancer genes from September 4, 2013 to August 29, 2014. We identified 1964 patients with ovarian cancer who were tested over this time period. All patient data regarding clinical history were obtained by health care provider report on test requisition forms.

Results: Gene panel testing identified 242 patients who were positive for 245 mutations. Of these mutations, 167 were in BRCA1/BRCA2, 11 were in one of the LS genes, and 67 were in one of the other cancer susceptibility genes, with the most common being ATM (n = 17), BRIPI (n = 14), CHEK2 (n = 9), and RAD51C (n = 9). The mean age of mutation carriers was very similar to the age of the population tested (60.3 compared to 60.7 years). LS mutation carriers had an average age of diagnosis of 56.4 years; BRCA1/BRCA2 carriers had an average age of diagnosis of 59.9 years. Only 54.5% of LS mutation carriers met National Comprehensive Cancer Network criteria for LS.

Conclusions: Gene panel testing provides more genes in one test than the typical single-syndrome approach. This analysis demonstrates that additional gene mutations were identified beyond BRCA1/BRCA2 using this broader approach.

doi:10.1016/j.ygyno.2015.01.014

13 — Scientific Plenary
Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer and a BRCA mutation: Overall survival adjusted for post-progression PARPi inhibitor therapy
U.A. Matulonis1, P. Harter2, C. Gourley3, M. Friedlander1, I.B. Vergote4, C.J.S. Rustin5, A. Fielding6, S. Spencer7, D. Parry8, J.A. Ledermann9, 1Dana-Farber Cancer Institute, Boston, MA, USA, 2Klinikum Essen-Mitte, Essen, Germany, 3University of Edinburgh Cancer Research UK Centre, Edinburgh, UK, 4Prince of Wales Cancer Centre, Randwick, Sydney, Australia, 5University Hospital Leuven, Leuven, Belgium, 6Mount Vernon Hospital, Middlesex, UK, 7AstraZeneca, Macclesfield, UK, 8University College London, London, UK

Objectives: Previously, we reported that maintenance treatment with the oral poly ADP ribose polymerase (PARP) inhibitor (PARPi) olaparib (400 mg bid; capsule formulation) led to a significant improvement in progression-free survival compared with placebo in patients (pts) with platinum-sensitive relapsed serous ovarian cancer (Ledermann et al. N Engl J Med. 2012), with the greatest clinical benefit observed in pts with a BRCA mutation (BRCAm) (Ledermann et al. Lancet Oncol. 2014). Although a statistically significant benefit in overall survival (OS) was not observed following an interim analysis (58% maturity), 12% of pts in the placebo arm (23% of BRCAm pts; 30% of germline BRCAm [gBRCAm] pts) received a PARPi after disease progression, which is hypothesized to have confounded the OS results. To explore this hypothesis, we performed an additional analysis of OS that excluded all pts from the sites where at least one pt received post-progression treatment with a PARPi.

Methods: Of the 82 investigational sites in this randomized, double-blind phase II trial (NCT00753545), pts from 11 sites received a PARPi post-progression, leading to the exclusion of 67/265 (25%) pts (39/136 [29%] BRCAm pts; 31/96 [32%] gBRCAm pts) from this posthoc analysis.

Results: Of the 198 pts in this analysis, 97 had a known BRCAm of whom 65 had a known gBRCAm. Interim OS data are shown in the Table.

Conclusions: This additional posthoc analysis of interim OS, which excluded all pts from sites where pts had received post-progression PARPi treatment, did not change the overall conclusion from this trial, which was that there is no significant difference in OS in the overall population. A larger proportion of pts in the BRCAm and gBRCAm populations received a PARPi post-progression. Reanalysis of OS, excluding the sites where crossover occurred, resulted in a numerical improvement in OS HR in all groups, especially the BRCAm group, suggesting that post-progression PARPi treatment could have a confounding influence on the original OS analyses. Given that, a higher proportion of gBRCAm pts received a subsequent PARPi than BRCAm pts in the placebo arm, the larger numerical decrease in OS HR in BRCAm pts vs. gBRCAm pts is unexpected. Further work is ongoing to explore these findings and other methods to account for post-progression treatment.

<table>
<thead>
<tr>
<th>BRCAm</th>
<th>gBRCAm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>136</td>
</tr>
<tr>
<td>Events: patients</td>
<td>59</td>
</tr>
<tr>
<td>Median, months</td>
<td>32</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.80 (0.55–1.16)</td>
</tr>
<tr>
<td>P</td>
<td>0.42</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio; and ITT, intent to treat.

Olaparib Placebo Olaparib Placebo Olaparib Placebo

102 | 103 | 59 | 95 |

| Median, months | 32.9 |
| HR (95% CI) | 0.80 (0.55–1.16) |
| P | 0.243 |

1 Includes patients with a known germline BRCA mutation (gBRCAm) and/or a known tumor BRCA mutation.

doi:10.1016/j.ygyno.2015.01.015

14 — Scientific Plenary
Olaparib monotherapy in patients with advanced relapsed ovarian cancer and a germline BRCA1/2 mutation: A multi-study sub-analysis
U.A. Matulonis1, R.T. Penson2, S.M. Domchek3, K. Kaufman4, M.W. Audel1, S.B. Kaye5, H. Mann6, J. Robertson7, R.L. Coleman7, 1Dana-Farber Cancer Institute, Boston, MA, USA, 2Massachusetts General Hospital/Harvard University, Boston, MA, USA, 3Basser Research Center and Abramson Cancer Center, Philadelphia, PA, USA, 4Sheba Medical Center, Tel Hashomer, Israel, 5Samuel Oschin Cancer Institute, Los Angeles, CA, USA, 6The Royal Marsden Hospital, London, UK, 7AstraZeneca, Macclesfield, UK, 8The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objectives: Olaparib is a novel poly ADP ribose polymerase (PARP) inhibitor with documented antitumor activity among women with relapsed ovarian cancer (OC) who carry a germline BRCA1/2 mutation.

was acceptable in patients who received platinum-sensitive recurrent ovarian cancer: Can we afford it?

PARP inhibitors as maintenance therapy for patients with H.J.

Methods: A total of 300 women with relapsed ovarian, fallopian tube, or peritoneal cancer who were enrolled in six prospective clinical trials (NCT00516373, NCT00494442, NCT00628251, NCT00679783, NCT00777582, NCT01078662) received olaparib 400 mg bid (capsule) monotherapy at the time of relapse. A pooled analysis was conducted using original patient outcomes data based on assessment definitions in the respective trials. Adverse events (AEs) were recorded throughout the trials and graded by Common Terminology Criteria for Adverse Events Version 3.0.

Results: All 300 patients were evaluable for safety; of these, 273 had measurable disease (by computed tomography/magnetic resonance imaging) and were evaluable for response by Response Evaluation Criteria in Solid Tumors 1.1 criteria. Table 1 presents the ORR and DoR for the overall patient population and for the subgroup of patients who had previously received ≥3 lines of chemotherapy. The safety profile was similar for both groups. In the overall population, 50% had ≥3 AEs, 30% had serious AEs (SAEs) (10% causally related SAEs), 5% had AEs leading to discontinuation (DAEs), and 3% (n = 8) had AEs leading to death. In patients who had received ≥3 lines of chemotherapy, 54% had grade ≥3 AEs, 34% had SAEs (12% causally related SAEs), 7% had DAEs, and eight patients (4%) had an AE leading to death. The AEs leading to death were: sepsis, intestinal perforation, suture rupture, acute leukemia, acute myeloid leukemia, cerebrovascular accident, chronic obstructive pulmonary disease, and pulmonary embolism (the incidence of each was 0.4% in this patient subgroup and none was considered causally related to olaparib).

Conclusions: Patients with relapsed gBRCAm OC who had received ≥3 lines of chemotherapy benefited from olaparib treatment and experienced durable responses (~8 months). The safety profile of olaparib was acceptable in patients who received ≥3 lines of chemotherapy.

| Table 1
<table>
<thead>
<tr>
<th>Patient population</th>
<th>Confirmed responders, n²</th>
<th>ORR, % [95% CI]¹</th>
<th>DoR months [95% CI]¹</th>
<th>Duration of treatment, median days [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population, n = 300</td>
<td>97/273</td>
<td>36 [30, 42]</td>
<td>7.4 [5.7, 9.1]</td>
<td>177 [1–819]</td>
</tr>
<tr>
<td>≥3 prior chemotherapy regimens, n = 223</td>
<td>64/205</td>
<td>31 [25, 38]</td>
<td>7.8 [5.6, 9.5]</td>
<td>168 [1–819]</td>
</tr>
</tbody>
</table>

¹ Response data shown are for patients who were evaluable for response: overall population, n = 273; ≥3 prior chemotherapy regimens, n = 205.

doi:10.1016/j.ygyno.2015.01.017

15 — Scientific Plenary

PARP inhibitors as maintenance therapy for patients with platinum-sensitive recurrent ovarian cancer: Can we afford it?

H.J. Smith, C.L. Walters Haygood, R.C. Arend, C.A. Leath III, J.M. Straughn Jr., University of Alabama at Birmingham, Birmingham, AL, USA

Objectives: To determine the cost-effectiveness of olaparib, a poly adenosine 5′-diphosphoribose polymerase (PARP) inhibitor, as maintenance therapy for patients with platinum-sensitive (PS) recurrent ovarian cancer.

Methods: A cost-effectiveness model compared the cost of observation vs. olaparib maintenance therapy in patients with PS recurrent ovarian cancer. All patients received six cycles of paclitaxel and carboplatin. Drug costs were estimated using 2014 wholesale acquisition costs. The cost of olaparib was estimated at $7000 per month. The cost of observation was based on National Comprehensive Cancer Network guidelines for ovarian cancer surveillance using 2014 Medicare reimbursement rates. Progression-free survival was determined from previously published data. Cost-effectiveness (C/E) ratios and incremental cost-effectiveness ratios (ICERs) per progression-free life-year saved (PF-LYS) were calculated for patients with BRCA mutations and for patients with wild-type BRCA. A sensitivity analysis estimated the cost at which olaparib would be cost-effective.

Results: We estimated that 5549 patients were diagnosed with PS recurrent ovarian cancer in the United States annually. The rate of germline BRCA mutation was assumed to be 20% (1110 patients). The cost of observation in patients with a BRCA mutation was $5.5 million (M) with a C/E ratio of $1.3 M vs. a cost of $91.3 M with a C/E ratio of $8.1 M for maintenance therapy with olaparib. The ICER for olaparib maintenance therapy in patients with a BRCA mutation was $135,672 per PF-LYS. If the cost of olaparib was decreased to $2500 per month, the ICER was $49,584. For the 4449 patients with wild-type BRCA, the cost of maintenance therapy was $244.1 M with a C/E ratio of $33.0 M; the ICER was $315,840 per PF-LYS.

Conclusions: Assuming a cost similar to that of other oral targeted agents, olaparib maintenance therapy would result in an increase in cost of $85.8 M compared to observation for patients with PS recurrent ovarian cancer and a deleterious BRCA mutation. Maintenance therapy with olaparib is not cost-effective with an ICER of $135,672. To achieve an ICER of less than $50,000, the cost of olaparib should be $2,500 or less per month. For wild-type BRCA patients, maintenance therapy with olaparib is unlikely to ever be cost-effective.

doi:10.1016/j.ygyno.2015.01.017

17 — Surgical Forum

Single port robotic sentinel lymph node biopsy and hysterectomy in endometrial cancer

A.K. Sinnoa, A. Nickles Faderb, S. Scheibc, E.J. Tanner IIIb, "Johns Hopkins Hospital, Baltimore, MD, USA, "Johns Hopkins School of Medicine, Baltimore, MD, USA

Laparoscopic single-site surgery (LESS) has been increasingly used for complex gynecologic conditions but has not achieved widespread use for oncologic indications. The robotic LESS platform has the potential to overcome some of the limitations of conventional single-port surgery and may result in increased utilization among surgeons. Similarly, sentinel lymph node biopsy has been suggested as a less invasive and safe
alternative to complete lymphadenectomy in endometrial cancer but has not been described using the single-port robotic platform. In this video, we describe a 67-year-old patient with FIGO grade 1 endometrial cancer undergoing robotic LESS hysterectomy and sentinel lymph node mapping. The video highlights our initial experience combining these innovative techniques, with an emphasis on set-up, operative techniques to improve visualization and tissue handling, and patient selection.

doi:10.1016/j.ygyno.2015.01.019

18 — Surgical Forum
Sentinel lymph node mapping using robotic-assisted fluorescence imaging
J.L. Mueller, M.M. Leitao. Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: Sentinel lymph node mapping is an increasingly accepted method of assessing nodal disease in early-stage gynecologic malignancies.

Methods: This teaching video was created for those who are refining this method using the robotic platform.

Conclusions: We use our experience in early endometrial cancer to emphasize an evidence-based algorithm that assists in the successful adaptation of the sentinel lymph node mapping technique.

doi:10.1016/j.ygyno.2015.01.020

Scientific Plenary IV: The Farr Nezhat Surgical Innovation Session
Sunday, March 29, 2015

Moderators:
Farr Nezhat, MD, FACOG, FACS, St. Luke’s-Roosevelt Hospital, New York, NY, USA
Anna Fagotti, MD, PhD, Catholic University of the Sacred Heart, Rome, Italy; St. Maria Hospital, University of Perugia, Terni, Italy

19 — Scientific Plenary
Robotic versus Open Type III radical hysterectomy: A multi-institutional experience for early stage cervical cancer
B.M. Sert1, J.F. Boggess2, S. Ahmad3, A.L. Jackson2, N.M. Stavitzski4, A.A. Dahil, R.W. Holloway5, 6. The Norwegian Radium Hospital, Oslo, Norway, 7University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, 8Florida Hospital Cancer Institute, Orlando, FL, USA, 4University of Cincinnati, UC Health Medical Arts Building, Cincinnati, OH, USA, 6Oslo University Hospital, Oslo, Norway

Objectives: Despite the rapid adoption of robotic-assisted radical hysterectomy (RRH) in gynecologic oncology, long-term survival outcomes data are limited. The aim of this study was to determine the comparative long-term recurrence-free and overall survival outcomes of RRH vs. open radical hysterectomy (ORH) for early-stage cervical cancer.

Methods: This retrospective multicenter study abstracted data from medical records for demographics, operative data, and long-term outcomes of 517 patients treated surgically for cervical cancer (RRH = 260 and ORH = 257) between 2005 and 2011. The association between operative technique, margin status, lymph node status, and long-term oncologic outcomes (recurrence, survival) was examined using chi square tests and univariate and multivariate logistic regression models to adjust for the confounding variables.

Results: Mean (± SD) follow-up time was 34.4 ± 21.6 months for RRH and 44.4 ± 28.1 months for ORH (P < 0.001). Recurrence and death rate were not statistically different for the two groups (P = 0.97 vs. P = 0.60, respectively). The groups did not differ significantly in age, body mass index, histology, postoperative complications, or postoperative chemotherapy. Mean operative time was significantly longer for RRH than ORH (3.40 vs. 2.37 h, P < 0.001). Mean estimated blood loss (EBL) and transfusion rate were significantly less for RRH than ORH (97 mL vs. 429 mL, P < 0.001) (3% vs. 8%, P = 0.009). Preoperative conization rate was significantly higher for RRH than ORH (67% vs. 42%, P < 0.001). Neoadjuvant chemotherapy was used significantly more for ORH than RRH (10% vs. 4%, P < 0.001). Postoperative adjuvant treatment was administered in 30% of patients after RRH and in 55% after ORH (P < 0.001). In multivariate regression analyses, longer operative time, less EBL, fewer perioperative complications, and more preoperative conization were significantly associated with RRH compared with ORH. Although overall complications were similar (P = 0.49), perioperative complications were less in the RRH than the ORH group (P = 0.002).

Conclusions: Recurrence and death rates for RRH were comparable to that of ORH, with statistically significant less blood loss and perioperative complications.

doi:10.1016/j.ygyno.2015.01.021

20 — Scientific Plenary
Personalized surgical therapy for advanced ovarian cancer
A.M. Nick, R.L. Coleman, P.T. Ramirez, K.M. Schmeler, P.T. Soliman, K.H. Lu, J.K. Burzawa, A.K. Sood. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objectives: Patients who have no gross postoperative residual disease (R0) appear to benefit the most from attempted cytoreduction. We sought to evaluate disease distribution by diagnostic laparoscopy (LS) as a means of assessing R0 resectability in patients with presumed advanced ovarian cancer.

Methods: Using a previously described triage algorithm, preoperatively defined parameters were analyzed with LS among women with presumed advanced ovarian cancer over a 1-year period. Disease distribution was described independently by two surgeons using the Fagotti score, with scores >8 resulting in triage to neoadjuvant chemotherapy (NACT). Patient outcomes and faculty compliance were tracked prospectively and R0 rates were compared to historical practice.

Results: A total of 99 patients with suspected advanced ovarian cancer presented during the study time period. Eleven were not offered LS due to medical comorbidities, including seven with active venous thromboembolism and 20 with extra-abdominal metastases. Two were not offered LS by their primary surgeon (98% compliance). Median age was 66 years (range, 39–90 years) and 90% had serous histology. Sixty-five patients underwent LS with a median operating room time of 36 min (range, 11–102 min) and median estimated blood loss of 5 mL (range, 0–50 mL). There was 99% concordance between the two surgeons (k = 0.97 [95% CI: 0.89–0.99]). Forty (63%) patients had a score >8 and 37 underwent primary TRS (3 opted for NACT secondary to risk of bowel resection). The remaining 25 underwent NACT. The accuracy of laparoscopic assessment for predicting R0 resection was 86% (compared to a historical R0 resection rate of 40% from 2007 to 2012, P < 0.001). Fourteen of 18 (78%) patients dispositioned to NACT have subsequently undergone interval TRS and achieved R0 resection. Median CA-125 values were greater in patients triaged to NACT by LS (893 vs. 161, P < 0.01). Similarly, median platelet counts prior to treatment were greater among those triaged to NACT (379 vs. 289.5, P < 0.01). Among those patients who underwent primary TRS, a postlaparotomy score sheet correlated with the primary surgeon’s laparoscopic score 96% of the time (R = 0.66, P < 0.01).

Conclusions: Laparoscopy is a highly reliable and reproducible method of determining ovarian cancer disease distribution. We anticipate that improved R0 rates will result in reciprocal improvements in survival among patients with advanced ovarian cancer.

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21 — Scientific Plenary
A multicenter assessment of the ability of preoperative computed tomography scan and serum CA-125 to predict gross residual disease at primary debulking surgery for advanced ovarian, fallopian tube and peritoneal cancer
R.S. Suidan1, P.T. Ramirez2, D. Sarasohn3, J. Teitcher3, S. Mironova4, R. Iyer5, Q. Zhou4, J. Densesopilis2, H. Hricak6, D.S. Chi4. 1Memorial Sloan Kettering Cancer Center, New York, NY, USA, 2The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objectives: To assess the ability of preoperative computed tomography (CT) scan and serum CA-125 to predict gross residual disease (RD) at primary cytoreduction in advanced epithelial ovarian cancer.

Methods: A prospective, nonrandomized, multicenter trial of patients (pts) who underwent primary debulking surgery for stage III–IV ovarian, fallopian tube, and peritoneal cancer previously identified nine criteria associated with suboptimal (>1 cm residual) cytoreduction. This secondary post hoc analysis looked at the ability to predict any RD, assessing 4 clinical and 18 radiologic criteria and developing a multivariable model predictive of RD.

Results: From 7/2001 to 12/2012, 669 pts were enrolled; 350 met eligibility criteria. The complete gross resection rate was 33.4% (117 pts). On multivariate analysis, 3 clinical and 8 radiologic criteria were significantly associated with the presence of any RD: age ≥ 60 years (odds ratio [OR] 1.5, 95% CI 1.1–1.9), CA-125 ≥ 600 U/mL (OR 1.3, 95% CI 1.2–1.4), American Society of Anesthesiologists (ASA) score of 3–4 (OR 1.6, 95% CI 1.6–1.7), lesions in the root of the superior mesenteric artery (OR 4.1, 95% CI 3.1–5.3), splenic hilum/ligaments (OR 1.4, 95% CI 1.1–1.6), lesser sac (>1 cm) (OR 2.2, 95% CI 1.5–3.3), gastrohepatic ligament/porta hepatitis (OR 1.4, 95% CI 1.2–1.7), gallbladder fossa/intersegmental fissure (OR 2, 95% CI 1.7–2.5), suprarenal retroperitoneal lymph nodes (OR 1.3, 95% CI 1.1–1.6), diffuse small bowel adhesions/thickening (OR 1.1, 95% CI 1.1–1.14), and moderate-severe ascites (OR 2.2, 95% CI 1.7–2.8). A “predictive score” was assigned to each criterion based on its multivariable OR, and the rate of having any RD for pts who had a total score of 0–2, 3–5, 6–8, and ≥9 was 45%, 68%, 87%, and 96%, respectively (Table). A receiver operating characteristic curve was generated, and a predictive model utilizing the 8 CT criteria, CA-125, ASA score, and age, demonstrating an AUC of 0.72.

Conclusions: In a two tertiary care cancer centers, we identified 11 factors associated with RD and developed a predictive model in which the rate of having any RD was directly proportional to a predictive score. Our results may be helpful in pretreatment pt assessment and in guiding clinical management.

<table>
<thead>
<tr>
<th>Total predictive score</th>
<th>Total patients n (%)</th>
<th>No residual disease (n)</th>
<th>Gross residual disease (n)</th>
<th>Rate of having gross residual disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2</td>
<td>107/350 (31%)</td>
<td>59</td>
<td>48</td>
<td>45%</td>
</tr>
<tr>
<td>3–5</td>
<td>151/350 (43%)</td>
<td>48</td>
<td>103</td>
<td>68%</td>
</tr>
<tr>
<td>6–8</td>
<td>68/350 (19%)</td>
<td>9</td>
<td>59</td>
<td>87%</td>
</tr>
<tr>
<td>≥9</td>
<td>24/350 (7%)</td>
<td>1</td>
<td>23</td>
<td>96%</td>
</tr>
</tbody>
</table>

doi:10.1016/j.ygyno.2015.01.024

22 — Scientific Plenary
The impact of intraoperative tumor fragmentation or morcellation in patients with early-stage uterine leiomyosarcoma
J.A. Duncie1, K. Fritton2, R. O’Cearbaill3, M.L. Hensley4, R.A. Soslow5, N.R. Abu-Rustum6, M.M. Leitao7, O. Zivanovic7. 1Memorial Sloan Kettering Cancer Center, New York, NY, USA, 2Thomas Jefferson University, Philadelphia, PA, USA, 3Weill Cornell Medical College, New York, NY, USA

Objectives: To examine the impact of intraoperative tumor fragmentation or morcellation on the outcomes of patients (pts) with stage I high-grade uterine leiomyosarcoma (uLMS).

Methods: We searched our institutional database for pts diagnosed with uterine-confined stage I uLMS diagnosed between 2000 and 2014. We excluded pts who presented with recurrent disease. All operative notes were reviewed. Intraoperative tumor fragmentation was defined as mechanical morcellation of a specimen, gross rupture of tumor through uterine serosa or tumor capsule, or cutting through of the tumor at the time of myometomy or supracervical hysterectomy with corroborating pathologic data (positive surgical margins).

Results: We identified 136 pts with stage I high-grade uLMS. Intraoperative tumor fragmentation was noted in 32 (23.5%) cases; of these, 15 (46.9%) underwent morcellation. The majority (n = 29; 91%) of pts with intraoperative tumor fragmentation or morcellation presented to our institution after initial surgery at outside hospitals. Intraoperative tumor fragmentation or morcellation was associated with younger age (P < 0.0001) and larger tumor size (P = 0.001). Median follow-up for all surviving pts was 47.2 months (range, 5.3–172.8 months). Median overall survival (OS) was 45.3 months (range, 39.1–151 months) in pts with intraoperative tumor fragmentation or morcellation compared with 105.2 months (range, 78.3–132.1 months) in the control group (P = 0.02). Age, tumor size, and mitotic index did not significantly affect OS in this cohort. Of the 12 pts who had second-look operation or completion surgery after initial intraoperative tumor fragmentation or morcellation, 6 (50%) were found to have early progressive disease.

Conclusions: In a stage I high-grade uLMS population, poor tissue handling with intraoperative tumor fragmentation, intraoperative tumor rupture, and morcellation were the only prognostic factors significantly associated with OS. In cases where uterine malignancy is suspected, proper tissue handling to avoid intraperitoneal tumor fragmentation is paramount.

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the NMOR cohort compared with 92.5% in the MOR cohort (P = 0.031), while 33% of the NMOR cohort underwent preoperative biopsy compared with 44.8% of the MORC cohort (P = NS). Median uterine weight was 296 g in the MOR and 184 g in the NMOR cohorts (P = 0.004). Two occult uterine cancers were detected in the entire cohort (0.00% malignancy risk, n = 2173 pts). Only one case of leiomyosarcoma (LMS; 0.04% risk) and one case of microinvasive cervical cancer were detected, both in the MOR cases. Both are without evidence of disease with overall survival of 45.6 (LMS case) and 18 months (cervical case), respectively. No occult uterine cancers were identified in women <50 years old in the entire cohort.

Conclusions: The risk of occult uterine malignancy in women undergoing uterine surgery for presumed benign disease at a high-volume MIS center was low, and was 0% in reproductive-age women. Comprehensive preoperative assessments and patient risk stratification for occult malignancy may optimize patient safety and reduce the risk of morcellator-associated morbidity.

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25 — Scientific Plenary
TP53 mutations in circulating tumor DNA for response monitoring in patients with high grade serous carcinoma of ovary
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Objectives: Circulating tumor DNA (ctDNA) is the DNA released by apoptotic and necrotic cells of the primary tumor into the blood circulation early in tumor development. This ctDNA can be extracted from blood, and the genetic and epigenetic alterations can be analyzed. This study investigated TP53 mutation in primary tumor tissue and ctDNA using digital polymerase chain reaction (PCR) in patients with high-grade-serous carcinoma of the ovary (HGS-OC).

Methods: We obtained tumor tissue and peripheral blood from 18 HGS-OC patients. We isolated DNA from their tumor tissues and ctDNA from their blood. Initially, we checked TP53 mutations in their tumor tissues using PCR and target gene exome sequencing. After detecting TP53 mutations, we sought the same mutations in ctDNA using digital PCR. We compared TP53 mutation in ovarian cancer tissue and those in ctDNA. We analyzed the change of ctDNA during the initial chemotherapeutic management and compared to CA-125.

Results: The average concentration of ctDNA was 2.12 ± 0.59 ng/mL. Among 18 patients, TP53 mutations were revealed in the tissue of 14 patients (77.8%). A single-point mutation (7 cases) or multipoint mutation (7 cases) was found in patient-derived tumor tissues, and we confirmed the same TP53 mutations from ctDNA in 9 patients. We investigated the intratumoral and intertumor heterogeneity in diverse tumor tissues of each patient and, interestingly, detected and monitored two different TP53 mutations from ctDNA in P-0039 simultaneously (p.L289R and p.R213L). In each case, we compared the performance of circulating biomarkers with the CA-125 values and ctDNA levels. We found that the amount of ctDNA decreased after initial debulking surgery, and chemotherapy and levels of ctDNA seemed to correspond with the CA-125 values, although with an individually different pattern.

Conclusions: We confirmed the concordance of genomic DNA in tissue and ctDNA in plasma from each HGS-OC patient. The analysis of ctDNA represents an alternative sensitive and specific disease monitoring method with several advantages, including noninvasive sampling and documentation of tumor heterogeneity. The biologic significance of these findings warrants further investigation in the context of genetic and epigenetic alteration in ctDNA from more patients.
Table 1
The results of the TP53 mutations identified by tumor tissue and blood from HGS-OC patients.

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Age</th>
<th>Cell type</th>
<th>Stage</th>
<th>Tumor site</th>
<th>TP53 mutation</th>
<th>Exon</th>
<th>Mutation type</th>
<th>ctDNA detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-001</td>
<td>77</td>
<td>PSA</td>
<td>IIIC</td>
<td>Peritoneum</td>
<td>C229S R282W</td>
<td>7</td>
<td>Missense</td>
<td>Not done</td>
</tr>
<tr>
<td>p-0002</td>
<td>62</td>
<td>PSA</td>
<td>IIIC</td>
<td>Peritoneum</td>
<td>p.C266R p.R175H</td>
<td>8</td>
<td>Missense</td>
<td>Positive</td>
</tr>
<tr>
<td>p-0032</td>
<td>44</td>
<td>PSA</td>
<td>IV</td>
<td>Right Ovary</td>
<td>p.T170T p.L289R</td>
<td>5</td>
<td>Coding silent</td>
<td>Not done</td>
</tr>
</tbody>
</table>

Objectives: High-grade serous cancer (HGSC) is diagnosed at an advanced stage due to the lack of a reliable early detection biomarker. Exosomes are microvesicles, 50–100 nm in size, that form when endosomes fuse with cell membranes and are released into the extracellular space. Modern genomic technology allows researchers to isolate and interrogate circulating serum exosomes. We hypothesize that tumor-derived serum exosomes contain microRNAs (miRNAs) that can serve as novel biomarkers for HGSC.

Methods: Exosomes were isolated from 500 μL of serum from 15 patients with stage IIIC or IV HGSC and 16 healthy, unaffected controls using the Exoquick kit (System Biosciences, Mountain View, CA). Exosomes were confirmed by size measurement using the NanoSight NS500 (Salisbury, UK) and the presence of common exosomal proteins (HSP70, CD9, CD81, and CD63) through Western blots. miRNAs were extracted from isolated exosomes using the Seramir kit (System Biosciences), and 800 commonly expressed human miRNAs were quantified with the NanoString nCounter platform (NanoString Technologies, Seattle, WA). miRNA expression was validated using Taqman real-time polymerase chain reaction (RT-PCR) with spike-in controls (Life Technologies, Norwalk CT). Two-sided statistical tests were used as appropriate.

Results: Expected exosome size was confirmed by Nanosight evaluation, and Western blots confirmed the presence of common exosome-associated proteins: HSP70, CD9, CD81, and CD63. Of the 800 miRNAs measured, 56 were found to have more than twofold higher expression in HGSC samples compared to controls at a strict Bonferroni-corrected P < 0.01. No miRNAs were overexpressed in the control samples. Taqman RT-PCR has validated relative gene expression for select miRNAs. The Figure shows nonsignificant differences in expression for mir-16 and significant differential expression for mir-200a and mir-1283 in the discovery and validation platforms for HGSC cases and unaffected controls.

Conclusions: Serum exosomal miRNAs are overexpressed in patients with advanced-stage HGSC compared to healthy controls. These findings suggest that serum exosomal miRNAs may serve as novel biomarkers for advanced HGSC. Future work will be required to determine if exosomal miRNA expression is sufficient for early detection.

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26 — Scientific Plenary
Tumor-derived serum exosomal microRNA as a novel biomarker for high-grade serous carcinoma
V. Broach, J.J. Mueller, B. Schlappe, F. Bogomolniy, M. Bisogna, F. Dao, P. Jelinic, D.A. Levine. Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: High-grade serous cancer (HGSC) is diagnosed at an advanced stage due to the lack of a reliable early detection biomarker. Exosomes are microvesicles, 50–100 nm in size, that form when endosomes fuse with cell membranes and are released into the extracellular space. Modern genomic technology allows researchers to isolate and interrogate circulating serum exosomes. We hypothesize that tumor-derived serum exosomes contain microRNAs (miRNAs) that can serve as novel biomarkers for HGSC.

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doi:10.1016/j.ygyno.2015.01.027

27 — Scientific Plenary
Serum mitochondrial DNA shows a greater effect size than CA-125 in predicting survival in epithelial ovarian cancer
K.S. Grzankowski, N. Khan, N.V. Kolomeyevskaya, K.M. Moysich, K. Eng, S.B. Lele, K.O. Odunsi, B.H. Segal. Roswell Park Cancer Institute, Buffalo, NY, USA
**Objectives:** Mitochondrial damage-associated molecular patterns, composed of mtDNA and formylated peptides, are released after cellular injury and activate innate immune responses. mtDNA is found in variable amounts in serum and the tumor microenvironment of epithelial ovarian cancer (EOC) patients. Because EOC is associated with cellular necrosis, we reasoned that extracellular mtDNA may be a molecular marker of prognosis. The prognostic significance of CA-125, the serum marker most closely associated with EOC, is widely published.

**Methods:** Serum from patients with advanced-stage EOC collected before primary surgical debulking (n = 41) was analyzed for mtDNA using quantitative polymerase chain reaction with cytochrome B primers specific for mtDNA. Defining the top 15% concentration of serum mtDNA as the high (hi) category and the remainder as low (lo), survival was determined for each category. Comparison using Cox regression model was performed. Progression-free survival (PFS) was the primary clinical endpoint. Log rank test was then used to correlate published CA-125 data with serum mtDNA.

**Results:** Patients within the serum mtDNA hi group had markedly reduced PFS (4.5 vs. 16.1 months; P = 0.00145) and overall survival (8.3 vs. 50.1 months; P = 0.00098) compared to the mtDNA lo group. Table 1A lists the patient characteristics, including disease stage, histology, grade, and mean patient age at diagnosis. Comparing pretreatment serum mtDNA levels to published results on serum CA-125 levels from a Gynecology Oncology Group study that analyzed 1299 patients with EOC, serum mtDNA hi was substantially better in predicting prognosis for PFS (HR = 4.3) and OS (HR = 5.4), as shown in Table 1B.

**Conclusions:** Comparing pretreatment serum mtDNA levels in a small cohort of the top 15% with published data on serum CA-125 levels, we observed significantly greater effect sizes with serum mtDNA in predicting prognosis in EOC, with the greatest effect in the high serum mtDNA category.

**Table 1A**

<table>
<thead>
<tr>
<th>mtDNA hi (top 15%) n = 6</th>
<th>mtDNA lo n = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean mtDNA concentration</td>
<td></td>
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<tr>
<td>48.7 (24.4–116.5)</td>
<td></td>
</tr>
<tr>
<td>65 (43–77)</td>
<td></td>
</tr>
<tr>
<td>Mean age Stage</td>
<td></td>
</tr>
<tr>
<td>III-5 (83%)</td>
<td></td>
</tr>
<tr>
<td>IV-1 (17%)</td>
<td></td>
</tr>
<tr>
<td>Unstated advanced</td>
<td></td>
</tr>
<tr>
<td>6 Serous (100%)</td>
<td></td>
</tr>
<tr>
<td>30 Serous (83.5%)</td>
<td></td>
</tr>
<tr>
<td>Grade</td>
<td></td>
</tr>
<tr>
<td>3–50%</td>
<td></td>
</tr>
<tr>
<td>1–0%</td>
<td></td>
</tr>
<tr>
<td>Median PFS (p = 0.00145, HR 4.3)</td>
<td></td>
</tr>
<tr>
<td>4.5 months</td>
<td></td>
</tr>
<tr>
<td>Median OS (p = 0.00098, HR 5.43)</td>
<td></td>
</tr>
<tr>
<td>8.3 months</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1B**

Comparison of pre-treatment serum mtDNA and CA-125 levels in predicting survival in patients with advanced epithelial ovarian cancer.

<table>
<thead>
<tr>
<th>Log-rank p-value</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>0.00145</td>
</tr>
<tr>
<td>OS</td>
<td>0.00022</td>
</tr>
</tbody>
</table>

**Surgical Forum II: Surgical Films**

**Sunday, March 29, 2015**

**28 – Surgical Forum**

**Laparoscopic retroperitoneal lymphadenectomy for bulky para-aortic ovarian cancer recurrence**

R. Ribeiro, M.A. Luz, J.L. Mattana, M. Zapparoli, W. Kondo, J.A. Guerreiro. Erasto Gaertner Hospital, Curitiba, Brazil; Diagnostico Avancado por Imagem, Curitiba, Brazil; Sugisawa Hospital, Curitiba, Brazil

**Objectives:** A 72-year-old patient presented for endometrioid ovarian cancer follow-up. She had no complaints and normal CA-125, but the computed tomography scan showed bulky retroperitoneal lymphadenopathy. She was treated 2 years ago with total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and peritoneal biopsies. No lymphadenectomy was performed at that time. She also had adjuvant chemotherapy (6 cycles of carboplatin/paclitaxel). She was referred for laparoscopic retroperitoneal lymphadenectomy.

**Methods:** The complete technique is demonstrated, starting with patient and team positioning and trocar placement. Step-by-step dissection of the retroperitoneal space, ureters, renal and lumbar vessels, sympathetic nerves, and all other important retroperitoneal structures is shown.

**Conclusions:** The film demonstrates how this approach can offer a less morbid, minimally invasive surgical treatment alternative.

**29 – Surgical Forum**

**Radical abdominal trachelectomy during pregnancy for stage IB1 cervical carcinoma**

A. Rodolakis, N. Thomakos, G. Vlachos, D. Loutridis. Alexandra Hospital, University of Athens, Athens, Greece; University of Athens School of Medicine, Alexandra Hospital, Athens, Greece

**Objectives:** Treatment of pregnancy complicated by malignancy constitutes a great clinical challenge balancing between optimal maternal therapy and fetal viability. Radical abdominal trachelectomy is a fertility-preserving alternative.

**Methods:** Routine Papanicolau smear of a 29-year-old woman (POGO) showed atypical squamous cells of unknown significance. Biopsy sampling (colposcopically directed) revealed squamous cell carcinoma, with moderate differentiation (cervical intraepithelial neoplasia 3, compatible with human papillomavirus). Magnetic resonance imaging showed a 2.1-cm tumor at a range of 7 mm from the internal cervical os. The patient was thoroughly informed about the current treatment of cervical cancer and the possible complications. Due to patient’s strong desire to preserve the pregnancy, she was given the alternative option of radical trachelectomy. The disease was reassessed at the 14th week of gestation. The tumor had increased to 2.9 cm at a range of 5 mm from the cervical os.

**Results:** Radical abdominal trachelectomy, bilateral lymphadenectomy, and a double loupe in the lower uterine segment were performed. Histologic examination showed adenosquamous cell cervical carcinoma, sized 3.5 × 2.9 × 0.7 cm, with poor differentiation and free surgical margins, at a range of 4 mm from the upper border. An extra 2.5 × 2-mm segment was removed and marked as also free from disease.

**Conclusions:** Radical trachelectomy can widen the therapeutic approach for early-stage cervical cancer in pregnant women who wish to preserve their fertility, providing a possibility of receiving the proper treatment with no delay.

**doi:** 10.1016/j.ygyno.2015.01.030
30 — Surgical Forum
Laparoscopic parametrectomy and pelvic lymphadenectomy for cervical cancer after simple hysterectomy with sentinel lymph node dissection
R. Ribeiro, M.V.A.A. Bernardes, M.A. Luz, C.L. Minari, J.C. Linhares. Erasto Gaertner Hospital, Curitiba, Brazil

Objectives: We present a case of a 32-year-old patient who previously underwent simple hysterectomy and bilateral pelvic sentinel lymph node biopsy for epidermoid carcinoma of the cervix. Pathology showed a 5-mm residual tumor at the cervix and the patient was referred for laparoscopic radical nerve-sparing parametrectomy and bilateral pelvic lymphadenectomy.

Methods: This video shows the complete technique of the surgery, including patient and team positioning, trocar placement, and step-by-step dissection of planes, vessels, nerves, and other pelvic structures. Snapshots of the surgery with all relevant anatomic structures identified are shown during the video.

Conclusions: This didactic surgical film demonstrates that parametrectomy, when systematically performed, is a reliable procedure with minimal complications.

doi:10.1016/j.ygyno.2015.01.032

31 — Surgical Forum
Full thickness skin graft for McIndoe neovagina to treat vaginal agenesis in Mayer–Rokitansky–Küster–Hauser syndrome
J.E. Wolford, K.S. Tewari. UC Irvine Medical Center, Orange, CA, USA

Objectives: The procedure that this video highlights is the creation of a neovagina using an adaptation of the McIndoe Abbe procedure, a full-thickness skin graft technique, for a patient with vaginal agenesis secondary to Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome. Surgical treatment for MRKH syndrome typically involves neovaginal construction using split-thickness skin grafts that, while successful in some patients, may result in vaginal contracture or foreshortening. With the use of full-thickness grafts, we have shown a decreased rate of contracture and an overall improved functional outcome.

Methods: In this video, we present our surgical technique for using full-thickness skin grafts for vaginal reconstruction.

Results: The video demonstrates step-by-step creation of the neovagina while discussing the benefits of the full-thickness grafts vs. the split-thickness grafts and elaborating on the postoperative care of the neovaginal patient.

Conclusions: We have found that vaginal reconstruction using full-thickness skin grafts is an underutilized surgical technique that is associated with a decreased rate of contracture and improved functional outcome.

doi:10.1016/j.ygyno.2015.01.033

32 — Surgical Forum
Pelvic and abdominal tumor debulking

A 41-year-old G2P1 woman presented with abdominal bloating and back pain of 3 months’ duration. Her medical history was significant for ulcerative colitis for which she underwent laparoscopic colectomy with rectal pouch anastomosis. On examination, she was found to have a 14-weeks’ gestation-size pelvic mass and a palpable right inguinal lymph node, which was found to be positive for malignancy. Imaging studies showed metastatic lesions in the spleen, upper abdomen, and pelvis. The patient was counseled extensively regarding her condition and chose to undergo exploratory laparoscopy with tumor debulking.

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33 — Surgical Forum
Mechanical morcellation of a solid ovarian mass in a pneumo-bag
D.M. Boruta II, M.R. Davis, University of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea

Objectives: The umbilical incision used for gynecologic laparoscopic single-site surgery (LESS) facilitates removal of adnexal specimens. Once separated from attachments, a cystic mass can be placed within an endoscopic bag. After exteriorizing the bag opening through the port, the cyst is drained without spillage of contents, and the solid portions are removed. Very large, solid adnexal masses present a more challenging problem for minimally invasive surgical removal.

Methods: This surgical video demonstrates a technique for mechanical morcellation of a solid ovarian mass within a gas-filled pneumo-bag as an oncologically sound means to facilitate minimally invasive surgical removal using LESS.

doi:10.1016/j.ygyno.2015.01.035

34 — Surgical Forum
Combined robotic and vaginal approach in radical hysterectomy for the patient with bulky cervical cancer
D. Kim, D.S. Suh, J.H. Kim, Y.M. Kim, Y.T. Kim, J.H. Nam. University of Ulsan College of Medicine, ASAN Medical Center, Seoul, South Korea

Objectives: Robotic surgery is gradually being incorporated into gynecologic oncology. Robotic radical hysterectomy offers some advantages over other surgical approaches with respect to operative time, blood loss, and hospital stay. Due to the necessary location of the robot docking system, however, there is not enough space to enable the performance of vaginal procedures. Therefore, robotic-assisted total radical hysterectomy is in the mainstream for early-stage cervical cancer treatment. In bulky cervical cancer, however, intrauterine manipulation is difficult to install and increases the risk of intra-abdominal tumor seeding. Especially difficult is determination of the level of vaginal cutting. For this reason, the vaginal approach is preferred for robot-assisted radical hysterectomy in bulky cervical cancer.

Methods: This case study examined the use of combined robotic and vaginal radical hysterectomy in a 47-year-old woman who was diagnosed with a FIGO stage IB2 (7.8 cm) squamous cell cervical carcinoma.

Results: Robotic surgery was performed for lymph node dissection, dissection to the origin of the ureter, and dissection of the ureter under direct vision. The vaginal approach was used to apply a precise incision of the vaginal cuff. The patient successfully voided on the seventh postoperative day and has been doing well with no problem.

Conclusions: The combination of robotic and vaginal radical hysterectomy in bulky cervical cancer reduces duration of surgery and decreases the rate of vaginal cuff dehiscence compared to robot-assisted radical hysterectomy alone. A vaginal approach with direct vision following robotic radical hysterectomy is highly effective in treatment of bulky cervical cancer.

doi:10.1016/j.ygyno.2015.01.036
Scientific Plenary VI

Sunday, March 29, 2015
Moderator: Rene Pareja, MD, Instituto de Cancerología, Las Américas, Medellín, Colombia
Audrey Tieko Tsunoda, MD, Barretos Cancer Hospital, Barretos, Brazil

35 – Scientific Plenary

Relative prevalence of high risk HPV genotypes in a US population: Insights before rollout of the next generation 9-valent HPV vaccine

W.K. Huh1, C.M. Behrens2, J. Monsonog3, T. Cox4, M.T. Sandried, P.S. Yap4, E.L. Franco1. 1University of Alabama at Birmingham, Birmingham, AL, USA, 2Roche Molecular Systems, Pleasanton, CA, USA, 3Institut du Col, Paris, France, 4University of California, Santa Barbara, CA, USA, 4Istituto European di Oncologia, Milan, Italy, 5McGill University, Montreal, QC, Canada

Objectives: There is limited information about the distribution of high-risk human papillomavirus (HPV) (hrHPV) genotypes in women in the United States (US), particularly in a low-risk population. The current analysis was undertaken to obtain insights concerning the relative prevalence of hrHPV genotypes in a US population undergoing cervical cancer screening before the rollout of the next-generation 9-valent HPV vaccine.

Methods: In the ATHENA study, approximately 47,000 US women 21 years and older underwent cytologic screening and hrHPV testing with cervical specimens collected in PreservCyt™ medium. HPV testing was performed by the modified Roche LINEAR ARRAY HPV Genotyping test™, which identifies 16 high-risk genotypes: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73, and 82. We calculated the prevalence of HPV genotypes in women with normal cytology (NILM) and in the overall population and the ratio of the prevalence of each type to that of HPV16. We also stratified the analysis between women 21 to 24 years of age and 25 years and older. A 2-sample z-test (2-sided) was used for statistical comparison of proportions.

Results: A total of 46,751 women had valid hrHPV test results and 45,914 of these had evaluable cytology results. HPV16 was the most prevalent genotype in single infections (Table). There was a statistical difference by age in the prevalence of all hrHPVs as well as types 16, 18, 52 and other types not in the 9-valent vaccine (P < 0.001).

Conclusions: Based on one of the largest HPV genotyping datasets in the US, prevalent hrHPVs in a low-risk population are included in the next-generation 9-valent HPV vaccine. We suggest the prevalence ratio relative to HPV16 as a possible baseline indicator of how common each type is relative to a key vaccine-targeted type, which could be used to monitor the impact of vaccination in a population in which different age cohorts may have reached screening age. The forthcoming 9-valent vaccine may substantially influence disease rates and screening recommendations in the US, but resources should be dedicated to tracking HPV genotype prevalence over time and the possibility of an imbalance on type distribution in the general population.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Overall</th>
<th>Pap NILM</th>
<th>Relative prevalence, overall to HPV type 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>All genotypes</td>
<td>11.5 (5382)</td>
<td>10.0 (4261)</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>1.9 (891)</td>
<td>1.5 (656)</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>0.7 (345)</td>
<td>0.6 (273)</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>0.8 (383)</td>
<td>0.7 (292)</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>0.2 (107)</td>
<td>0.2 (89)</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>0.6 (297)</td>
<td>0.6 (252)</td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>1.1 (508)</td>
<td>1.0 (414)</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>0.7 (321)</td>
<td>0.6 (260)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5.4 (2532)</td>
<td>4.7 (2025)</td>
<td></td>
</tr>
</tbody>
</table>

doi:10.1016/j.jygyno.2015.01.037
Objectives: To quantify the cumulative risk of cervical intraepithelial neoplasia (CIN)3 or more severe diagnoses (CIN3+) and invasive cervical cancer (ICC) in three successive rounds of human papillomavirus (HPV) and Papanicolaou (Pap) co-testing at Kaiser Permanente Northern California, which adopted this approach in 2003.

Methods: We defined 3-year cumulative risk to include diagnosis immediately following each screen (using logistic regression) and subsequently up to the next screening round (using Weibull survival models). Between 01/01/2003 and 06/30/2013, 1,002,898 women aged 30 to 64 years who underwent co-testing and did not have ambiguous or non-cervical outcomes were included in this analysis; 532,858 women whose first co-test was negative completed a second round of co-testing and 212,990 women whose second co-test was negative completed a third round of co-testing. Results are presented as the 1st round/2nd round/3rd round and were tested for difference between 1st and 2nd rounds and between 2nd and 3rd rounds.

Results: The population 3-year ICC risks were 0.048%/0.015%/0.0087% (p1vs.2 = 0.0001; p2vs.3 = 0.14). Three-year risks following successive negative co-tests were 0.050%/0.038%/0.033% for CIN3+ (p1vs.2 = 0.025; p2vs.3 = 0.55) and 0.0075%/0.0050%/0.0023% for ICC (p1vs.2 = 0.4; p2vs.3 = 0.28) (B&D). Three-year risks following successive negative HPV tests were 0.072%/0.052%/0.048% for CIN3+ (p1vs.2 < 0.0001; p2vs.3 = 0.72) and 0.011%/0.0074%/0.0027% for ICC (p1vs.2 = 0.10; p2vs.3 = 0.16) (A&C). Three-year risks following successive negative Pap tests were 0.15%/0.087%/0.081% for CIN3+ (p1vs.2 < 0.0001; p2vs.3 = 0.63) and 0.019%/0.0093%/0.0061% for ICC (p1vs.2 = 0.0004; p2vs.3 = 0.44) (A&C).

Conclusions: We noted significant declines in risks between the 1st and 2nd rounds but less pronounced, nonsignificant declines between the 2nd and 3rd rounds of co-testing, suggesting that there may be an irreducible cervical cancer risk with screening. A negative HPV test provides greater reassurance than Pap testing and nearly the same reassurance as a negative co-test against CIN3+ and ICC.

doi:10.1016/j.ygyno.2015.01.040

38 – Scientific Plenary

High-resolution microendoscopy (HRME): A low-cost, point-of-care alternative to colposcopy and biopsies?

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Objectives: Eighty-five percent of cervical cancer cases and deaths occur in low- and middle-income countries (LMICs), where cervical cancer is the first or second leading cause of cancer among women. High-resolution microendoscopy (HRME) is a novel, low-cost optical imaging method that provides similar morphologic information to a cervical biopsy (nuclear to cytoplasmic [N/C] ratio, nuclear crowding, and atypia) in real time, allowing for immediate diagnosis of cervical dysplasia and treatment if indicated (See & Treat). The objective of this study was to compare HRME imaging to cervical biopsy.

Methods: A prospective study of 59 patients undergoing colposcopy for abnormal Papanicolaou test results was performed at Barretos Cancer Hospital in Brazil. All patients underwent colposcopy per standard of care, with any acetowhite (ACW) lesions recorded. HRME images were obtained for all lesions noted by colposcopy. Biopsies of abnormal areas were obtained and reviewed by two independent, blinded pathologists and compared to HRME findings.

Results: A total of 79 ACW lesions were noted in 46 patients, with biopsies performed of all lesions. Adequate HRME images were obtained for 59 of these lesions (75%). Biopsy results showed normal tissue (n = 9, 15%), cervical intraepithelial neoplasia (CIN)1 (n = 16, 27%), CIN2 (n = 12, 20%), CIN3 (n = 19, 32%), and invasive cancer (n = 3, 5%). The corresponding percentages indicated as positive by HRME were 22% for normal, 31% for CIN1, 83% for CIN2, 95% for CIN3, and 100% for cancer. The sensitivity and specificity of HRME for biopsy-proven CIN2+ (n = 34) were 89% and 77%, respectively.

Conclusions: Our results suggest that HRME imaging may provide a low-cost, accurate, point-of-care alternative to colposcopy and directed cervical biopsies for the diagnosis of cervical dysplasia in low-resource settings, where there is often a lack of colposcopy and pathology services. Further evaluation in large prospective studies is ongoing.

doi:10.1016/j.ygyno.2015.01.039

Focused Plenary I — Pre Clinical Discovery

Monday, March 30, 2015

Moderators: Ernst Lengyel, MD, PhD, University of Chicago Medicine, Chicago, IL, USA
Walter Gotlib, MD, Jewish General Hospital, Montreal, Quebec, Canada

39 – Focused Plenary

Post-chemotherapy tumors in the PDX model identify ribosomal synthesis as a novel targeting strategy in ovarian cancer

Z.C. Dobbin1, A.A. Katre2, D.H. Jeong3, B.K. Erickson3, R.D. Alvarez4, D.A. Schneider1, C.N. Landen Jr.5, *University of Alabama at Birmingham, Birmingham, AL, USA, 2Busan Paik Hospital, Inje University, Busan, South Korea, 3University of Virginia School of Medicine, Charlottesville, VA, USA

Objectives: The objectives of this study were to use the heterogeneity of the patient-derived xenograft (PDX) model to characterize the surviving population for de novo mediators of chemotherapy resistance and subsequently target pathways contributing to such resistance. Identification of ribosomal RNA synthesis as a major mediator of survival led to a strategy to target this pathway and revealed it is a potential means to overcome chemotherapy resistance in ovarian cancer.

Methods: Tumors removed during primary tumor-reductive surgery were implanted directly into severe combined immunodeficiency disease mice. Mice with PDX tumors were treated with combination carboplatin/paclitaxel. Surviving residual tumors were compared to untreated matched tumors and subjected to RNA sequencing and pathway analysis. Ribosomal RNA synthesis was inhibited with the novel agent CX-5461 in vitro and in vivo in chemosensitive and chemoresistant models. Viability, cell cycle analysis, and tumor reduction were the primary endpoints of therapy.

Results: At the mRNA level, the original patient tumor was similar to PDX tumors in mice, as assessed by an 84-oncogene expression panel. Patient responses also correlated well with responses in mice.
PDX tumors collected after treatment showed that the survival population was significantly more dormant than the original tumor. RNA sequencing analysis of treated and untreated PDX tumors (n = 6 pair) demonstrated that numerous factors with roles in ribosomal synthesis were significantly altered by treatment. In vitro, an inhibitor of ribosomal synthesis, CX-5461, caused significant G2/M-phase arrest, and effects were much more profound in chemoresistant cells than corresponding chemosensitive cells. In vivo, of the five PDX models that were treated with CX-5461, two had progression, one had stable disease, one had a 60% reduction in tumor growth, and one had a complete response to single-agent therapy, still without recurrence after 3 months.

**Conclusions:** The ovarian PDX model exhibits similarity to patient tumors. Postchemotherapy tumors reveal severe alteration of ribosomal synthesis. Treatment with an inhibitor of ribosomal RNA synthesis was highly effective in vitro and in vivo, offering a novel opportunity to specifically target the chemoresistant population in ovarian cancer.

doi:10.1016/j.ygyno.2015.01.041

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**41 — Focused Plenary**

**Pre-surgical window study of metformin in obesity-driven endometrial cancer**


**University of Manchester, Manchester, UK, bCentral Manchester University Hospitals Foundation Trust, Manchester, UK, cTameside Hospital NHS Foundation Trust, Manchester, UK, dPennine Acute Hospitals NHS Trust, Oldham, UK

**Objectives:** Metformin use in patients with type 2 diabetes is associated with reduced cancer risk in some observational studies. Preclinical studies in endometrial cancer show that metformin reduces cellular proliferation by inhibition of the PI3K–mTOR pathway. We hypothesized that metformin would reduce cellular proliferation in vivo in atypical endometrial hyperplasia (AEH) and endometrioid endometrioid adenocarcinoma (EC).

**Methods:** Women with AEH or EC who were recruited to receive metformin 850 mg BD or no drug in the 1- to 4-week presurgical window between diagnosis and hysterectomy. Blood and endometrial tumour samples were obtained at recruitment and at hysterectomy. Cellular proliferation by Ki67 proliferation index and intracellular phosphorylation of AKT (P-S6, respectively). Observer intraclass correlations of 0.94, 0.88, and 0.92 for Ki-67, P-AKT, and S6, respectively. Results: The study group comprised 28 metformin-treated and 12 control women. Median age was 64 years in the metformin-treated and 66 years in the control group. More than 60% of all patients were obese; 55% of patients had undiagnosed diabetes (n = 4, fasting glucose >7.0 mmol/L) or insulin resistance (HOMA-IR >2.8). Metformin was taken for a median of 20 days (range, 7–34 days). In the metformin-treated group, Ki-67 was 16.9% lower at hysterectomy than at recruitment (95% CI 6.7 to 27.1, P = 0.002) after adjusting for baseline Ki-67, Ki-67 change in untreated controls, age, body mass index (BMI), and HOMA-IR. There were no significant changes in phosphorylation states of AKT (P = 0.30) and S6 (P = 0.73) or HOMA-IR (P = 0.88) in the treated relative to untreated patients after adjusting for baseline biomarker values, age and BMI.

**Conclusions:** Undiagnosed insulin resistance/diabetes was common in our study population. Short-term presurgical metformin was associated with a reduction in Ki-67 proliferation index. Changes associated with mTOR inhibition were not demonstrated in contrast to studies without contemporaneous controls. Our findings warrant placebo-controlled studies to explore the therapeutic effect of metformin in endometrial cancer and identification of relevant biomarkers.

doi:10.1016/j.ygyno.2015.01.041
42 — Focused Plenary
The effects of NT1014, a novel AMPK activator, compared to metformin, on ovarian cancer cell proliferation, apoptosis, and tumor growth

W.Z. Wysham, J.E. Kilgore, A.L. Jackson, H. Qiu, C. Zhou, K.W. Batchelor, V.L. Bae-Jump. "University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. 4Houston Methodist Hospital, Houston, TX, USA, 4University of Cincinnati, Cincinnati, OH, USA. 6NovaTarg Therapeutics, Research Triangle Park, NC, USA

Objectives: Antidiabetic biguanide drugs such as metformin may have antitumorigenic effects by behaving as adenosine monophosphate-activated protein kinase (AMPK) activators and mTOR inhibitors. Metformin requires organic cation transporters (OCTs) for entry into cells, and NT1014 (NovaTarg Therapeutics) is an AMPK activator designed to have greater affinity for two of these transporters, OCT1 and 3. We sought to compare the effects of metformin and NT1014 on cell proliferation in ovarian cancer (OC) cell lines and on tumor growth in a serous OC mouse model.

Methods: Cell proliferation was assessed in two OC cell lines, SKOV3 and IGROV1, by MTT assay after exposure to metformin and NT1014. Apoptosis was analyzed by Annexin V-FITC assay. Cell cycle progression was evaluated by flow cytometry. Phosphorylated (phos)-S6 and phos-AMPK were evaluated by Western immunoblotting. For in vivo studies, we utilized the K18-gT121/fl−/−, p53−/−, Brca1+/- (KpB) OC mouse model. Mice were treated with placebo, metformin (200 mg/kg/day), or NT1014 (75 µg/kg/day) following tumor onset for 4 weeks. Immunohistochemistry was used to evaluate expression of Ki-67, phos-AMPK, and phos-S6 in the OC tumors after treatment with placebo, metformin, or NT1014.

Results: Metformin and NT1014 significantly inhibited proliferation in a dose-dependent manner in both OC cell lines after 72 h of exposure, coincident with G1 cell cycle arrest. The mean inhibition concentration of IC50 values were lower for NT1014 (SKOV3 = 380 µM; IGROV1 = 150 µM) than metformin (SKOV3 = 1000 µM; IGROV = 850 µM). Apoptosis occurred in both OC cell lines exposed to metformin but only in the IGROV1 cells exposed to NT1014. Metformin and NT1014 increased phosphorylation of AMPK and decreased phosphorylation of S6, a key downstream target of the mTOR pathway. As compared to placebo, NT1014 inhibited tumor weight in the KpB mice by 61% (P < 0.0015), while metformin inhibited tumor weight by only 32% (P = 0.047). Treatment with metformin and NT1014 in the OC tumors decreased Ki-67 and phos-S6 staining and increased phos-AMPK.

Conclusions: Metformin and NT1014 suppressed OC cell and tumor growth through AMPK activation and mTOR pathway inhibition, with increased efficacy of NT1014 found in vitro and in vivo. This suggests that NT1014 may have improved potency over metformin and should be further explored in the treatment of OC.

doi:10.1016/j.ygyno.2015.01.045

Focused Plenary II — Genetics of Uterine Cancer
Monday, March 30, 2015
Moderator: Diane S. Yamada, MD, University of Chicago, Chicago, IL
Summer B. Dewdney, MD, Rush University Medical Center, Chicago, IL

43 — Focused Plenary
Identification of potential therapeutic targets by molecular profiling of 628 cases of uterine serous carcinoma

N.L. Jones, J. Xiu, S.K. Reddy, A.I. Tergas, W.M. Burke, J.D. Wright, J.Y. Hsia. "NYP/Columbia University Medical Center, New York, NY, USA, 5Caris Life Sciences, Irving, TX, USA

Objectives: Therapeutic options are limited for uterine serous carcinoma (USC), an uncommon but aggressive subtype of endometrial cancer that is often resistant to traditional cytotoxic chemotherapy. We aim to identify potential treatment options for USC patients by evaluating patterns of molecular, genomic, and protein changes in a large cohort of patients with USC.

Methods: A total of 3133 endometrial cancer specimens were evaluated by Caris Life Sciences from March 2011 to July 2014 via multiplet platform profiling, which included a combination of sequencing (Sanger or next generation sequencing [NGS]), protein expression (immunohistochemistry [IHC]), and/or gene amplification (chromogenic in situ hybridization [CISH] or fluorescence in situ hybridization [FISH]). Based on reported pathology, 628 USCs were identified and analyzed.

Results: Of 47 genes sequenced, 31 showed mutations; the most frequent were TP53 (76%), PIK3CA (29%), FBXW7 (12%), and KRAS (9.3%). BRCA1 and 2 were mutated in 9.1% and 6.3%, respectively, and FGFR2 in 3.4%. Of proteins implicated in DNA repair, ERCC1 was absent in 81% and MGMT was absent in 46%, suggesting potential benefit from platinum and alkylating agents, respectively. Although not traditionally considered hormone-dependent, our USC cohort showed high estrogen receptor-α (60%), progestereceptor (32%), and androgen receptor (27%) expression. Her2 overexpression was 10% via IHC, amplification was 17% via CISH/FISH, and mutation was 2% via NGS. While low in Pten mutation frequency (7%), 45% of USCs showed Pten loss on IHC. Twenty-nine-nineteen percent harbored PIK3CA mutation, suggesting upregulation of the P13K/akt/mTOR pathway in a subset of patients. Eleven percent expressed PDL1 and 6% expressed PDI, suggesting potential benefit from anti-PDI/PDL1 agents in a subset of patients. Interestingly, 89.5% overexpressed TOP2A protein and 6.8% showed TOP2A amplification, among which half showed coamplification of Her2 with TOP2A, suggesting increased anthracycline susceptibility in a subgroup of USC patients.

Conclusions: Our findings suggest that USC is a genetically heterogeneous disease, but molecular profiling of a large cohort of 628 tumors using multiple technologies identified potential pathways for therapeutic exploitation. Drugs targeting specific pathways, including the PI3K, DNA repair, and PDI/PDL1 pathways, as well as anthracyclines and hormonal agents may have benefit in a selected subset of patients with this disease.

doi:10.1016/j.ygyno.2015.01.044

44 — Focused Plenary
Using multi-gene testing to broaden the understanding of inherited endometrial cancer

L.E. Panos, E. Chao, R. McFarland, H. LaDuca. Ambyr Genetics, Aliso Viejo, CA, USA

Objectives: Aside from Lynch syndrome and Cowden syndrome, little is known about the possible genetic contribution to endometrial cancer susceptibility. In this study, we explored the clinical and molecular characteristics of endometrial cancer patients, with pathogenic mutations and likely pathogenic variants identified on multi-gene panel testing.

Methods: Multi-gene cancer panel results and clinical history information were reviewed for 429 endometrial cancer patients referred by clinicians to a clinical diagnostic laboratory. The number of cancer susceptibility genes analyzed for each patient varied, among which half showed coamplification of Her2 with TOP2A, suggesting increased anthracycline susceptibility in a subgroup of USC patients.

Results: A total of 68 endometrial cancer patients were identified as having at least one pathogenic mutation or likely pathogenic variant (15.9%). Variants of unknown significance were identified in 25.9% of patients (n = 111). The most commonly mutated gene in this cohort was CHEK2, accounting for 21.7% of all mutations identified. Other commonly mutated genes included MSH6 (18.2%), ATM (8.7%), BRCA2 (8.7%), and MSH2 (8.7%). Sixty-five positive patients reported an age of diagnosis of endometrial cancer, with 73.8% diagnosed between 40 and 59 years of age.

Conclusions: Our findings suggest that USC is a genetically heterogeneous disease, but molecular profiling of a large cohort of 628 tumors using multiple technologies identified potential pathways for therapeutic exploitation. Drugs targeting specific pathways, including the PI3K, DNA repair, and PDI/PDL1 pathways, as well as anthracyclines and hormonal agents may have benefit in a selected subset of patients with this disease.

doi:10.1016/j.ygyno.2015.01.045
Table 1
The frequency of mutations identified in an endometrial cancer population.

<table>
<thead>
<tr>
<th>Category (N)</th>
<th>Number positive</th>
<th>% positive</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial cancer (429)</td>
<td>68</td>
<td>15.9%</td>
<td>APC, ATM, BRCA1, BRCA2, BRIPI1, CDH1, CHEK2, MLH1, MRE11A, MSH2, MSH6, MUTYH, PMS2, PNL2, PTF1, TP53</td>
</tr>
<tr>
<td>Age at endometrial cancer diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 (20)</td>
<td>0</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>30–39 (51)</td>
<td>8</td>
<td>15.7%</td>
<td></td>
</tr>
<tr>
<td>40–49 (103)</td>
<td>23</td>
<td>22.3%</td>
<td></td>
</tr>
<tr>
<td>50–59 (113)</td>
<td>25</td>
<td>22.1%</td>
<td></td>
</tr>
<tr>
<td>60–69 (89)</td>
<td>8</td>
<td>9.0%</td>
<td></td>
</tr>
<tr>
<td>70+ (41)</td>
<td>4</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>Endometrial cancer with no other primaries (143)</td>
<td>18</td>
<td>12.6%</td>
<td></td>
</tr>
<tr>
<td>Multiple primary cancers (286b)</td>
<td>50</td>
<td>17.5%</td>
<td></td>
</tr>
<tr>
<td>2 primary cancers (182)</td>
<td>24</td>
<td>13.2%</td>
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</tr>
<tr>
<td>Endometrial and ovarian primaries (100)</td>
<td>14</td>
<td>14.0%</td>
<td></td>
</tr>
<tr>
<td>Endometrial and breast primaries (160)</td>
<td>32</td>
<td>20.0%</td>
<td></td>
</tr>
<tr>
<td>Endometrial and colorectal primaries (36)</td>
<td>8</td>
<td>22.2%</td>
<td></td>
</tr>
<tr>
<td>3 primary cancers (79)</td>
<td>21</td>
<td>26.6%</td>
<td></td>
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<td></td>
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<td></td>
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</tbody>
</table>

* Includes one individual with two CHEK2 mutations.

b Excludes skin cancer.

45 — Focused Plenary
Clinicopathologic features associated with defective DNA mismatch repair (MMR): A GOG 0210 cohort study of 1041 endometrioid endometrial cancer cases
D.G. Mutch*, M.A. Powell†, A. Schmid†, R. Broadus‡, N. Ramirez‡, D. Tritchler§, S. Ali†, H. Lankes¶, D.M. O’Malley¶, P.J. Goodfellow‡.
*Washington University School of Medicine, St. Louis, MO, USA. †The University of Texas MD Anderson Cancer Center, Houston, TX, USA. ‡Gynecologic Oncology Group Tissue Bank, Biopathology Center, Research Institute at Nationwide Children’s Hospital, Columbus, OH, USA. §Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA. ¶Roswell Park Cancer Institute, Buffalo, NY, USA. †The Ohio State University, James Cancer Hospital, Columbus, OH, USA. ‡The Ohio State University Medical Center, Columbus, OH, USA.

Objectives: To systematically classify DNA mismatch repair (MMR) status in a large series of endometrioid endometrial cancers enrolled in a single trial and determine the relationship between MMR defects and clinicopathologic features, focusing on outcomes.

Methods: MMR status was investigated in 1041 endometrioid endometrial cancer specimens from the GOG 0210 cohort (open enrollment phase 9/03–9/07). MMR immunohistochemistry (IHC) was scored by a single expert pathologist. Microsatellite instability (MSI) and MLH1 methylation testing were performed using multiplexed polymerase chain reaction and pyrosequencing. Statistical analyses were performed in a centralized statistics and data management center.

Results: MSI, IHC, and methylation analyses were successfully completed for 993 tumor specimens. Based on tumor MMR typing, subjects were assigned to one of three groups: no defect (n = 637), epigenetic loss attributable to MLH1 methylation (EL) (n = 244), or probable genetic disease (n = 112). Age, body mass index (BMI), grade, stage, and lymphovascular space involvement (LVI) were significantly associated with MMR status. Tumors with MMR defects were more likely to have LVI (P = 1.4 × 10^{-7}) and to be higher grade (P = 3.0 × 10^{-2}) and higher stage (P = 0.01). As previously described, BMI was lower and age was higher for patients in the EL group. There was no difference in progression-free or overall survival among the three groups (P = 0.08 and 0.33, respectively).

Conclusions: Endometrial cancer MMR status measured using combined IHC and DNA analyses is not associated with disease-free or overall survival, despite the increased prevalence of poor prognostic features in MMR-deficient tumors, including higher stage and grade and presence of LVI. This finding points to a complex interplay between conventional prognostic features, elevated mutation status, and other changes in tumors with MMR defects. MMR defects appear to blunt the expected adverse effects associated with higher grader, higher stage, and LVI in endometrial cancers. The variable results seen with prior studies assessing the relationship between MMR abnormalities and outcomes could be explained, in part, by a difference in methods used to...
dichotomize MMR status and by combining cases with epigenetic and probable genetic causes rather than treating them as etiologically and clinically distinct groups.

doi:10.1016/j.ygyno.2015.01.047

46 — Focused Plenary
Homologous recombination deficiency in endometrioid uterine cancer: An unrecognized phenomenon
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Objectives: PTEN mutations are frequently observed in endometrioid uterine cancer and lead to hyperactivation of the PI3K/Akt pathway. However, the role of BRCA1 and 2 mutations, leading to homologous recombination deficiency, is not known in this disease. We sought to determine the frequency and clinical significance of BRCA mutations in patients with uterine cancer and PTEN mutations.

Methods: We assessed PTEN, BRCA1, and BRCA2 mutation status for 248 uterine tumor samples using level 3 data from The Cancer Genome Atlas (TCGA). We performed mutation analysis for PTEN, BRCA1, and BRCA2 for an additional 251 samples from TCGA using ANNOVAR. A total of 499 patients were included in the analysis. Clinical data, including stage, tumor histology, and overall survival, were also extracted. Fisher's exact tests were used to identify the association between mutation status and histologic subtype. Kaplan–Meier plots were constructed to demonstrate survival differences between groups.

Results: Among the samples analyzed, 335 (67%) had endometrioid histology, 76 (15%) had serous histology, 18 (44%) had mixed histology, and histology was unknown in the remainder of cases. Of the patients with endometrioid histology, 260 (78%) had a PTEN mutation, 23 (7%) had both BRCA1 and 2 mutations, 4 (1%) had mutations in BRCA1 only, and 25 (8%) had mutations in BRCA2 only. A total of 52/335 patients (16%) had mutations in either BRCA1 or 2; 18/52 (35%) of these had stage II or above disease and the remainder had stage I disease. No survival advantage was detected in patients with BRCA1 mutations over wild-type BRCA1, independent of PTEN mutation status (P = 0.16 and 0.19, respectively). Patients with both PTEN and BRCA2 mutations had improved overall survival compared to patients with wild-type PTEN and BRCA2 (P = 0.03). A single mutation in BRCA1, BRCA2, or PTEN did not confer a significant survival advantage compared to wild-type (P = 0.15).

Conclusions: BRCA1 and 2 mutations are prevalent in patients with endometrioid uterine cancer, and PTEN/BRCA2 double mutations are associated with prolonged patient survival. These findings may have significant clinical and treatment implications.

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Focused Plenary III — Novel Approaches to Surgery
Monday, March 30, 2015
Moderator: Heidi J. Gray, MD, University of Washington Medical Center, Seattle, WA
Camille Catherine Gunderson, MD, The University of Oklahoma, Oklahoma City, OK

47 — Focused Plenary
ROMA guided conservative management for women diagnosed with an ovarian cyst or pelvic mass
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Objectives: Results-oriented management assessment (ROMA) has been cleared by the United States Food and Drug Administration to assist non-oncology physicians in risk assessment of a pelvic mass and to triage women at high risk for malignancy to gynecologic oncologists. Most women presenting with a pelvic mass have benign disease, and many who are asymptomatic still have surgery. The objective of this study was to evaluate the use of ROMA to assist in identifying women who can safely undergo conservative management.

Methods: All patients referred to Women's Oncology with a pelvic mass are evaluated at our multidisciplinary tumor board (TB), where ROMA and imaging are used to reach management recommendations. This institutional review board-approved trial evaluated women presented to the TB from 2009 to 2012 with a pelvic mass who had either surgical or conservative management. Patient demographics, imaging, ROMA scores, TB recommendations, and pathology were collected. Basic statistical parameters were determined.

Results: Among the 500 patients eligible for analysis (173 pre- and 327 postmenopausal), the median age was 56 years (range: 15–90 years). There were 392 patients with benign disease, 22 with low malignant potential (LMP) tumors, 28 with stage I–II epithelial ovarian cancer (EOC), 36 with stage III–IV EOC, and 20 with non-EOC. Initial TB recommendation for patient management had a sensitivity for detecting malignancy of 100% (95% CI: 95.7–100%), specificity of 47.8% (95% CI: 42.8–52.9%), and negative predictive value (NPV) of 100% (95% CI: 98.0–100%). Actual patient management had a sensitivity of 98.8% (95% CI: 93.5–100%), specificity of 46.0% (95% CI: 41.0–51.1%) and NPV of 99.4% (95% CI: 97.0–100%). ROMA alone for the detection of EOC had a sensitivity of 95.3% (95% CI: 86.9–99.0%), specificity of 65.8% (95% CI: 60.6–70.3%), and NPV 98.8% (95% CI: 96.7–99.8%). For Stage I–II EOC, ROMA had a sensitivity of 89.3% (95% CI: 71.8–97.7%). All 84 malignancies, including 28 early-stage EOC, were recommended for surgery. Only 1 of 22 patients with an LMP tumor was assigned to observation. Clinical assessment in conjunction with ROMA identified 187 (37.4%) women for conservative management.

Conclusions: ROMA, in conjunction with clinical assessment, can safely identify women for conservative management. No women with a malignancy were assigned to the observation group, and one third of patients who were originally referred for consideration for surgery safely underwent conservative management.

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48 — Focused Plenary
Impact of sentinel lymph node mapping on FIGO stage and GOG risk stratification in early endometrial cancer: A comparative analysis
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Objectives: To determine the impact of sentinel lymph node (SLN) mapping on FIGO stage and Gynecologic Oncology Group (GOG) risk stratification in patients with endometrial cancer by comparing patients surgically staged with and without SLN mapping.

Methods: A robotic surgery database was queried for endometrial cancer cases (07/2006 to 06/2013) that underwent robotic hysterectomy with pelvic ± aortic lymphadenectomy. A total of 781 cases were identified that had ≥8 pelvic lymph nodes (LN)s resected: Group A had pelvic ± aortic lymphadenectomy (n = 662) and Group B had SLN mapping with lymphadenectomy (n = 119). SLN mapping was accomplished with isosulfan blue dye and indocyanine green with near-infrared imaging. Patients were staged by FIGO 2009 criteria and assessed for GOG risk stratification. Criteria compared in both groups were clinicopathologic data, FIGO stage, GOG risk, and postoperative therapies.
Results: Groups A and B were comparable for body mass index, histology (Grade 3, Type I vs. Type II), depth of invasion, and lymphovascular space invasion. Group B cases were older (65.5 ± 9.2 vs. 63.0 ± 10.9 years, P = 0.02) and had more pelvic LNs harvested (26.4 ± 10.5 vs. 18.8 ± 8.5, P < 0.0001). Aortic LN yields were identical (9.0 ± 5.6 vs. 9.0 ± 6.0). More pelvic LN metastases were detected in Group B (30.3% vs. 13.6%, P < 0.0001). Group B had more Stage III/1 cases (19.3% vs. 6.0%, P < 0.0001), fewer Stage IIIA cases (0.8% vs. 6.6%, P < 0.01), more GOG high-risk cases (32.8% vs. 19.8%, P < 0.01), fewer low-risk cases (21.8% vs. 36.3%, P < 0.01), and more patients receiving combination chemotherapy + radiation (28.6% vs. 16.3%, P < 0.003). A total of 18/36 (50%) Group B cases with LN metastases were isolated to the SLN, and 12/18 (66.7%) of these were micrometastases or isolated tumor cells that were missed on hematoxylin-and-eosin pathology.

These 12 upstaged cases would have been considered GOG low-risk (n = 4), low-intermediate risk (n = 2), and high-intermediate risk (n = 6) without SLN mapping.

Conclusions: This study suggests that compared to traditional pelvic lymphadenectomy, the addition of SLN mapping identifies more pelvic lymph node metastases and shifts GOG low- and intermediate-risk cases to high-risk cases, possibly resulting in administration of more postoperative chemotherapy and radiation therapy.

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50 — Focused Plenary

Outcomes in low-volume lymph node metastasis discovered during sentinel lymph node mapping for endometrial carcinoma


Objectives: Pathologic ultrastaging in endometrial carcinoma has led to increased detection of “low-volume” lymph node metastasis in the form of isolated tumor cells (ITCs) and micrometastases (MMs). We sought to characterize treatment patterns and oncologic outcomes in this patient population to further inform the discussion regarding optimal postoperative management.

Methods: We identified endometrial cancer cases treated surgically at our institution from September 2005 to April 2013 in which sentinel lymph node mapping was performed. All grades, stages, and histologies were included. MMs was defined as tumor within a lymph node measuring 0.2 to 2.0 mm. ITCs were those identified on hematoxylin-and-eosin (H&E) measuring <0.2 mm. Cytokeratin-positive cells not seen on H&E were considered node-negative. Standard statistical analysis was performed using SPSS.

Results: A total of 844 patients met the inclusion criteria for evaluation. Median age was 61 years (range, 30–90 years), and median body mass index was 30 (range, 16–69). Histology: endometrioid, 724 (86%); serous, 104 (12%); and clear cell, 16 (2%). Of the endometrioid cases, 479 (66%) were FIGO grade 1, 177 (25%) were grade 2, and 68 (9%) were grade 3. The median number of lymph nodes resected was 6 (range, 0–60); the median number of sentinel lymph nodes was 2 (range, 0–15). A total of 753 patients (89%) were node-negative, 23 (3%) had ITCs only, 21 (2.5%) had MMs only, and 47 (6%) had micrometastasis. Adjuvant chemotherapy was given to 106/753 (14%) node-negative patients, 19/23 (83%) patients with ITCs, 17/21 (81%) patients with MMs, and 42/47 (89%) patients with micrometastasis. Median follow-up was 26 months (range, 0–108 months). Three-year recurrence-free survival was as follows: node-negative patients, 90 ± 1.5%; ITCs only, 86 ± 9.4%; MMs only, 86 ± 9.7%; and macrometastasis, 71% ± 7.2% (P < 0.001). These data were similar when stratified by histology.

Conclusions: In this cohort, patients with ITCs and MMs frequently received adjuvant therapy and appeared to have oncologic outcomes similar to those with negative lymph nodes. Further prospective
51 — Scientific Plenary

A phase I trial of pegylated liposomal doxorubicin (PLD), carboplatin, bevacizumab, and veliparib (ABT-888) in recurrent, platinum-sensitive ovarian, primary peritoneal, and fallopian tube cancer: A Gynecologic Oncology Group study

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Objectives: To determine the maximum tolerated dose (MTD) and dose-limiting toxicities (DLT) of two different regimens of ABT-888 when administered with carboplatin and PLD in recurrent platinum-sensitive epithelial ovarian, primary peritoneal, and fallopian tube cancer. A second component of the study was to examine the tolerability of these treatment regimens in combination with bevacizumab (10 mg/kg on days 1 and 15) at the MTD.

Methods: Patients received PLD (30 mg/m², IV) and carboplatin (AUC 5, IV) on day 1, with ABT-888 on days 1–7 (intermittent) or days 1–28 (continuous) starting at a dose of 50 mg PO BID. Standard 3 + 3 design was used in the dose escalation phase, with DLTs based on the first cycle. Once the MTDs were determined for both arms of ABT-888, cohorts of 6 evaluable patients were enrolled in each regimen with bevacizumab to assess feasibility. The first four cycles of treatment were assessed to determine DLTs in the bevacizumab cohorts.

Results: The MTD for ABT-888 was determined to be 80 mg PO BID for both the intermittent and continuous arms. In the dose-escalation phase, 27 patients were treated, and all were DLT- evaluable. Six evaluable patients had DLTs with the first cycle of treatment. These DLTs included grade 4 thrombocytopenia (4), prolonged neutropenia > 7 days (2), and grade 3 hyponatremia (1). Twelve evaluable patients were treated with bevacizumab in combination with PLD, carboplatin, and ABT-888 at MTD of 80 mg PO BID. Four of the six evaluable patients on the intermittent dosing arm had DLTs over four cycles of treatment: grade 4 thrombocytopenia (2), prolonged neutropenia > 7 days (1), and grade 3 hypertension (2). Five of six evaluable patients on the continuous dosing arm had DLTs over four cycles of treatment: grade 4 thrombocytopenia (3), grade 3 hypertension (3), and prolonged neutropenia > 7 days (1).

Conclusions: The MTD of ABT-888, when administered in combination with PLD (30 mg/m², IV) and carboplatin (AUC 5, IV) in a population of recurrent platinum-sensitive ovarian cancer patients, is 80 mg PO BID, with bone marrow suppression as the DLT. In a population of platinum-sensitive recurrent ovarian cancer patients treating at the first recurrence, ABT-888 is tolerated only at low doses in combination with PLD and carboplatin.

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53 — Scientific Plenary

A phase II trial of trebananib (AMG 386), a selective angiopoietin 1/2 neutralizing peptibody in patients with persistent/recurrent carcinoma of the endometrium: A Gynecologic Oncology Group study

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Objectives: Angiogenesis has a role in endometrial cancer (EC) progression and prognosis. A phase II trial of bevacizumab in recurrent EC with one or two prior therapies documented a response rate (RR) of 13% and 6-month progression-free survival of 40%. Ang1 (angiopoietin-1) and Ang2 (angiopoietin-2) interact with Tie-2 receptor expressed on endothelial cells to mediate vascular remodeling in an angiogenesis signaling pathway that is distinct from the vascular endothelial growth factor axis. Trebananib is a peptide Fc fusion protein that binds both Ang1 and Ang2 and prevents interaction with the Tie2 receptor.

Methods: The primary objective of the study was to evaluate the efficacy of the study agent through the frequency of patients (pts) with objective tumor responses (ORR) and the those who survived event-free for at least 6 months (6-month EFS) and determine toxicity of AMG386 15 mg/kg intravenously QW. Recurrent/persistent epithelial EC, measurable disease, and one or two prior chemotherapy lines were required. Prior biologic treatment was not allowed.

Results: A total of 35 pts were enrolled and 32 were eligible and treated. Thirty-four percent of pts enrolled were age 60–69 years and 44% were 70 years and older. Histology was evenly split between G1/2 endometrioid (n = 10, 31%), G3 endometrioid (n = 9, 28%), and serous (n = 10, 31.3%). Seventy-eight percent of pts had only one prior regimen. Pts received 1–9+ cycles of AMG 386; 24 pts (75%) received ≤2 cycles. One pt had a partial response (3.1%) and 8 pts had stable disease (25%). Five pts (15.6%) had 6-month EFS. Median progression-free survival and overall survival were 1.97 months (90% CI 1.77–2.1) and 6.6 months (90% CI 4.01–14.75), respectively. The most common adverse events (AE), regardless of attribution, were fatigue, anemia, constipation, abdominal pain, nausea, anorexia, hypertension, and limb edema. Respective grade 3 and 4 AEs occurred in the following categories: gastrointestinal 31% and 0%; vascular disorders 22% and 0%; metabolism/nutrition 19% and 3%; and general administration site (including edema) 16% and 0%. Four grade 5 AEs were reported. One pt died due to a pneumothorax reported as related to treatment site (including edema). Clinical trial information: NCT01210222.

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54 — Scientific Plenary

A personalized paradigm in the treatment of platinum-resistant ovarian cancer: A cost utility analysis of genomic versus cytotoxic therapy

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Objectives: To assess the cost utility of a strategy of using genomic-based tumor testing to guide therapy for platinum-resistant ovarian cancer compared with standard cytotoxic chemotherapy.

Methods: A decision tree was generated to compare treatments: 1) standard of care (SOC) arm: sequential therapy with pegylated liposomal doxorubicin, then bevacizumab/paclitaxel, then topotecan; or 2) genomic arm: genomic tumor testing with targeted therapy based on identifying a mutation with a drug to treat this target. Cost estimates of chemotherapy as well as the price of a genomic tumor test ($5800 for FoundationOne) were derived from Medicare. Targeted therapy was nominally priced at $8737/month, based on a weighted average. In the base case, equivalent survival and quality of life (QoL) between strategies was assumed. Pertinent uncertainties (cost of targeted therapy and genomic testing, response to targeted therapy, probability of a tumor having a targetable mutation, and impact of QoL) were evaluated in a series of one and two-way sensitivity analyses.

Results: A strategy of genomic testing and targeted therapy was more costly ($85,620 vs. $77,246) than SOC. When QoL was assumed to be better with targeted therapy compared with SOC, the incremental cost-effectiveness ratio (ICER) of the genomic strategy was >$300,000 per quality-adjusted life year saved (QALY). Results were insensitive to the degree of difference in QoL during targeted vs. SOC treatments, and to the probability of identifying a therapeutic target. The cost-effectiveness of the genomic strategy was sensitive to the costs of the genomic test and targeted therapy, but both need to be significantly lower to make genomic testing cost-effective (Fig. 1). When the cost of genomic testing is decreased by 50% and the cost of targeted therapy is decreased by 25%, the genomic strategy becomes potentially cost-effective with an ICER of $92,321/QALY.

Conclusions: Under baseline assumptions, genomic-based targeted therapy is more expensive and not cost-effective compared with SOC. The model was sensitive to the cost of the genomic test and the cost of targeted therapy but not the rate of response to these agents. As personalized medicine becomes more widely adopted, costs of targeted treatment may decrease to levels that maximize their value.

Fig. 1. Two-way sensitivity analysis: Effect of the costs of genomic testing and targeted therapies on the cost-effectiveness of the genomic strategy (Shading indicates a strategy is cost-effective within this range).

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55 – Scientific Plenary
Incidence of VTE by type of gynecologic malignancy in the National Surgical Quality Improvement Program

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Objectives: The objective of this study was to determine the frequency of venous thromboembolism (VTE) in surgical gynecologic oncology patients, stratified by origin of malignancy.

Methods: Using the American College of Surgeons National Surgical Quality Improvement Program database, 104,368 gynecologic surgeries were identified from 2006 to 2012. Patient demographics, 30-day postoperative complications, and operative diagnosis were abstracted. Patients were stratified by origin of gynecologic malignancy. The primary outcome was the frequency of VTE. Institutional Board Review exemption was obtained.

Results: A total of 104,436 gynecologic surgeries were identified and found to have a frequency of deep venous thrombosis (DVT) of 2.3% in 2006 (n = 242) and a frequency of pulmonary embolism (PE) of 2.9% in 2000 (n = 299). One-fifth (n = 49) of patients with DVT had a simultaneous PE. Of all gynecologic surgeries, 1.6% (n = 1657) were performed for ovarian cancer; 3.8% (3941) for uterine cancer; 0.6% (n = 619) for cervical cancer; and 0.3% (n = 310) for vulvar cancer. The rate of DVT observed within the ovarian cancer group was 1.9% (n = 32) compared to 0.9% (n = 37) in the uterine cancer group; and for PE was 1.3% (n = 21) and 1.1% (n = 42), respectively. The odds ratio (OR) of postoperative DVT in ovarian cancer compared to all gynecologic surgeries was 9.41 (CI: 6.25–13.73). When comparing ovarian cancer to uterine cancer, the adjusted OR of postoperative DVT was 1.899 (CI: 1.12–3.22, P = 0.017), while the OR of PE was 9.31 (CI: 6.54–12.96). In contrast, there were only three DVTs and two PEs within the cervical cancer group and no DVTs or PEs within the vulvar cancer group.

Conclusions: The incidence of VTE among postoperative gynecologic patients is higher for ovarian cancer patients compared to other gynecologic malignancies in current clinical practice, based on this nationally representative cohort. This surgical sentinel event may not be able to be completely eliminated in this higher-risk population. However, continued attention must be directed to decrease VTE risk and to develop feasible benchmarks and clinical practice guidelines in conjunction with national organizations such as the Joint Commission.

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57 – Scientific Plenary
Impact of treatment-induced neutropenia and thrombocytopenia on survival in patients with advanced ovarian cancer treated with chemotherapy plus bevacizumab: An NRG Oncology/Gynecologic Oncology Group ancillary data study

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Objectives: Emerging data for many solid tumors, including ovarian cancer, suggest that chemotherapy-induced neutropenia may represent a biomarker with prognostic significance. Thrombocytopenia, on the other hand, may impart a worse prognosis and the effect (if any) of treatment-induced thrombocytopenia on survival has not been elucidated. Because chemotherapy plus antiangiogenesis therapy can lower white blood cell and platelet counts, we evaluated the impact on survival of treatment-induced neutropenia and/or thrombocytopenia in ovarian carcinoma.

Methods: This is an ad hoc analysis of 1720 eligible patients from Gynecologic Oncology Group 218, a phase III randomized, double-blind, placebo-controlled trial that studied bevacizumab in primary (n = 569) and maintenance (n = 570) therapy. Categorical variables were compared using Pearson chi square test and continuous variables by Wilcoxon–Mann–Whitney test. Survival was estimated using Kaplan–Meier. The Cox proportional hazards model evaluated prognostic factors and their effects on progression-free survival (PFS) and overall survival (OS).

Results: Approximately 93% (n = 1603) of patients had neutropenia (absolute neutrophil count <1500 mm$^3$) and 49% (n = 851) had thrombocytopenia (nadir platelets <100 × 10$^9$ L$^{-1}$). In neutropenic patients, the adjusted HR for disease progression (median PFS: 12.7 vs. 10.2 months) was 0.76 (95% CI 0.61, 0.95; P = 0.014) and the adjusted
HR for death (median OS: 42.8 vs. 32.5 months) was 0.73 (95% CI 0.57, 0.94; \( P = 0.014 \)). There was no preferential benefit from being in a particular treatment arm. In an exploratory analysis, thrombocytopenia during bevacizumab maintenance was significant for OS (adjusted HR 0.46; 95% CI 0.23, 0.91; \( P = 0.025 \)). Both pretreatment neutrophil and platelet counts were significant in some PFS and OS models.

**Conclusions:** Neutropenia induced by chemotherapy with and without bevacizumab may represent a clinical biomarker associated with improved survival. Treatment-induced neutropenia may represent an in vivo bioassay to track dose intensification and treatment efficacy. Pretreatment systemic inflammatory status, reflected by baseline neutrophils and platelets, may impart prognostic significance in some cases.

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**58 — Scientific Plenary**

**Changes in metabolic profiles before and after bariatric surgery in high risk morbidly obese women: Obesity-related carcinogenesis is not all about hormones**

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**Objectives:** Obesity markedly increases cancer risk, yet whether the primary mechanisms are hormonal, inflammatory, or metabolic remains uncertain. The study objectives were to determine baseline endometrial histology in morbidly obese women undergoing bariatric surgery and to evaluate serum metabolic parameters before and after surgical intervention.

**Methods:** This prospective trial enrolled women undergoing bariatric weight loss surgery. Clinicopathologic data, serum, and endometrial tissue (if uterus was intact) were collected preoperatively and serum was collected postoperatively. Serum global biochemical profiles of 732 compounds were assessed pre/postoperatively (Metabolon Inc.) and endometrial histology was examined. Welch’s two sample t-tests and paired t-tests were used to identify significant differences (\( P < 0.05 \)).

**Results:** The mean age of the 71 women enrolled was 44.2 years (range, 21–68 years), the mean body mass index (BMI) was 50.9 (range, 34.2–82.6), and the mean weight loss was 45.5 kg (range, 11.2–89.4 kg). A subset of 20 women had both pre/postoperative blood samples available for metabolic analysis and did not differ significantly from the entire study population. The primary pathways affected were energy metabolism, with improvements in glucose homeostasis; branched-chain amino acid metabolism that indicated improved insulin responsiveness; and lipid metabolism with diminished free fatty acids. Tryptophan, phenylalanine, and heme metabolism were also affected by baseline neutrophil and showed improved anti-inflammatory processes that indicated improved insulin responsiveness; and lipid metabolism with diminished free fatty acids. Branched-chain amino acid metabolism that indicated improved insulin responsiveness; and lipid metabolism with diminished free fatty acids. Other pathways included the dehydroepiandrosterone sulfate and 4-androsten metabolites, which consistently showed significant decreases. Endometrial biopsy results were: proliferative (12/30; 40%), insufficient (9/30; 35%), secretory (6/30; 20%), and hyperplasia (3/30; 10%, with 1 complex atypical and 2 simple).

**Conclusions:** The findings in this study demonstrate that bariatric surgery is accompanied by an improvement in glucose homeostasis, insulin responsiveness, inflammation, and redox homeostasis to a greater extent than changes in hormonal milieu. All of these pathways are implicated in carcinogenesis and could be potential biomarkers or therapeutic targets for at-risk morbidly obese women.

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**59 — Scientific Plenary**

**Does adjuvant pelvic radiation therapy improve survival in patients with uterine serous carcinoma who received adjuvant chemotherapy?**

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**Objectives:** To investigate the impact of adjuvant pelvic radiation on survival in patients with uterine serous carcinoma (USC) who received adjuvant chemotherapy.

**Methods:** Patients with stages I–IV USC were identified from the Surveillance, Epidemiology, and End Results (SEER) program 2000–2009. The patients were included if they underwent surgery with at least hysterectomy and received adjuvant chemotherapy. The patients were divided into two groups: those who received adjuvant radiation (USC_RT/CT) and those who received only adjuvant chemotherapy (USC_CT). Kaplan–Meier curves and Cox regression proportional hazards models were used.

**Results:** Of the 1708 patients who were included in this study, 67.7% (1157) had advanced-stage disease (III–IV) and 32.3% (551) had early-stage disease (I–II). Adjuvant pelvic radiation was associated with a significant improvement in overall survival (log rank \( P = 0.001 \)) and disease-specific survival (log rank \( P < 0.001 \)) in patients with advanced-stage (III–IV) USC but not for early-stage (I–II) USC (\( P = 0.23 \) and 0.28, respectively). Among the patients with stage III disease, those who received combined adjuvant pelvic radiation and chemotherapy had longer overall survival (\( P = 0.005 \)) and trend toward longer disease-specific survival (\( P = 0.06 \)) compared to those who received adjuvant chemotherapy alone.

The impact of adjuvant radiation was influenced by the extent of lymphadenectomy and nodal status. In multivariable analysis adjusting for age, race, and extent of lymphadenectomy in patients with advanced-stage USC, adjuvant pelvic radiation was a significant predictor of overall survival (HR 0.65, 95% CI 0.52–0.82, \( P = 0.0003 \)) and disease-specific survival (HR 0.72, 95% CI 0.55–0.93, \( P = 0.013 \)).

**Conclusions:** In the USC patients who received adjuvant chemotherapy, adding pelvic radiation therapy was associated with a significant improvement in overall survival and disease-specific survival in advanced-stage disease but not early-stage disease. The impact of adjuvant pelvic radiation was influenced by the extent of surgical staging and nodal status.

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**60 — Scientific Plenary**

**KRAS variant rs61764370 is not associated with ovarian cancer risk or survival in the Ovarian Cancer Association Consortium (OCAC) or Consortium of Modifiers of BRCA1 and BRCA2 (CIMBA)**

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**Objectives:** Some inherited variants in microRNAs or their targets have been reported to confer increased cancer risks. A variant in the 3’ untranslated region of the KRAS gene (rs61764370) has been reported to confer an increased risk of ovarian cancer (OC). An increased risk was also seen among BRCA1 mutation carriers and women with familial OC or both breast cancer and OC lacking BRCA1/2 mutations. rs61764370 was also associated with measures of poor OC outcome, including shorter survival among women diagnosed after age 52 years, platinum-resistant disease, and suboptimal debulking after neoadjuvant chemotherapy. Because a
genetic test for this variant has been available since 2010, our genetic epidemiology consortia sought to validate reported associations with risk and outcome.

**Methods:** We performed centralized genotyping and analysis of 54 variants within 100 kb of the KRAS gene, including rs61764370, in 68,843 women of European ancestry from 96 studies using a custom Illumina iSelect BeadChip. Ovarian Cancer Association Consortium (OCAC) subjects included 15,358 OC cases and 30,816 controls, and the Consortium of Modifiers of BRCA1 and BRCA2 (CMBA) subjects included 14,765 BRCA1 mutation carriers (2232 with OC) and 7904 BRCA2 mutation carriers (599 with OC).

**Results:** We found no overall association of rs61764370 with sporadic OC risk (odds ratio [OR] 0.99, 95% CI 0.94–1.04, P = 0.74), among BRCA1 or BRCA2 mutation carriers (BRCA1 carriers, OR 1.09, 95% CI 0.97–1.23, P = 0.14; BRCA2 carriers, OR 0.89, 95% CI 0.71–1.13, P = 0.34), or among BRCA1/2-negative cases with a family history of OC. The most significant association was with a decreased risk of low-grade serous OC (OR 0.76, 95% CI 0.59–0.97, P = 0.034), but this finding was not significant after adjustment for multiple testing. Null results were also obtained for associations with overall OC survival (HR 0.94, 95% CI 0.83–1.07, P = 0.38) and for all other previously reported outcome associations.

**Conclusions:** KRAS variant rs61764370 is not associated with OC risk or outcome and should not be used clinically. These results demonstrate the power of large consortia to refute false associations. They also highlight the dangers of developing and marketing genetic predictive tests without appropriate data from carefully conducted, large-scale studies to establish their clinical validity.

<table>
<thead>
<tr>
<th>Minor allele frequency</th>
<th># cases</th>
<th># controls</th>
<th>Cases</th>
<th>Controls</th>
<th>Relative risk (95% CI)</th>
<th>p-Value</th>
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</thead>
<tbody>
<tr>
<td>All invasive</td>
<td>15,358</td>
<td>30,816</td>
<td>0.0914</td>
<td>0.0949</td>
<td>0.99 (0.94–1.04)</td>
<td>0.74</td>
</tr>
<tr>
<td>Histology</td>
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<tr>
<td>High-grade serous</td>
<td>6938</td>
<td>30,816</td>
<td>0.095</td>
<td>0.0949</td>
<td>1.04 (0.97–1.11)</td>
<td>0.26</td>
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<tr>
<td>Endometrioid</td>
<td>2151</td>
<td>30,816</td>
<td>0.083</td>
<td>0.0949</td>
<td>0.90 (0.80–1.00)</td>
<td>0.06</td>
</tr>
<tr>
<td>Clear cell</td>
<td>1015</td>
<td>30,816</td>
<td>0.099</td>
<td>0.0949</td>
<td>1.09 (0.94–1.27)</td>
<td>0.27</td>
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<tr>
<td>Mucinous</td>
<td>1000</td>
<td>30,816</td>
<td>0.09</td>
<td>0.0949</td>
<td>0.99 (0.85–1.16)</td>
<td>0.91</td>
</tr>
<tr>
<td>Low-grade serous</td>
<td>485</td>
<td>30,816</td>
<td>0.07</td>
<td>0.0949</td>
<td>0.76 (0.59–0.97)</td>
<td>0.03</td>
</tr>
<tr>
<td>First-degree family history</td>
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<tr>
<td>Ovarian cancer</td>
<td>483</td>
<td>342</td>
<td>0.081</td>
<td>0.092</td>
<td>0.87 (0.60–1.27)</td>
<td>0.47</td>
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<tr>
<td>Breast or ovarian cancer</td>
<td>477</td>
<td>18,442</td>
<td>0.097</td>
<td>0.092</td>
<td>1.09 (0.93–1.28)</td>
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<tr>
<td>BRCA1/BRCA2 negative</td>
<td>346</td>
<td>15,492</td>
<td>0.105</td>
<td>0.0997</td>
<td>1.09 (0.85–1.41)</td>
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<tr>
<td>BRCA1/2 carriers</td>
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<tr>
<td>BRCA1 carriers</td>
<td>2332</td>
<td>12,432</td>
<td>0.0954</td>
<td>0.0922</td>
<td>1.09 (0.97–1.23)</td>
<td>0.14</td>
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<td>BRCA2 carriers</td>
<td>559</td>
<td>7305</td>
<td>0.0852</td>
<td>0.096</td>
<td>0.89 (0.71–1.13)</td>
<td>0.34</td>
</tr>
<tr>
<td>Enrolled within two years of diagnosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All ovarian cancer</td>
<td>10,121</td>
<td>30,815</td>
<td>0.0942</td>
<td>0.0949</td>
<td>0.99 (0.95–1.04)</td>
<td>0.68</td>
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<tr>
<td>BRCA1 carriers</td>
<td>1095</td>
<td>10,802</td>
<td>0.095</td>
<td>0.094</td>
<td>1.05 (0.90–1.23)</td>
<td>0.52</td>
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<tr>
<td>BRCA2 carriers</td>
<td>270</td>
<td>6509</td>
<td>0.0907</td>
<td>0.0979</td>
<td>0.85 (0.60–1.20)</td>
<td>0.34</td>
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<tr>
<td>Menopausal status</td>
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<tr>
<td>Pre- or peri-menopausal</td>
<td>4264</td>
<td>8789</td>
<td>0.0915</td>
<td>0.0927</td>
<td>1.02 (0.92–1.13)</td>
<td>0.68</td>
</tr>
<tr>
<td>Post-menopausal</td>
<td>11,058</td>
<td>15,903</td>
<td>0.0916</td>
<td>0.0951</td>
<td>0.99 (0.93–1.06)</td>
<td>0.81</td>
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<td>Prior breast cancer</td>
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<tr>
<td>Enrolled within two years of diagnosis</td>
<td>426</td>
<td>30,815</td>
<td>0.0943</td>
<td>0.0949</td>
<td>0.91 (0.71–1.17)</td>
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<tr>
<td>Post-menopausal ovarian cancer</td>
<td>341</td>
<td>15,903</td>
<td>0.081</td>
<td>0.0951</td>
<td>0.90 (0.68–1.21)</td>
<td>0.49</td>
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<tr>
<td>First degree breast or ovarian cancer family history</td>
<td>202</td>
<td>30,815</td>
<td>0.0916</td>
<td>0.0949</td>
<td>0.99 (0.70–1.40)</td>
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</table>

<table>
<thead>
<tr>
<th># cases</th>
<th># events</th>
<th>Hazard ratio (95% CI)</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>All-cause mortality</td>
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<td></td>
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<tr>
<td>All cases</td>
<td>3096</td>
<td>1421</td>
<td>0.94 (0.83–1.07)</td>
</tr>
<tr>
<td>Suboptimally debulked</td>
<td>1114</td>
<td>784</td>
<td>0.94 (0.78–1.13)</td>
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<tr>
<td>Post-menopausal ≤52 years</td>
<td>2226</td>
<td>1276</td>
<td>0.97 (0.84–1.12)</td>
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<tr>
<td>Progression-free survival</td>
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<tr>
<td>All cases</td>
<td>3096</td>
<td>2144</td>
<td>1.01 (0.90–1.13)</td>
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<tr>
<td>Suboptimally debulked</td>
<td>1114</td>
<td>961</td>
<td>1.03 (0.87–1.21)</td>
</tr>
<tr>
<td>Post-menopausal ≤52 years</td>
<td>2226</td>
<td>1603</td>
<td>1.02 (0.90–1.16)</td>
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</table>

doi:10.1016/j.ygyno.2015.01.062

**Featured Posters I: Meet the Professor: Connecting Minds for a Better Future**
**Saturday, March 28, 2015**

**61 — Featured Poster Session**

**Predictive value of p16INK4a and Ki-67 immunohistochemical staining in expectant management of cervical intraepithelial neoplasia grade 2**

F. Miralpeix, G. Mancebo, J.M. Sole-Sedeno, J. Genoves, B. Lloveras, J. Gimeno, F. Alameda, B. Bellosillo, R. Carreras. Hospital del Mar, Barcelona, Spain

**Objectives:** To describe the outcome of cervical intraepithelial neoplasia (CIN)2 in selected women followed without treatment during 12 months and to evaluate regression rate according to p16 and Ki-67 staining.

**Methods:** Patients newly diagnosed with CIN2 cervical biopsy, older than 18 years, who agreed to a follow-up every 4 months for at least 2 years were prospectively recruited. Unsatisfactory colposcopy and immuno-suppressive treatment were considered exclusion criteria. Previous abnormal colposcopy and high-risk human papillomavirus (HPV) were reported at baseline. p16 and Ki-67 expressions were analyzed in all biopsies. Regression was defined as CIN1 biopsy or two consecutive negative cytologies, persistence as CIN2 biopsy, and progression as...
histologic diagnosis of CIN3. All the patients with CIN3 biopsy were treated by cone excision. Statistical analyses were performed with two-sided tests and considered significant at a P value of <0.05.

**Results:** A total of 102 patients were included. The mean age was 30 years (range, 18–56 years) and the mean age (standard deviation) of the first sexual intercourse was 17.4 (2.5) years. They had the mean of 8 (6) total sexual partners, 45.1% used condoms, and 39.2% used contraceptive pills. A total of 73.5% of women were nulliparous and 53.9% were smokers. The sexual intercourse was 17.4 (2.5) years. They had the mean of 8 (6) contraception method of measureable disease and a greater likelihood of CR in the irradiated pelvis. The CR is associated with prolonged OS. Genomic sequencing of archived tumor is indicated to identify molecular predictors of CR.

**Conclusions:** CRs occurred in 44/452 patients (9.7%) (Ctx + B n = 28; Ctx n = 16). The median time to CR was 4.5 months (2.9–6.8 months), with the median duration of CR lasting 13.6 months (8.0–25.5 m). The majority had squamous histology (n = 31; 70%), recurrent/persistent disease (n = 39; 81%), and previously irradiation (n = 37; 84%). Disease sites included cervix (n = 15; 34%), lung (n = 9; 20%), and lymph nodes (n = 28; 64%). Eighteen patients (41%) achieved CR in the irradiated field, most of whom received Ctx + B (n = 11; 61%). There was a trend for Ctx + B patients to achieve CR sooner (4.4 vs. 5.2 months), especially those receiving topotecan–paclitaxel–bevacizumab (4.8 vs. 7.5 months). The median progression-free survival and overall survival in patients with CR were 18.3 months and 39.3 months, respectively. The median overall survival for patients with CR on the cisplatin–paclitaxel–bevacizumab arm has not been reached.

**Conclusions:** Ctx + B may be associated with a more rapid clearance of measureable disease and a greater likelihood of CR in the irradiated pelvis. The CR is associated with prolonged OS. Genomic sequencing of archived tumor is indicated to identify molecular predictors of CR.

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**Abstracts / Gynecologic Oncology 137 (2015) 2–91**

63 — Featured Poster Session

**Evaluation of WHO-endorsed “see and treat” cervical cancer screening in HIV-positive and HIV-negative women in Cameroon**

L.S. Bradford, G.A. DeGregorio, P. Tih, R. Wama, Z. Sando, E. Welty, T. Welty, L. Kennedy-Sheldon, J.G. Ogembo, University of Massachusetts, Worcester, MA, USA, University of Massachusetts Medical School, Worcester, MA, USA, Cameroon Baptist Convention Health Services, Bamenda, Northwest Province, Cameroon, Northwestern University, Boston, MA, USA, University of Yaoundé, Yaoundé, Cameroon, Cameroon Baptist Convention Health Board, Bamenda, Northwest Province, Cameroon, University of Massachusetts Medical Center, Worcester, MA, USA

**Objectives:** In August 2014, the United States Food and Drug Administration approved bevacizumab for use in the treatment of recurrent, persistent, and advanced-stage cervical cancer based on the findings of Gynecologic Oncology Group (GOG) 240. We sought to evaluate the clinicopathologic features of patients who achieved a complete response (CR) on the study.

**Methods:** This is a posttrial ad hoc analysis of GOG protocol 240, a phase III randomized clinical trial that evaluated the impact of bevacizumab on survival in patients with advanced-stage, persistent, or recurrent cervical cancer. Participants were treated every 21 days to progression/unacceptable toxicity. Tumor measurements were made using Response Evaluation Criteria in Solid Tumors (RECIST v1). CR was defined as disappearance of all target and nontarget lesions and no evidence of new lesions on two assessments 4 weeks apart.

**Results:** CRs occurred in 44/452 patients (9.7%) (Ctx + B n = 28; Ctx n = 16). The median time to CR was 4.5 months (2.9–6.8 months), with the median duration of CR lasting 13.6 months (8.0–25.5 m). The majority had squamous histology (n = 31; 70%), recurrent/persistent disease (n = 39; 81%), and previously irradiation (n = 37; 84%). Disease sites included cervix (n = 15; 34%), lung (n = 9; 20%), and lymph nodes (n = 28; 64%). Eighteen patients (41%) achieved CR in the irradiated field, most of whom received Ctx + B (n = 11; 61%). There was a trend for Ctx + B patients to achieve CR sooner (4.4 vs. 5.2 months), especially those receiving topotecan–paclitaxel–bevacizumab (4.8 vs. 7.5 months). The median progression-free survival and overall survival in patients with CR were 18.3 months and 39.3 months, respectively. The median overall survival for patients with CR on the cisplatin–paclitaxel–bevacizumab arm has not been reached.

**Conclusions:** Ctx + B may be associated with a more rapid clearance of measureable disease and a greater likelihood of CR in the irradiated pelvis. The CR is associated with prolonged OS. Genomic sequencing of archived tumor is indicated to identify molecular predictors of CR.

**doi:** 10.1016/j.ygyno.2015.01.064
Results: Of the 33,660 cases with valid VIA data, 9.5% of women considered screened were VIA-positive, 62.7% were VIA-negative, and 27.8% were rural screening location, gravidity, age at sexual debut, and number of lifetime sexual partners. Among 3115 women eligible for same-day cryotherapy, only 43% accepted treatment. Pathology specimens (n = 750) collected from women with VIA-positive lesions ineligible for cryotherapy identified 30% of cases as ICC and 70% as CIN. 

Conclusions: The CBCHS successfully implemented the “see-and-treat” screening program in Cameroon, screening more than 34,000 women in 7 years. However, fewer than half of the eligible patients opted for the same-day treatment. Further studies are required to better identify barriers to implementing same-day treatment protocols.

doi:10.1016/j.ygyno.2015.01.065

64 — Featured Poster Session
High- versus low-dose rate brachytherapy for locally advanced cervical cancer
S.S. Patankar1, A.I. Tergas2, W.M. Burke3, J.Y. Hou3, C. Anantha4, Y. Huang5, A. Neugut6, D. Hershman7, J.D. Wright8, aColumbia University College of Physicians and Surgeons, New York, NY, USA, bNYP/Columbia College of Physicians and Surgeons, New York, NY, USA

Objectives: Intracavitary brachytherapy plays an important role in the treatment of advanced cervical cancer. Although small international trials have shown comparable survival outcomes between high-dose rate (HDR) and low-dose rate (LDR) intracavitary brachytherapy, little data are available in the United States. We examined the utilization and outcomes of HDR brachytherapy for locally advanced cervical cancer.

Methods: Women with locally advanced (stages IIB–IVA) cervical cancer treated with combination (external beam and brachytherapy) radiotherapy between 2003 and 2011 and recorded in the National Cancer Database (NCDB) were analyzed. Multivariable hierarchical regression models accounting for clinical, oncologic, and hospital factors as well as hospital-specific random intercept were used to predict the use of HDR. Survival was examined using Kaplan–Meier analyses and Cox proportional hazards models adjusted for the above characteristics and other metrics of treatment quality.

Results: A total of 10,564 women, including 2681 (25.4%) who received LDR and 7883 (74.6%) who received HDR, were identified. The use of HDR increased by 67% between 2003 (50.2%) and 2011 (83.9%; P < 0.0001). In a multivariable model, year of diagnosis was the strongest predictor of the use of HDR. Although patients in the Midwest (relative risk [RR] = 0.87; 95% CI, 0.79–0.96) and South (RR = 0.88; 95% CI, 0.80–0.97) were less likely to receive HDR, there were no other clinical, hospital, tumor, or socioeconomic characteristics associated with receipt of HDR. In a multivariable Cox model, survival was equivalent for HDR compared to LDR (HR = 0.93; 95% CI 0.83–1.03). A series of Kaplan–Meier analyses stratified by stage demonstrated no difference in survival based on type of brachytherapy for stage IIB (P = 0.68), IIB (P = 0.17), or IVA (P = 0.16) tumors.

Conclusions: The use of HDR has increased rapidly and is now the predominant method of brachytherapy delivery for cervical cancer. For women with locally advanced cervical cancer, survival is equivalent for HDR brachytherapy and LDR brachytherapy.

doi:10.1016/j.ygyno.2015.01.067

66 — Featured Poster Session
Cervical stenosis following abdominal radical trachelectomy: A report of a 10-year experience
J.L. Li, X. Wu. Fudan University Shanghai Cancer Center, Shanghai, China

Objectives: Cervical stenosis is the major and unique postoperative complication associated with abdominal radical trachelectomy (ART). The purpose of the study was to investigate the incidence of cervical stenosis in patients after ART and to present our experience in preventing and managing stenosis during the past 10 years.

Methods: We conducted a retrospective review of a prospectively maintained database of patients undergoing ART at our institution from 2004 to 2014. Each patient was asked to complete a survey evaluating symptoms that may relate to cervical stenosis (e.g., abdominal pain, irregular menstrual cycle, hematomata) at follow-ups. To prevent cervical stenosis, we have been placing a tailed T-introuterine device (IUD) before the uterovaginal reconstruction since 2007. We also sutured the endometrium to the fibromyometrial wall of the uterus at 3, 6, 9 and 12 o’clock orientation to prevent stenosis. Dilation of the cervical os and then without ultrasonic guidance was used to treat patients with severe cervical stenosis.

Results: A total of 220 patients underwent ART at our institution. According to the follow-up survey, approximately 20% had mildly symptomatic stenosis not requiring neocervical dilation. Among them, 56% complained about abdominal pain and 42% noted prolonged menstruation. Fourteen (6.4%) patients had severe cervical stenosis that
required neocervical dilation. Among them, three patients required repeated dilation eight times; all recovered eventually. Four patients had late occurrence of cervical stenosis after withdrawal of the tailed T-IUDs. Clinicians recommended that they have neocervical dilation every 2 weeks until they became pregnant. Four patients had difficulty removing their T-IUDs because the tail had dropped, and ultrasonographic-guided neocervical dilation was used to remove the device.

**Conclusions:** Cervical stenosis was the major and unique post-tracheectomy complication, with a total incidence of 26.4% of all patients. Abdominal pain and prolonged menstruation were the most common symptoms. Although stenosis could be effectively prevented by installation of a tailed T-IUD, late occurrence after withdrawal of the device did occur with some patients. Repeated dilation of the neovix may need to be performed to obtain optimal results in patients with severe cervical stenosis.

doi:10.1016/j.ygyno.2015.01.068

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**67 — Featured Poster Session**

**Chemoradiation versus neoadjuvant chemoradiation followed by radical surgery for FIGO stage III cervical cancer: Analysis of complications and 3-year survival**


*Catholic University of the Sacred Heart, Milan, Italy, Istituto Nazionale Tumori Regina Elena, Rome, Italy, European Institute of Oncology, Milan, Italy, S. Orsola-Malpighi Hospital, Bologna, Italy, Catholic University of the Sacred Heart, Rome, Italy*

**Objectives:** To compare rates of early and late complications and survival in a consecutive series of patients with FIGO stages IIIa–IIIb cervical cancer submitted to chemoradiation and neoadjuvant chemoradiation followed by radical hysterectomy.

**Methods:** This retrospective multicenter analysis included 150 patients with FIGO stages IIIa–IIIb cervical cancer: 77 patients submitted to chemoradiation (Group A) and 73 submitted to neoadjuvant chemoradiation and radical surgery (Group B). Exclusive chemoradiation consisted of a concurrent platinum-based chemotherapy plus a median of 50 Gy of external beam radiation with median 30 Gy of vaginal brachytherapy. Neoadjuvant treatment involved concomitant platinum-based chemotherapy plus a median dose of 45 Gy of external beam radiation followed by radical hysterectomy.

**Results:** The baseline characteristics of the two groups were superimposable. We observed lower intraoperative/early urinary and gastrointestinal complications in Group B compared to Group A. We registered 47 (61.0%) urinary complications in Group A, all often grade 1, and 10 (13.5%) in Group B (P<0.001). A lower rate of gastrointestinal complications was observed in Group B (2.7% vs. 75.3%; P<0.001). Vascular complications were registered only in Group B (16.2%) (P<0.001). No statistical differences were observed in terms of late complications. Median follow-up time, overall survival (OS), and progression-free interval (PFI) rates were similar in both groups. We did not observe statistically significant differences in terms of pattern of local and distant systemic recurrence (local: 22.1% vs. 10.9% and distant: 18.2% vs. 15.06%; P=0.141). Median PFI was 19 and 22 months in Group A and Group B, respectively (P=0.078). Median OS rates were 35 and 33 months in Group A and Group B, respectively (P=0.164).

**Conclusions:** The early complications rate was higher in Group A except for vascular complications. After 30 days from the end of treatment, no differences were observed in terms of complication rate. There were no significant differences in terms of PFI and OS between the two groups. Further randomized studies with quality of life assessment are mandatory to identify the best treatment modality of advanced cervical cancer patients.

doi:10.1016/j.ygyno.2015.01.069

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**68 — Featured Poster Session**

**Is parametrectomy in early stage cervical cancer always necessary?**


**Objectives:** Increasing data suggest that a group of patients with early-stage cervical cancer may benefit from less radical surgery because patients with favorable pathologic characteristics have a low risk of parametrial involvement (PI). Our aim was to evaluate the clinicopathologic factors related to PI and identify a group of patients at low risk.

**Methods:** We analyzed a series of 236 patients from a cohort of 406 patients who had radical hysterectomies for cervical cancer from May 1982 to December 2008 at AC Camargo Cancer Center. Thirteen (5.5%) patients had PI: 11 (84.6%) unilateral and 2 (15.4%) bilateral.

**Results:** Forty (17.1%) cases were adenocarcinoma, 10 (4.3%) adenosquamous, and 184 (78.5%) squamous cell carcinoma. The median age was 47 years (range, 27–73 years). The median tumor size and depth of invasion were 2.7 cm (range, 0.4–10 cm) and 9 mm (range, 0.3–45 mm), respectively. Eighty-three (41.3%) of 201 patients had lymphovascular space invasion (LVSI), 20.6% (41/199) had perineural invasion, 23.5% (47/200) had histologic grade 3, and 18.6% (44/236) had lymph node metastasis. Regarding tumor size among the 179 patients, 30.7% had ≤2 cm (n=55), 46.4% had >2 cm to ≤4 cm (n=83), and 22.9% had >4 cm (n=41). Among the 201 patients with depth invasion described, 41.3% had >10 mm (n=83). Patients with adenocarcinoma or adenosquamous histologic types were more likely to have PI (12% vs. 3.8%, P=0.036), and the presence of LVSI also correlated with PI (12% vs. 0.8%, P=0.001). Tumor size (P=0.27), depth invasion (P=0.66), histologic grade 3 (P=0.68), perineural invasion (P=0.12), and lymph node status (P=0.072) did not correlate with PI. LVSI (HR 21.5, 95% CI 2.5–179, P=0.005) and histologic type (HR 6.5, 95% CI 1.7–24.9, P=0.006) remained risk factors for PI in multivariate analysis. Notably, only one (1.8%) patient with tumor size of 2 cm had PI, but she also had lymph node metastasis and LVSI. Furthermore, all 24 patients (10.2%) with tumor <2 cm and no LVSI had no PI, despite the presence of other variables.

**Conclusions:** Our data suggest that histologic type and the presence of LVSI correlate with PI. No patient with tumor <2 cm and absence of LVSI had PI. Our data may contribute to selecting patients for more conservative approaches, such as simple hysterectomy or simple tracheectomy associated with pelvic lymphadenectomy.

doi:10.1016/j.ygyno.2015.01.070

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**69 — Featured Poster Session**

**Abdominal radical tracheectomy for early stage cervical cancer: Fertility sparing approach**

A. Rodolakis, N. Thomakos, I. Koutroumpa, M. Sotiropoulou, D. Haidopoulou, G. Vlachos, D. Loutradis. *Alexandra Hospital, University of Athens, Athens, Greece, University of Athens School of Medicine, Alexandra Hospital, Athens, Greece*

**Objectives:** The recommended surgical treatment for stages IA2–IB1 cervical cancer is radical hysterectomy with bilateral pelvic lymphadenectomy and consequent loss of fertility. Recent literature describes...
abdominal radical trachelectomy (ART) as a procedure that preserves the uterus without increasing the risk of recurrence while affording the opportunity to retain childbearing potential. This study was performed to assess the feasibility and safety of this fertility-preserving surgery for early-stage cervical cancer. We describe the surgical, oncologic, and fertility outcomes of patients treated with ART.

Methods: We conducted a retrospective review of patients undergoing fertility-sparing ART at our institution from 2002 to 2014.

Results: A total of 70 patients who underwent ART with pelvic lymphadenectomy were followed for 2–106 months. Twenty-eight patients had undergone conization before surgery. The characteristics of the patients included tumor diameter of 8–32 mm (stage IA2 = 9, stage IB1 [3.2 cm] = 61), average age of 29.5 years (range, 26–43 years), mean operative time of 185 min (range, 142–245 min), and average blood loss of 350 mL (range, 150–750 mL). Uterine arteries were identified at their origin from the internal iliac artery and gently preserved in 67 cases. There were two recurrences in the paraaortic area treated with chemoradiation (n = 1) and radical hysterectomy (n = 1). Three patients developed high-grade squamous intraepithelial lesions and were successfully treated by loop excision. Forty women attempted to conceive and 29 successful pregnancies were recorded (73%). All of the pregnancies resulted in live births, with a rate of preterm delivery 17.2% (5/29).

Conclusions: ART can be successfully performed by gynecologic oncologists experienced in radical surgery. It is a well-established, safe procedure with good oncologic and obstetric outcomes and low morbidity and mortality. Young women diagnosed with cervical cancer who desire future fertility should discuss fertility-sparing procedures with their gynecologists.

doi:10.1016/j.ygyno.2015.01.072

71 — Featured Poster Session
Utility of HPV genotyping in the management of low-grade squamous intraepithelial cervical lesions (LSIL)

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Objectives: Evaluate the utility of human papillomavirus (HPV) genotyping in the management of low-grade squamous intraepithelial cervical lesions (LSIL).

Methods: We analyzed newly diagnosed LSIL in our area (Hospital del Mar, Barcelona, Spain). HPV genotyping was performed by the COBAS HPV test (Roche Molecular Diagnostics, Pleasanton, CA). That technique allowed us to classify lesions as HPV16-positive, HPV18-positive, or high-risk HPV others than HPV16 or HPV18 (HPVn16n18). We calculated progression and regression rates overall and by age groups.

Results: The mean age of the patients was 33.8 ± 11.1 years. Of all lesions, 19.6% were positive for HPV16, 4.9% for HPV18, and 63.6% for HPVn16n18. The different age distribution was significant only for HPV18, which was more frequent in patients older than 39 years. At 2 years of follow-up, the cure rate for LSIL was 74.1%, persistence rate was 16.3%, progression to cervical intraepithelial neoplasia (CIN)2+ was 9.8%, and progression to CIN3 was 2.1%. HPV16 positivity was more frequent in lesions that progressed to CIN2+, while nondeletion of high-risk HPV (hrHPV) was more frequent for lesions that regressed. The absolute risk for progression to CIN2+ was 32.1% for HPV16, 14.3% for HPV18, and 5.8% for HPVn16n18. None of the HPV-negative (HPVneg) cases evolved to CIN2+. None of the LSIL caused by HPV16 in patients older than 39 years progressed to CIN2+. The presence of HPV16 conferred a 7.4 times greater risk of developing CIN2+ than its absence. This relative risk was the only statistically significant risk. In patients older than 39 years, the relative risk was lower than for younger patients. The absolute risks for healing were 53.6% for HPV16, 57.1% for HPV18, 75.4% for HPVn16n18, and 87.5% for HPVneg. In older patients, the absolute risk of cure was higher than for younger patients. The relative risks for healing of HPV16 and HPVneg (0.7 and 1.3, respectively) were the only ones statistically significant, which were higher for patients older than 39 years.

Conclusions: LSIL lesions caused by HPV16 are more likely to progress to CIN2+, so tight control and immediate colposcopy is crucial. LSIL lesions in which we could not detect a high-risk HPV did not progress to CIN2+, suggesting that its control should be different from other LSILs. Conservative management seems could be acceptable from a clinical point of view according to our data.

doi:10.1016/j.ygyno.2015.01.073
72 — Featured Poster Session
Association between statin use and disease-specific endometrial cancer survival

Objectives: Statins, 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase inhibitors, are commonly used by patients with hyperlipidemia and high-risk cardiovascular disease. Statin use has been associated with decreased incidence and/or death from cancers of the ovary, breast, colon, pancreas, gastrointestinal tract, and liver. The purpose of this study was to evaluate the association of statin use with disease-specific survival (DSS) from endometrial cancer.

Methods: After institutional review board approval, data from 984 patients treated for uterine cancer from January 1999 through December 2009 at a single institution were retrospectively reviewed to examine the association of statin therapy with DSS from endometrial cancer. DSS was estimated by Kaplan–Meier survival estimates. A Cox proportional hazards model was used to study the risk of death. All statistical tests were two-sided.

Results: A total of 230 patients died of disease (82% of deceased patients) and median follow-up was 3.36 years. DSS was greater for patients with hyperlipidemia who were using statin therapy at the time of surgical staging/biopsy for diagnosis compared to women who were not taking statin therapy (log rank test \( P = 0.03 \)). The survival advantage persisted after stratification by histologic subtype for type II cancers \( (P < 0.01) \) (Fig. 1). Statin use was associated with a decreased hazard of death in patients with type II endometrial cancers \( (HR = 0.54, 95\% CI 0.36 \text{ to } 0.83, P < 0.01) \) after adjusting for age, body mass index, histologic type, clinical stage, grade, hypertension, diabetes, aspirin, metformin, radiation, chemotherapy, and presence of hyperlipidemia.

Conclusions: Statins may be a useful adjuvant therapy in the treatment of type II endometrial cancers. Prospective evaluation of statins as adjuvant therapy should be investigated.

doi:10.1016/j.ygyno.2015.01.075

74 — Featured Poster Session
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Objectives: To describe recent trends in lymphadenectomy and the identification of lymph node metastasis among patients undergoing surgery for endometrioid adenocarcinoma of the endometrium.

Methods: The Surveillance, Epidemiology, and End Results registry was queried for patients who underwent surgery for endometrioid adenocarcinoma of the endometrium between 1998 and 2010. Year
of surgery was categorized into periods (Table). Lymphadenectomy and lymph node metastasis status as well as patient and tumor characteristics were abstracted. Frequencies, risk differences, and 95% confidence intervals were calculated. Differences in proportions were evaluated with chi square test.

Results: During the study period, 73,224 patients underwent surgery. Frequency of lymphadenectomy differed significantly by time period \((P < 0.001)\), increasing by 17.3% \((95\% \text{ CI} 16.2–18.4)\) from 1998–2001 to 2008–2010, and this trend was observed irrespective of age, tumor grade, primary tumor size, or extent of myometrial invasion. Lymph node metastases were identified among 11.1% \((95\% \text{ CI} 10.8–11.4)\) of patients who underwent lymphadenectomy, and this did not vary with time period \((P = 0.4)\). Among patients undergoing surgery, the fraction identified with lymph node metastasis differed significantly by time period \((P < 0.001)\), increasing by 1.9% \((95\% \text{ CI} 1.4–2.4)\) from 1998–2001 to 2008–2010. The portion of patients who underwent a negative lymphadenectomy increased by 15.5% \((95\% \text{ CI} 14.4–16.6)\).

Conclusions: Between 1998 and 2010, the proportion of patients with endometrioid adenocarcinoma of the endometrium whose surgery included excision of lymph nodes increased significantly, irrespective of risk factors for lymph node involvement. Consequently, there was a modest but significant increase in the proportion of subjects identified with lymph node metastasis, and a larger increase in the proportion of patients who had negative lymph node dissections.


<table>
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</thead>
<tbody>
<tr>
<td>All subjects n = 11,841</td>
<td>n = 18,143</td>
<td>n = 20,203</td>
<td>n = 23,037</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph nodes excised (47.9%)</td>
<td>54.4% (56.1%)</td>
<td>63.1% (63.8%)</td>
<td>65.2% (65.9%)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis identified</td>
<td>5.2% (6.0%)</td>
<td>6.4% (6.8%)</td>
<td>6.7% (7.4%)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Negative lymph node excision</td>
<td>42.7% (48.2%)</td>
<td>49.0% (55.4%)</td>
<td>56.1% (55.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects with lymph node excision</td>
<td>n = 5671</td>
<td>n = 10,042</td>
<td>n = 12,754</td>
<td>n = 15,030</td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis identified</td>
<td>10.9% (10.1–11.7)</td>
<td>11.5% (10.9–12.2)</td>
<td>11.1% (10.6–11.7)</td>
<td>10.9% (10.4–11.4)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

a Percent (95% Confidence Interval). P-value is for \(\chi^2\) test.
endometrioid endometrial carcinoma between two international cohorts.

Methods: All patients surgically staged with endometrioid endometrial cancer were identified through institutional databases at one United States (US) and one Denmark (DK) cancer centers. For the purposes of this analysis, patients with unknown stage and gross intraabdominal or distant metastases were excluded. Patients treated at the US center were surgically staged according to an institutional sentinel lymph node (SLN) mapping algorithm. Patients in the DK center underwent lymphadenectomy if they had FIGO grade 3 histology, >50% myometrial invasion, and/or cervical involvement.

Results: A total of 302 patients were identified: 174 (57.6) in the DK cohort and 128 (42.4) in the US cohort. Median age was 69 years (range, 40–96 years) and 65 years (range, 30–90 years) in the DK and US cohorts, respectively (P < 0.0001). Median body mass index was 27.6 (range, 16–58) and 29.3 (range, 16–55) (P = 0.01). The number of patients with FIGO grade 1 disease was 81 (46.6%) in the DK cohort and 29 (22.7%) in the US cohort (P < 0.0001), and the respective distribution of FIGO grade 3 disease was 40 (23.0%) and 68 (53.1%) (P < 0.0001). Stage IIIIC disease was diagnosed more often in the US cohort (P = 0.001). More chemotherapy was administered to patients in the US cohort (n = 51, 39.8%) than the DK cohort (n = 38, 21.8%) (P = 0.001). Median follow-up time was 33 months (range, 0–101 months) and 31 months (range, 3–84 months) in the DK and US cohorts, respectively (P = 0.3). Median overall survival (OS) was not reached in either cohort; 5-year OS was 86.7% (SD ± 3.5%) vs. 87.6% (SD ± 5.7%) in the DK and US cohorts, respectively (P = 0.4).

Conclusions: Using an SLN mapping algorithm increases the detection of nodal disease and does not compromise OS in patients with intermediate- and high-risk endometrioid endometrial cancer. Either the SLN algorithm or selective lymphadenectomy appears a reasonable strategy for staging of uterine endometrioid malignancy.

<table>
<thead>
<tr>
<th>N</th>
<th>DK (57.6)</th>
<th>US (42.4)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>69 (40–96)</td>
<td>65 (30–90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median BMI, kg/m² (range)</td>
<td>27.6 (16–58)</td>
<td>29.3 (16–55)</td>
<td>0.01</td>
</tr>
<tr>
<td>FIGO grade, N (%)</td>
<td>33 (0–101)</td>
<td>31 (3–84)</td>
<td>0.3</td>
</tr>
<tr>
<td>Grade 1</td>
<td>81 (46.6)</td>
<td>29 (22.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Grade 2</td>
<td>46 (26.4)</td>
<td>31 (24.2)</td>
<td>0.5</td>
</tr>
<tr>
<td>Grade 3</td>
<td>40 (23.0)</td>
<td>68 (53.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stage IIIIC detection, N (%)</td>
<td>19 (10.9)</td>
<td>29 (22.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>IIIIC1</td>
<td>1 (0.6)</td>
<td>4 (3.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>IIIIC2</td>
<td>7 (4.0)</td>
<td>16 (12.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Positive cytology, N (%)</td>
<td>16 (9.2)</td>
<td>46 (35.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥50%</td>
<td>158 (90.8)</td>
<td>82 (64.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lymph node sampling, N (%)</td>
<td>110 (63.2)</td>
<td>127 (99.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjuvant therapy</td>
<td>38 (21.8)</td>
<td>51 (39.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Chemotherapy ± radiation therapy</td>
<td>115 (66.1)</td>
<td>15 (11.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-year OS, % (SD)</td>
<td>86.7% (±3.5)</td>
<td>87.6% (±5.7)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

DK = Danish cohort; US = US cohort; OS = overall survival.

Conclusions: Using an SLN mapping algorithm increases the detection of nodal disease and does not compromise OS in patients with intermediate- and high-risk endometrioid endometrial cancer. Either the SLN algorithm or selective lymphadenectomy appears a reasonable strategy for staging of uterine endometrioid malignancy.

doi:10.1016/j.ygyno.2015.01.079

78 – Featured Poster Session
Patterns of practice and outcomes of definitive radiation therapy in early stage inoperable endometrial cancer
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Objectives: Endometrial carcinoma frequently presents in the elderly, many of whom have comorbidities restricting surgical management. Definitive radiation alone, frequently incorporating brachytherapy (BT), has been previously reported with acceptable outcomes. Using the National Cancer Data Base (NCDB), a population-based analysis was conducted to more extensively evaluate the impact of radiation modalities among inoperable patients.

Methods: Query of the NCDB was completed for patients with biopsy-proven FIGO stage I endometrioid adenocarcinoma from 1998 to 2006 treated with radiotherapy. Patients treated surgically or with inadequate follow-up were excluded. Factors associated with BT utilization were established using multivariate logistic regression. The Kaplan–Meier method and Cox regression modeling were used to assess survival and related variables.

Results: A total of 853 patients were identified, with the majority receiving external beam radiotherapy (EBRT) alone (45.0%), followed by EBRT + BT (31.3%) and BT alone (23.7%). BT utilization trends remained stable over time, varying from 48.1% to 59.5% patients/year (P = 0.71). BT utilization was lower for patients of Hispanic ethnicity (odds ratio [OR] 0.13, 95% CI 0.03–0.62, P = 0.01) and from community cancer facilities (OR 0.34, 95% CI 0.14–0.81, P = 0.02). Higher utilization was found in urban/suburban regions (OR 3.48, 95% CI 1.80–6.71, P = 0.01) and in the Pacific facility location (OR 7.20, 95% CI 1.65–31.5, P = 0.01). With a median follow-up of 36 months (range, 1–170 months), the unadjusted median survivals for EBRT alone, BT alone, and EBRT + BT were 29.1 months (95% CI 24.7–33.6), 44.6 months (95% CI 33.1–56.0), and 57.1 months (95% CI 48.2–66.0; P < 0.01). In addition to
older age, lower community educational attainment level, higher Charlson–Deyo comorbidity score, and poorly differentiated tumors, multivariate survival analysis revealed inferior survival if receiving EBRT alone (HR 1.66, 95% CI 1.23–2.23, P < 0.01).

**Conclusions:** BT utilization for inoperable endometrial cancer remains low, with most patients receiving external beam radiotherapy alone. Despite concerns of overtreatment in a population with competing causes of death, BT appears to result in improved survival and should be used in this subset.

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### 79 — Featured Poster Session

**Impact of surgical staging and adjuvant therapy on recurrence risk and outcome in stage I non-invasive uterine papillary serous carcinoma**

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**Objectives:** To determine the impact of surgical staging and adjuvant treatment on rate and patterns of recurrence and outcome in stage I noninvasive uterine papillary serous carcinoma (UPSC).

**Methods:** This retrospective study involved four United States academic centers from 2000 to 2012. Only patients with noninvasive (limited to the endometrium) stage IA UPSC were included. All patients underwent surgical treatment with at least total hysterectomy. The Kaplan–Meier method and Cox proportional hazards regression modeling were used.

**Results:** Among the 115 patients who were included, the median age was 66 years (range, 49–90 years). Eighty-four percent underwent stage IIA (9/115), pelvic in 3.5% (4/115), and extra-pelvic in 14.7% (17/115). Among the entire cohort, adjuvant chemotherapy did not affect risk of recurrence (P = 0.85). Patients who underwent lymphadenectomy had a lower risk of recurrence than those who did not (P = 0.019), especially extra-pelvic recurrence (P = 0.027). Adjuvant chemotherapy or pelvic radiation did not affect risk of recurrence in subgroups of patients who underwent lymphadenectomy (P = 0.56) or extended (P = 0.52) or nonextended surgical staging (P = 0.78). Among patients who did not have lymphadenectomy, adjuvant chemotherapy or pelvic radiation was associated with longer mean progression-free (P = 0.04) and overall survival (P = 0.025). In multivariable analysis adjusting for age, surgical staging, chemotherapy, and pelvic radiation, only staging lymphadenectomy was a significant predictor of progression-free survival (HR 0.34, 95% CI 0.12–0.95, P = 0.04) and overall survival (HR 0.35, 95% CI 0.12–1.02, P = 0.05). Furthermore, extended surgical staging was a significant predictor of progression-free (HR 0.24, 95% CI 0.61–0.96, P = 0.04) and overall survival (HR 0.26, 95% CI 0.64–1.02, P = 0.05). Neither adjuvant chemotherapy nor pelvic radiation was a predictor of progression-free or overall survival.

**Conclusions:** In patients with stage I noninvasive UPSC, surgical staging was a significant predictor of recurrence and outcome and, therefore, should be considered in these patients. Adjuvant chemotherapy or pelvic radiation did not affect recurrence and outcome. However, it should be considered in nonstaged noninvasive UPSC.

doi:10.1016/j.ygyno.2015.01.081

### 80 — Featured Poster Session

**Do stages I–II uterine clear cell carcinoma patients need to be treated as aggressively as patients with serous carcinoma?**

T.J. Yang, N. Desai, M. Kollmeier, V. Makker, M.M. Leitao, N.R. Aburustum, K. Alektiar, Memorial Sloan Kettering Cancer Center, New York, NY, USA

**Objectives:** The treatment paradigm for stages I–II uterine clear cell carcinoma (CC) is often linked to serous carcinoma (SC), yet it is unclear if women with these histologies have similar outcomes and if tailored therapy should be offered to women with CC. This study compared the oncologic outcomes between women with CC and SC.

**Methods:** From 4/1992 to 12/2011, 181 women with stages I–II uterine CC (41 patients, 23%) or SC (140, 77%) underwent hysterectomy and salpingo-oophorectomy at our institution. A total of 139 (76%) had FIGO 2009 stage IA disease, 21 (12%) had stage IB, and 21 (12%) had stage II disease. One hundred forty-seven patients (81%) received adjuvant radiation therapy (RT) and 103 (57%) received adjuvant platinum and taxane-based chemotherapy. Clinicopathologic characteristics and therapies received were compared between CC and SC patients using chi square test. Kaplan–Meier estimate was used to assess disease-free survival (DFS), disease-specific survival (DSS), overall survival (OS), and recurrence rates (RR) at 5 years.

**Results:** The median follow-up was 57 months. There were no significant differences in the clinicopathologic characteristics between patients with CC vs. SC, respectively, including: number of women ≥60 years of age (77% vs. 68%, P = 0.17), myometrial invasion ≥50% (13% vs. 17%, P = 0.32), lymphovascular invasion (32% vs. 25%, P = 0.25), or stage (IA: 78% vs. 76%, IB: 15% vs. 12%, II: 7% vs. 12%, P = 0.53). While there was no difference in the number of patients who received adjuvant RT (CC = 83% vs. SC = 81%, P = 0.47), significantly fewer CC patients received adjuvant chemotherapy (34% vs. 64%, P = 0.001). At 5 years, no significant differences in DFS (CC = 82% vs. SC = 83%, P = 0.89), DSS (94% vs. 90%, P = 0.97), or OS (92% vs. 86%, P = 0.57) was found. Additionally, there were no differences in the 5-year locoregional and distant RR (Table 1).

**Conclusions:** The oncologic outcomes and recurrence patterns of women with stages I–II uterine CC compared favorably to women with SC, despite a significantly less use of adjuvant chemotherapy. Potential reduction in adjuvant therapy should be studied prospectively in women with CC.

**Table 1** Comparison of 5-year RR between women with uterine CC vs. SC.

<table>
<thead>
<tr>
<th>Relapse sites</th>
<th>CC</th>
<th>SC</th>
<th>P</th>
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<tbody>
<tr>
<td>Vaginal</td>
<td>7 (0–16)</td>
<td>4 (1–7)</td>
<td>0.73</td>
</tr>
<tr>
<td>Pelvic</td>
<td>13 (1–25)</td>
<td>10 (5–15)</td>
<td>0.95</td>
</tr>
<tr>
<td>Paraortic</td>
<td>7 (0–17)</td>
<td>5 (1–9)</td>
<td>0.95</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>11 (0–23)</td>
<td>9 (6–12)</td>
<td>0.80</td>
</tr>
<tr>
<td>Other distant sites</td>
<td>12 (1–23)</td>
<td>10 (5–15)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

doi:10.1016/j.ygyno.2015.01.082

### 81 — Featured Poster Session

**The impact of adjuvant therapy on survival in uterine clear cell carcinoma patients**

A.A. Gockley, J.A. Rauh-Hain, J.T. Clemmer, R.M. Clark, T.R. Hall, A. Goodman, D.M. Borutali, M. del Carmen, W.B. Growdon, J.O. Schorge, Massachusetts General Hospital, Boston, MA, USA, Massachusetts General Hospital/Harvard University, Boston, MA, USA

**Objectives:** Uterine clear-cell carcinoma (UCCC) is a rare variant of endometrial cancer associated with a poor prognosis. Many adjuvant therapies have been instituted in attempts to improve prognosis. The
objective of this investigation was to examine the patterns of care, predictors, and impact of chemotherapy and radiation on survival in women diagnosed with UCCC.

**Methods:** The Surveillance, Epidemiology and End Results (SEER) — Medicare database was used to identify women diagnosed with UCCC from 1992 to 2009. Standard univariate analyses and multivariable analyses with logistic regression were performed. Kaplan–Meier survival analysis was used to generate overall survival (OS) data. Factors predictive of outcomes were compared using the log-rank test and Cox proportional hazards model.

**Results:** A total of 468 patients met eligibility criteria; 50% of women presented with stage I disease, 11.5% with stage II, 14.5% with stage III, and 21.3% with stage IV. The majority of patients (82.8%) underwent definitive surgery. Chemotherapy, radiation, and chemotherapy combined with radiation were administered in 16.5%, 32.5%, and 13.2% of women; 37.8% of women did not receive adjuvant therapy. Utilization of chemotherapy became more frequent over time across all stages. After adjusting for race, period of diagnosis, marital status, stage, age, surgery, lymph node dissection, socioeconomic status, and comorbidity index, there was no association between receipt of chemotherapy (HR 0.7; 95% CI, 0.4–1.1; P = 0.2), combination of chemotherapy and radiation (HR 0.9; 95% CI, 0.5–1.5; P = 0.7), or radiation (HR 0.9; 95% CI, 0.6–1.4; P = 0.9) and improved survival. There was no improvement in survival over the study period.

**Conclusions:** The overall rates of chemotherapy utilization have increased over time in patients with UCCC. Chemotherapy, radiation, and the combination of chemotherapy and radiation were not associated with increased survival.

**doi:**10.1016/j.ygyno.2015.01.083

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82 — Featured Poster Session

**Statin use significantly improves overall survival in high-grade endometrial cancer**


**University of Chicago, Pritzker School of Medicine, Chicago, IL, USA, bDrexel University College of Medicine, Philadelphia, PA, USA, cUniversity of Chicago, Chicago, IL, USA**

**Objectives:** In vitro data suggest that statins have antiproliferative and antimetastatic properties in endometrial cancer cells. An epidemiologic study showed that statin use after endometrial cancer diagnosis is associated with improved survival. We hypothesized that women with high-grade endometrial cancer treated with statins during definitive therapy would have improved overall survival (OS).

**Methods:** We retrospectively identified 103 patients who received chemotherapy and/or radiation in the setting of uterine clear cell carcinoma (UCC), uterine papillary serous carcinoma (UPSC), grade 3 endometrioid tumor, and mixed high-grade (MHG) endometrial cancer from 1995 to 2010. OS was estimated using the Kaplan–Meier method and compared using the log-rank test. Cox proportional hazards regression models were used for univariate and multivariate analyses.

**Results:** Histologies for the patients were 41% UPSC, 28% grade 3, 22% MHG, and 9% UCC. Median age at diagnosis was 67 years (range, 33–88 years), and 31% of patients were Caucasian, 65% African American, and 4% other. Median survival after diagnosis was 34 months. Twenty-nine (28%) patients had hyperlipidemia treated with statins, 8 (8%) had hyperlipidemia not treated with statins, and 66 (64%) were not diagnosed with hyperlipidemia. Median OS for patients with hyperlipidemia taking statins, hyperlipidemia not taking statins, and non-hyperlipidemic patients was 61.0 months (95% CI: 42.0–86.2), 32.0 months (95% CI: 17.9–52.1), and 30.5 months (95% CI: 35.1–53.2), respectively. Hyperlipidemic patients who used statins had improved OS compared to hyperlipidemic patients not using statins (P < 0.05). On multivariate analysis, statin use remained an independent predictor of survival (HR = 0.28, P < 0.05) after controlling for age, body mass index, race, diabetes status, and stage. Statin use was also significant when adjusting for treatment modality (P < 0.05).

**Conclusions:** Hyperlipidemic high-grade endometrial cancer patients receiving chemotherapy and/or radiation with concurrent statin use had a 47.5% increase in OS compared with those not treated with statins, which was significantly higher than the 1.4% increase in OS seen with statin use in the general population. This contributes to the growing research on antitumor effects of statins and supports additional study of statins as adjuvant therapy for women with endometrial cancer.

<table>
<thead>
<tr>
<th>Hyperlipidemia on statin</th>
<th>Hyperlipidemia without statin</th>
<th>Non-hyperlipidemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS (months)</td>
<td>61</td>
<td>32</td>
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<td></td>
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**doi:**10.1016/j.ygyno.2015.01.084

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83 — Featured Poster Session

Is VTE prophylaxis overkill? A comparison of VTE incidence in robotic and laparoscopic surgeries for endometrial cancer

A.H. Freeman, A. Barrie, L. Lyon, C. Garcia, L.H. Abbott, R.D. Littell, B. Powell, aKaiser Permanente San Francisco Medical Center, San Francisco, CA, USA, bKaiser Permanente Medical Group Division of Research, San Francisco, CA, USA

**Objectives:** To compare rates of venous thromboembolism (VTE) between robotic and traditional laparoscopic surgery for endometrial cancer and to determine the overall rate in minimally invasive approaches.

**Methods:** In this retrospective cohort analysis, consecutive patients undergoing minimally invasive hysterectomy for endometrial cancer or complex hyperplasia with atypia were identified between January 2009 and January 2014. Patient data, including age, cancer stage, cancer grade, procedure type, length of hospital stay, use of pharmacologic prophylaxis, and diagnosis of VTE were collected retrospectively by electronic medical record chart review. The primary outcome was the incidence of deep vein thrombosis (DVT) or pulmonary embolism (PE) within 30 days following surgery. Fischer’s exact tests were performed to evaluate factors associated with VTE.

**Results:** During the study period, 1434 patients underwent minimally invasive surgery (MIS) for endometrial cancer (740 robotic, 677 laparoscopic). Seventeen women were excluded due to known thrombophilia, history of VTE, or long-term anticoagulation. All patients were managed in a closed electronic health record system and all events were captured with no patient lost to follow-up. There were five VTEs in the robotic arm (0.68%) and three VTEs in the laparoscopic arm (0.44%) for an overall rate of VTE of 8/1417 (0.56%). There was no increased risk of VTE associated with robotic vs. laparoscopic approach (P = 0.728). Among all women, 39% had no perioperative therapy or had sequential compression devices (SCDs) only, 42% had preoperative pharmacologic prophylaxis only, 17% had both pre- and postoperative pharmacologic prophylaxes, and 2% had postoperative pharmacologic prophylaxis only. A total of 91 patients had posthospitalization extended prophylaxis. There was no increased risk of VTE associated with: age >65 years vs. <65 years (P = 0.72), advanced vs. early-stage disease (P = 0.56), same-day stay vs. longer (P = 1.00), use of pharmacologic prophylaxis (P = 1.00), or posthospitalization prophylaxis (P = 0.553).

**Conclusions:** The rate of VTE in patients undergoing MIS for endometrial cancer is low, and the rates are comparable between
84 — Featured Poster Session
Universal screening for Lynch syndrome in endometrial cancer results in increased acceptance of genetic counseling and testing

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Objectives: To evaluate the effect of a universal screening protocol for all newly diagnosed endometrial cancers for Lynch syndrome (LS) using immunohistochemistry staining (IHC) for mismatch repair (MMR) enzyme expression on subsequent genetic counseling and genetic testing referral and acceptance rates.

Methods: We performed a retrospective cohort study of all women who underwent a hysterectomy for endometrial cancer at Barnes Jewish Hospital in St. Louis, MO, between January 1, 2011 and December 31, 2013, (n = 637). A universal screening protocol was initiated on December 17, 2012, and used IHC for MMR enzymes MLH1, MSH2, MSH6, and PMS2. Cases with absent MLH1 staining were reclassified to MLH1 promoter methylation testing. The first cohort (Pre Em-USP) consisted of women who presented prior to initiation of the screening protocol and were selectively screened (n = 395). In the second cohort (Em-USP), women presented after initiation of this protocol and were all screened for LS (n = 242). Genetic counseling and genetic testing referrals in both cohorts were based on risk factors (family or personal history) and/or IHC results. Categorical variables were compared using the Fisher’s exact tests and continuous variables were compared using the Kruskal–Wallis test.

Results: Overall, a greater proportion of individuals in the Em-USP cohort underwent genetic testing than in the Pre Em-USP (9.1% vs. 4.8%, P < 0.05). Of the individuals with an IHC screening result suggestive of LS, those in the Em-USP cohort were significantly more likely to accept genetic counseling compared to those in the Pre-Em-USP cohort (95% vs. 64%, P = 0.013). Age >60 (OR 12.2, P = 0.002), BMI >35 (OR 2.26, P = 0.046), diabetes mellitus (OR 3.05, P = 0.022), and CHA (OR 8.46, P = 0.049) were independent predictors of concurrent endometrial carcinoma. The risk of concurrent endometrial carcinoma rose dramatically with increasing numbers of risk factors (none: 0%; 1 risk factor: 7%; 2 risk factors: 18.6%; 3 risk factors: 34.6%; and 4 risk factors: 45.5%, P = 0.001, Fig. A).

Conclusions: Older age, obesity, diabetes mellitus, and CHA are predictive of concurrent endometrial carcinoma in patients with endometrial hyperplasia. This information is valuable when counseling patients with endometrial hyperplasia on treatment options and stratifying their individual risk of concurrent malignancy.

doi:10.1016/j.ygyno.2015.01.086

85 — Featured Poster Session
Clinicopathologic factors predictive of concurrent endometrial carcinoma in women with a preoperative diagnosis of endometrial hyperplasia

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Objectives: Although certain fractions of endometrial hyperplasia can have concurrent endometrial carcinoma, patient characteristics associated with concurrent malignancy are not well described. The aim of our study was to identify predictive clinicopathologic factors for concurrent endometrial carcinoma among patients with endometrial hyperplasia.

Methods: We conducted a retrospective study of consecutive cases of biopsy-proven endometrial hyperplasia in women who underwent subsequent hysterectomy at a single institution from 2003 to 2014. We evaluated the following clinicopathologic factors: age, ethnicity, gravidity, medical comorbidities, body mass index (BMI), biopsy–hysterectomy time interval, and endometrial biopsy histology. Independent risk factors for concurrent endometrial carcinoma were identified by multivariate logistic regression analysis.

Results: A total of 211 endometrial hyperplasia cases were examined (simple hyperplasia with or without atypia [n = 24], complex hyperplasia without atypia [n = 58], and complex hyperplasia with atypia [CHA] [n = 129]). Endometrial carcinoma was diagnosed in 43 (20.4%) hysterectomy specimens; the majority were grade 1 (86.0%) and stage I (81.4%). Age 40 to 59 years (odds ratio [OR] 3.87, P = 0.013), age >60 (OR 12.2, P = 0.002), BMI >35 (OR 2.26, P = 0.046), diabetes mellitus (OR 3.05, P = 0.022), and CHA (OR 8.46, P = 0.049) were independent predictors of concurrent endometrial carcinoma. The risk of concurrent endometrial carcinoma rose dramatically with increasing numbers of risk factors (none: 0%; 1 risk factor: 7%; 2 risk factors: 18.6%; 3 risk factors: 34.6%; and 4 risk factors: 45.5%, P = 0.001, Fig. A).

Conclusions: Older age, obesity, diabetes mellitus, and CHA are predictive of concurrent endometrial carcinoma in patients with endometrial hyperplasia. This information is valuable when counseling patients with endometrial hyperplasia on treatment options and stratifying their individual risk of concurrent malignancy.

doi:10.1016/j.ygyno.2015.01.087

86 — Featured Poster Session
Same-day discharge after laparoscopic hysterectomy for endometrial cancer

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Objectives: To investigate the relationship between same-day discharge (SDD) and postoperative complications within 30 days of laparoscopic hysterectomy for endometrial cancer and endometrial intraepithelial neoplasia (EIN).

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Methods: This single-institution retrospective cohort included all patients who underwent laparoscopic hysterectomy for endometrial cancer or EIN by one of four gynecologic oncologists in a single tertiary care academic hospital between 2011 and 2013. Frequencies of SDD, and postoperative complications were evaluated longitudinally over the study periods. Rapid adoption of routine SDD within the institution was conceptualized as a natural experiment, and a noninferiority analysis, with composite postoperative complications as the outcome of interest, was conducted using a two–one-sided test approach with an equivalence margin set at 7%. A multivariate logistic regression model was also constructed to evaluate the association between SDD and postoperative complications.

Results: Six hundred ninety-four patients were included in the study. All patients underwent laparoscopic hysterectomy. 38.2% had pelvic and 3.0% had para-aortic lymphadenectomy, and 9.4% underwent omentectomy. The rate of SDD increased from 3.9% in the first quarter of 2011 to 70.9% in the final quarter of 2013 ($P < 0.001$). During this period, the frequency of postoperative readmission, unscheduled surgery, infection, and composite complications within 30 days of hysterectomy did not differ by year ($P = 0.1$ for all). The absolute risk difference in the rate of the composite complication for patients who had surgery in 2013 compared to 2011 was $3.3\%$ (95% CI $-7.7$ to $1.0$), which supports the hypothesis of noninferiority. Patients who had SDD were younger (mean difference $= 4.1$ years, $P < 0.001$), had shorter duration of surgery (MD 28 min, $P < 0.001$), and had fewer comorbidities (relative risk for Charlson comorbidity index $> 5 = 0.6$, $P < 0.001$) compared with those who were admitted. After controlling for demographic, intraoperative, and comorbid factors, patients who had SDD were not at increased risk for postoperative complications.

Conclusions: SDD is safe for the majority of patients undergoing laparoscopic surgery for endometrial cancer and EIN.

Objectives: To compare the approach to and oncologic outcome of surgical staging in low-risk endometrial cancer between a European (EUC) and an American (USC) cancer center.

Methods: We identified all patients with low-risk endometrial cancer from two institutions. Low risk was classified as: endometrioid adenocarcinoma, myometrial invasion (MI) $< 50\%$, and FIGO grade 1 and 2. The EUC did not routinely perform lymphadenectomy in this low-risk group. Intraoperative macroscopic evaluation by a gynecologic pathologist was used to determine MI. Bulky nodes were always removed. The USC used a sentinel lymph node (SLN) algorithm and pathologic ultrastaging protocol. Isolated tumor cells and micro- and macrometastases were all considered node-positive for this analysis. Clinicopathologic data were compared. Appropriate statistical tests were used.

Results: A total of 891 patients were identified: 596 from the USC (March 2006–April 2013) and 295 from the EUC (December 2005–May 2013). When applying the SLN algorithm, 551 (92%) of 596 patients had at least 1 LN removed compared to 50 (17%) of 295 patients in the selective LN dissection group ($P < 0.005$). Positive pelvic LNs were detected in 30 (5%) of the USC patients and in 5 (1.7%) of the EUC patients ($P = 0.01$). There was no significant difference in detection of positive paraaortic LNs. Adjuvant therapy was administered in 135 (23%) of the USC patients and 39 (13%) of the EUC patients ($P = 0.001$). Administration of brachytherapy, 7 (2.4%) in the EUC group vs. 104 (17.4%) in the USC group, accounted for the main difference in adjuvant therapy ($P = 0.0005$). The median follow-up was 25 months (range, 0.4–90.1 months) for USC compared to 41.5 months (range, 0.2–103.1 months) for EUC patients. Two-year recurrence-free survival was 97.5% ($\pm 0.7\%$) in the USC vs. 95% ($\pm 1.4\%$) ($P = 0.06$) in the EUC group.

Conclusions: There is no international uniform approach to surgical staging of low-risk endometrial cancer. Applying an SLN algorithm for this low-risk population results in significantly higher detection

### Table

<table>
<thead>
<tr>
<th>Age, yrs</th>
<th>European Center (EUC)</th>
<th>US Center (USC)</th>
<th>$P$-value</th>
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<tbody>
<tr>
<td>n = 295</td>
<td>n = 596</td>
<td></td>
<td></td>
</tr>
<tr>
<td>64 (30–93)</td>
<td>59 (33–89)</td>
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<tr>
<td>27 (17–53.6)</td>
<td>30.4 (18–69)</td>
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<tr>
<td>246 (83.4%)</td>
<td>450 (75.5%)</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>49 (16.6%)</td>
<td>146 (24.5%)</td>
<td>0.008</td>
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</tr>
<tr>
<td>3 (1%)</td>
<td>61 (11%)</td>
<td>&lt;0.0005</td>
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<tr>
<td>Stage (FIGO 1988)</td>
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<td></td>
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<tr>
<td>IA</td>
<td>50 (17%)</td>
<td>335 (56%)</td>
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<tr>
<td>IB</td>
<td>189 (64%)</td>
<td>183 (31%)</td>
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<td>IC</td>
<td>0</td>
<td>0</td>
<td>&lt;0.0005</td>
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<tr>
<td>IIA</td>
<td>13 (4.4%)</td>
<td>2 (0.3%)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>IIB</td>
<td>23 (8%)</td>
<td>4 (0.7%)</td>
<td>&lt;0.0005</td>
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<tr>
<td>IIIA</td>
<td>6 (2%)</td>
<td>39 (6.5%)</td>
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<td>IIIC</td>
<td>5 (1.7%)</td>
<td>33 (5.5%)</td>
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<td>Unspecified</td>
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<tr>
<td>Pelvic LN removal</td>
<td>43 (15%)</td>
<td>482 (81%)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Pos pelvic LN</td>
<td>5 (1.7%)</td>
<td>30 (5%)</td>
<td>0.010</td>
</tr>
<tr>
<td>Pelvic and para-aortic LN</td>
<td>6 (2%)</td>
<td>69 (12%)</td>
<td>&lt;0.0005</td>
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<tr>
<td>LN removal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos para-aortic LN</td>
<td>2 (0.7%)</td>
<td>4 (0.7%)</td>
<td>1</td>
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<tr>
<td>Unknown LN removal status</td>
<td>11 (4%)</td>
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<tr>
<td>Adjuvant therapy</td>
<td>39 (13.2%)</td>
<td>135 (22.7%)</td>
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</tr>
<tr>
<td>WPRT</td>
<td>17 (5.8%)</td>
<td>19 (3.2%)</td>
<td>0.072</td>
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<tr>
<td>Brachytherapy</td>
<td>7 (2.4%)</td>
<td>104 (17.4%)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>21 (6.4%)</td>
<td>33 (5.5%)</td>
<td>0.372</td>
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<td>Hormonal therapy</td>
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<td>Unknown</td>
<td>0</td>
<td>2 (0.3%)</td>
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<tr>
<td>Recurrences</td>
<td>20 (6.8%)</td>
<td>16 (2.7%)</td>
<td>0.004</td>
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<tr>
<td>Local</td>
<td>10 (3.4%)</td>
<td>10 (1.7%)</td>
<td>0.147</td>
</tr>
<tr>
<td>Distant</td>
<td>10 (3.4%)</td>
<td>2 (0.3%)</td>
<td>&lt;0.0005</td>
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<tr>
<td>Multiple</td>
<td>0</td>
<td>4 (0.7%)</td>
<td>0.308</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>41.5 (0.2–103.1)</td>
<td>25 (0.4–90.1)</td>
<td></td>
</tr>
<tr>
<td>2-year recurrence free survival</td>
<td>95% ($\pm 1.4%$)</td>
<td>97.5% ($\pm 0.7%$)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Data are expressed as median (range), % or number (%).
of positive LNs compared to a selective LN dissection approach. There appears to be a possible advantage in recurrence-free survival with the SLN approach, perhaps due to higher identification of stage IIIC disease and more targeted adjuvant therapy. These data require additional validation and study.

doi:10.1016/j.ygyno.2015.01.089

88 — Featured Poster Session
Impact of obesity on sentinel lymph node mapping in patients with newly diagnosed uterine cancer undergoing robotic surgery
Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: To determine the impact of obesity on the rate of successful sentinel lymph node (SLN) mapping in patients with uterine cancer undergoing robotic surgery and compare blue dye and indocyanine green (ICG) SLN detection rates.

Methods: We reviewed robotic cases undergoing SLN mapping with a cervical injection for the time period 1/2011–12/2013 using either blue dye or ICG with near-infrared (NIR) fluorescence imaging. Data were stratified by body mass index (BMI) as normal and overweight (BMI < 30), obese (BMI ≥ 30–40), and morbidly obese (BMI ≥ 40) as well as dye used. Overall and bilateral mapping rates were compared only among cases in which either ICG or blue dye was used exclusively. Appropriate statistical tests were applied.

Results: A total of 472 cases were identified. Bilateral mapping was successful in 352 (75%) cases, unilateral mapping was successful in 19 (24%), and 7 (9%) did not map. Median BMI was slightly higher in those with no mapping (BMI 38) compared with unilateral or bilateral mapping (BMI 34.7 for both) (P = 0.001). There was a significant decrease in successful bilateral mapping rates for both ICG (P < 0.001) and blue dye groups (P = 0.004) with increasing BMI. Overall mapping also decreased with increasing BMI in the ICG (P = 0.008) and blue dye groups (P = 0.036) (Table). However, use of ICG resulted in better bilateral (P = 0.002) and overall (P = 0.011) mapping rates compared to the use of blue dye in all BMI groups (Table 1).

Conclusions: ICG results in higher overall and bilateral detection of SLNs in patients with uterine cancer. Successful mapping decreases with increasing obesity irrespective of dye used but is improved with the use of ICG.

89 – Featured Poster Session
Adherence to a standard algorithm results in high negative predictive value of sentinel lymph node assessment using indocyanine green (ICG) and isosulfan blue (ISB) dyes in endometrial cancer
F.J. Backes, D.M. O’Malley, R. Salani, D.E. Cohn, L.J. Copeland, J.M. Fowler. The Ohio State University, James Cancer Hospital, Columbus, OH, USA

Objectives: To prospectively evaluate the detection rate, sensitivity, and negative predictive value (NPV) of sentinel lymph node (SLN) assessment using isosulfan blue (ISB) and indocyanine green (ICG) dyes with fluorescence imaging.

Methods: All patients with endometrial cancer scheduled for robotic surgical staging were eligible to participate. Patients were prospectively enrolled after signing informed consent. ISB dye 1 mL and ICG dye 1 mL were injected submucosally in the cervix at 3 and 9 o’clock positions. After identification and dissection of the SLNs, a complete lymphadenectomy (LND) was performed in all patients. All lymph nodes (LNs) were evaluated with hematoxylin-and-eosin only (no ultrastaging).

Results: Between 4/2013 and 7/2014, 78 patients were included. The median age was 60 years (range, 37–79 years). Median body mass index (BMI) was 34.5 (range, 19.7–47.7). Sixty-four (82%) patients were diagnosed with stage I, 1 (1%) with stage II, and 13 (17%) with stage III disease. The mean number of pelvic LNs was 9.7 (left) and 9.8 (right). Sixty-eight percent of patients underwent aortic LND (mean, 7 PALN). In 70 (89%) cases, SLNs were identified with ICG (median, 3 SLNs) and in 56 (72%) with ISB (median, 2 SLNs). ICG resulted in 55% bilateral mapping and ISB in 38%. Using both dyes, bilateral mapping was successful in 52 (67%) cases, unilateral mapping was successful in 19 (24%), and 7 (9%) did not map. Median BMI was slightly higher in those with no mapping (BMI 38) compared with unilateral or bilateral mapping (BMI 34 for both) (P = 0.44). Ten (13%) patients had positive LNs. Six patients had positive SLNs with negative non-SLNs. Sensitivity of SLN evaluation was 68% (95% CI 62.4–78.6). Four of 10 of patients with positive LNs had negative SLNs. In three of four cases, positive LNs were found on the side of negative mapping. Only in one case were sentinel LNs identified bilaterally and a unilateral positive non-sentinel LN found (LN enlarged bilaterally). NPV was 94.4% (95% CI 86.4–98.4).

Conclusions: Despite four cases with positive non-sentinel LNs, no positive LNs would have been missed as long as the surgeon adhered to the algorithm of full dissection in case of negative mapping and removal of any enlarged LNs. BMI was not a significant factor for successful mapping in our cohort.

doi:10.1016/j.ygyno.2015.01.090

90 — Featured Poster Session
Pulmonary resection in the treatment of high-risk gestational trophoblastic neoplasia
M.L. Kanis, J.R. Lurainiili. Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Objectives: To evaluate the role of pulmonary resection in the management of high-risk gestational trophoblastic neoplasia (GTN).

Methods: Patients who underwent pulmonary resection as part of their treatment for high-risk GTN from 1986 to 2014 were
retrospectively analyzed. All patients had received one or more multiagent chemotherapy regimens preoperatively. Patient and disease characteristics, including age, FIGO stage and score, antecedent pregnancy, number of pulmonary metastases, other sites of disease, human chorionic gonadotropin (hCG) levels before and after surgery, and number and type of preoperative and postoperative chemotherapy regimens, were evaluated with respect to outcome.

**Results:** Fifteen (26%) of 58 patients treated for high-risk GTN underwent pulmonary resection with curative intent. Mean age of patients was 29 years (range, 19–37 years). FIGO stage was III in 12 patients and IV in 3. FIGO scores ranged from 5 to 20 (mean, 10). Antecedent pregnancy was nonmolar in 11 patients (73%). Adjuvant surgical procedures other than pulmonary resection were performed in eight patients (53%). The number of preoperative chemotherapy regimens ranged from 1 to 12 (median, 4) and courses numbered from 2 to 32 (median, 14). Preoperative hCG levels ranged from 2 to 2786 mIU/mL (median, 177 mIU/mL). Pulmonary wedge resections or lobectomies were performed via video-assisted thoracoscopic surgery (11) or thoracotomy (4). Two patients underwent pulmonary resections on two separate occasions. No patient had complications as a result of these procedures. Eleven patients (73%) were cured. In these 11 patients, hCG levels decreased to <2 mIU/mL within 6 to 52 days (mean, 22 days) postoperatively. Of the four patients who were not cured, mean FIGO score was 13, three had preoperative hCG levels >1700 mIU/mL, two had brain metastases, and one was noncompliant with follow-up chemotherapy.

**Conclusions:** Pulmonary resection of chemotherapy-resistant GTN was an important component of treatment in 26% of high-risk patients, resulting in a 73% cure rate. Ideal candidates have disease isolated to the lungs and low hCG levels. However, even some patients with multiple lesions in one lung requiring more than one primary resection or recurrent pulmonary disease requiring repeat surgery may still be curable. Postoperative chemotherapy should be administered.

doi:10.1016/j.ygyno.2015.01.092

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91 - Featured Poster Session

**A multicenter prospective assessment of surgical findings associated with suboptimal cytoreduction at primary debulking surgery for advanced ovarian, fallopian tube and peritoneal cancer**

R.S. Suidan\(^a\), P.T. Ramirez\(^b\), D.A. Levine\(^c\), Y. Sonoda\(^d\), N.R. Abu-Rustum\(^e\), M.M. Leitao\(^f\), Q. Zhou\(^g\), M.K. Amanugban\(^h\), C.F. Levenback\(^i\), D.S. Chi\(^j\), \(^a\)Memorial Sloan Kettering Cancer Center, New York, NY, USA, \(^b\)The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Objectives:** To identify surgical findings associated with suboptimal (>1 cm residual disease) primary cytoreduction in advanced epithelial ovarian, fallopian tube, and peritoneal cancer.

**Methods:** This was a prospective multicenter study of patients who underwent primary debulking surgery for stage III–IV ovarian, fallopian tube, and peritoneal cancer. Surgical findings and disease locations were recorded by an attending gynecologic oncologist at the time of laparotomy. Five clinical and 16 surgical criteria were assessed, and a multivariable model predictive of suboptimal debulking was developed.

**Results:** From 7/2001 to 12/2012, 669 patients were enrolled, with 382 meeting eligibility criteria. The optimal debulking rate was 76% (292 patients). On multivariate analysis, five surgical criteria were found to be significantly associated with suboptimal debulking: lesser sac lesions >1 cm (odds ratio [OR] 3.5, 95% CI 1.8–7.1); widespread small bowel serosal involvement ≥1 cm (OR 4.7, 95% CI 3.8–5.8); disease in the mesentery, around its root, or around the root of the superior mesenteric artery ≥1 cm (OR 3.9, 95% CI 1.01–8.9); presacral extraperitoneal disease ≥1 cm (OR 2.1, 95% CI 1.6–2.8); and anterior abdominal wall invasion ≥1 cm (OR 1.9, 95% CI 1.1–3.3). A receiver operating characteristic curve was generated, and a predictive model utilizing the five surgical criteria had an AUC of 0.829. A “predictive score” was assigned to each criterion based on its multivariate OR, and the suboptimal debulking rates of patients who had a total score of 0, 1–2, 3–4, 5–6, and ≥7 were 6%, 20%, 38%, 54%, and 84%, respectively (Table).

**Conclusions:** In two high-volume ovarian cancer centers, we identified five surgical criteria associated with suboptimal cytoreduction and developed a predictive model in which the suboptimal rate was directly proportional to a predictive score, with an overall accuracy of 0.829. This model could form the basis of a preoperative laparoscopic assessment to identify patients who are at high risk for suboptimal cytoreduction and who may be better suited for neoadjuvant chemotherapy.

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<thead>
<tr>
<th>Total predictive score</th>
<th>Total patients n (%)</th>
<th>Optimal (n)</th>
<th>Suboptimal (n)</th>
<th>Suboptimal rate</th>
</tr>
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<tr>
<td>0</td>
<td>188/382 (49%)</td>
<td>177</td>
<td>11</td>
<td>6%</td>
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<td>1–2</td>
<td>84/382 (22%)</td>
<td>67</td>
<td>17</td>
<td>20%</td>
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<td>3–4</td>
<td>42/382 (11%)</td>
<td>26</td>
<td>16</td>
<td>38%</td>
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<tr>
<td>5–6</td>
<td>37/382 (10%)</td>
<td>17</td>
<td>20</td>
<td>54%</td>
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<tr>
<td>≥7</td>
<td>31/382 (8%)</td>
<td>5</td>
<td>26</td>
<td>84%</td>
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doi:10.1016/j.ygyno.2015.01.093

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92 - Featured Poster Session

**Ovarian cancer patients selected for neoadjuvant chemotherapy versus primary debulking surgery are not similar: A National Cancer Data Base study**

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**Objectives:** We sought to characterize the types of patients with epithelial ovarian cancer (EOC) who received neoadjuvant chemotherapy (NACT) vs. primary debulking surgery (PDS) using the National Cancer Data Base (NCDB).

**Methods:** We identified patients with stages IIIIC and IV EOC in the NCDB diagnosed from 2003 to 2011. Patients who received chemotherapy (CT) prior to surgery were classified as receiving NACT; if surgery preceded CT, it was classified as PDS. Data collected from the NCDB included: demographics, comorbidity index, plus cancer, treatment, and hospital characteristics. Univariable and multivariable analyses were performed using chi square test, logistic regression, log-rank test, and Cox proportional hazards modeling as indicated. Statistical significance set at P < 0.05.

**Results:** A total of 62,726 patients with stages IIIIC and IV EOC were identified. The sequence of surgery and CT was identified, with 6922 (11%) having NACT and 31,279 (50%) having PDS. NACT was more frequently done in stage IV than in stage IIIIC disease (13% vs. 9%), and its use markedly increased over time. NACT was more frequently performed than PDS in the following situations: age >50 years and those with higher comorbidities, stage IV disease, and higher-grade EOC. NACT patients were more likely to receive treatment from hospitals that were adherent to National Comprehensive Cancer Network guidelines, high-volume facilities, those in the Midwest and West, and academic centers. Other factors significantly different between NACT and PDS were unplanned 30-day readmission: 3.6% vs. 7.0% (P < 0.001) and 30-day mortality: 1.3% vs. 0.6% (P < 0.001).
Survival analysis estimated median overall survival for stage III/IIIC with PDS as 42.7 months compared with NACT as 32.9 months ($P < 0.001$), but median survival was the same for stage IV disease (30.2 vs. 30.6 months). In multivariate analysis, patients who received NACT compared to PDS with stage III/IIIC disease had a slightly greater mortality risk ($HR = 1.23$), but the relative risk was less profound than age $>71$ years (1.64), comorbidities (1.62), grade 3 disease (1.70), CT alone (2.12), or surgery alone (1.64).

**Conclusions:** Evidence suggests that patients with greater adverse risk factors are more likely to receive NACT than PDS. Although patients who receive NACT have a somewhat worse mortality compared to PDS, this may be a reflection of older, medically infirm patients with advanced disease rather than an inherently inferior treatment option.

**References:**


**Fig. 1.** Kaplan-Meier Survival curves for overall survival (main outcome effects) stratified by SCS risk category.

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**93 — Featured Poster Session**

**Surgical complexity score and oncologic outcomes following optimal or complete cytoreductive surgery for ovarian, fallopian tube and primary peritoneal cancers**

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**Objectives:** Appropriate surgical candidate selection and maximum surgical effort are critical to the management of advanced ovarian cancer. This study sought to determine what effect surgical complexity has on postoperative morbidity, disease recurrence, and survival following primary or interval cytoreductive surgery for the treatment of advanced ovarian cancer.

**Methods:** A single-institution retrospective review identified all patients undergoing optimal ($<1$ cm) or complete (no gross residual disease [NGRD]) cytoreduction during primary or interval debulking for stage III and IV ovarian, fallopian tube, or peritoneal cancers between 1/95 and 12/08. Surgical, postoperative, and survival data were extracted from the medical record. Surgical complexity scores (SCSs) were calculated based on the number and relative difficulty of the procedures performed. The primary endpoints were progression-free survival (PFS) and overall survival (OS). Fisher’s exact test, Kaplan–Meier survival analysis, and multivariable Cox proportional hazards regression were used.

**Results:** Two hundred ninety-seven cases were analyzed. On univariate analysis, high SCS was associated with complete cytoreduction but also more major complications ($P < 0.05$). Kaplan–Meier analysis indicated that neither PFS nor OS was significantly different between the simple vs. complex SCS risk categories (median PFS, 21.5 vs. 15.8 months, $P = 0.18$; median OS, 50.5 vs. 35.6 months, $P = 0.26$) (Fig. 1). Cox proportional hazards regression confirmed that high SCS did not independently predict OS (HR 1.42; 95% CI 0.98–2.06), despite superior PFS (HR 1.50; 95% CI 1.07–2.10). Stage IV disease, age $>75$ years, American Society of Anesthesiologists score $>3$, and major complications were associated with worse OS. The absence of visible residual disease was the only covariate associated with improved PFS (HR 0.73; 95% CI 0.56–0.94) and OS (HR 0.73; 95% CI 0.55–0.97).

**Conclusions:** Quality care for advanced ovarian cancer should include any necessary procedures to minimize the amount of residual carcinoma remaining after initial debulking surgery. After controlling for NGRD, survival is equivalent regardless of how this benchmark is achieved (i.e., low or high SCS). The increased risk of short-term morbidity with high SCS is likely justified by the survival advantage conferred by reaching NGRD for many patients.

SCS calculated based on previously published point-scale used to quantify the extent of surgical complexity developed at the Mayo Clinic.

**doi:** 10.1016/j.ygyno.2015.01.094

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**94 — Featured Poster Session**

**Setting the bar: Compliance with ovarian cancer quality indicators at a National Cancer Institute (NCI)-designated Comprehensive Cancer Center (CCC)**

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**Objectives:** Quality measures are being developed for ovarian cancer and will be tracked to improve health care delivery and determine payment processes. Our objective was to evaluate compliance at a National Cancer Institute-designated comprehensive cancer center (CCC) with eight ovarian cancer quality indicators proposed by the Society of Gynecologic Oncology (Table 1).

**Methods:** A total of 123 patients underwent primary staging or cytoreductive surgery and adjuvant chemotherapy for invasive ovarian cancer from 2010 to 2012 at a single CCC. Patients were excluded if they received any treatment at another institution. Descriptive statistics were performed to determine compliance.

**Results:** Quality indicator (QI) #1: A total of 121/123 (98.4%) patients had an operative report documenting residual disease dictated within 48 h of cytoreduction. QI #2: Complete surgical staging was performed in 25/55 (45.5%) patients with stage I–IIIB disease. Peritoneal biopsies and bilateral pelvic and bilateral paraaortic lymphadenectomy were each omitted in about one third of patients. QI #3 & 4: In patients with optimally debulked stage III disease, 52/56 (92.9%) were offered intraperitoneal (IP) chemotherapy, with 29/56 (51.8%) receiving IP and 19 of these within 42 days. Most patients who did not receive IP were due to comorbidities or randomization in a clinical trial. QI #5: All 105 patients for whom adjuvant chemotherapy was indicated received platin or taxane and 79/105 (75.2%) within 42 days. QI #6: Venous thromboembolism prophylaxis was provided in 122/123 (99.2%) patients by mechanical prophylaxis.
Means and 98/123 (79.7%) by pharmacologic means within 24 h of surgery. QI #7 & 8: A total of 119/121 (98.3%) patients received prophylactic parenteral antibiotics within 60 min of cytoreduction and these were discontinued in 120/121 (99.2%) cases.

**Conclusions:** These data can help establish benchmark criteria for integrating ovarian indicators into actual practice. The surprisingly low percentage of “completely staged” patients deserves additional exploration as to whether this is a flaw in reporting or a lack of compliance. The study not only identifies areas for improvement but also demonstrates the importance of documentation when medical reasons prevent indicators from being met. Further validation requires prospective evaluation of these indicators and their correlation to patient outcomes, such as survival.

**Table 1**

<table>
<thead>
<tr>
<th>SGO ovarian indicators</th>
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<tr>
<td>1. Operative report with documentation of residual disease within 48 h of</td>
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<tr>
<td>2. Complete staging with invasive stage I–III ovarian, fallopian tube, or peritoneal</td>
</tr>
<tr>
<td>3. Intraperitoneal chemotherapy offered within 42 days of optimal cytoreduction to</td>
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<tr>
<td>4. Intraperitoneal chemotherapy administered within 42 days of optimal cytoreduction</td>
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<tr>
<td>5. Platin or taxane administered within 42 days following cytoreduction to women</td>
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<tr>
<td>6. Venous thromboembolism prophylaxis administered within 24 h of cytoreduction to</td>
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<tr>
<td>7. Order for prophylactic parenteral antibiotic administration within 1–2 h before</td>
</tr>
<tr>
<td>8. Order for prophylactic parenteral antibiotic discontinuation within 24 h after</td>
</tr>
</tbody>
</table>

**Results:** In ADV, 77% (64%–87%) of patients received guideline-concordant care with a level 1 evidence-based chemo regimen or research protocol and 64% completed at least 6 cycles. Of the 251 non-concordant patients, the most common reason for nonconcordance was no therapy within 90 days (25%). The most common alternative regimens were modifications of the GOG 172 intraperitoneal/IV regimen (36%). Single-agent carbo was given to 11% of the population, and another 5% did not receive a platinum and taxane. In early-stage disease, 78% (63%–88%) initiated the recommended or research based therapy within 30 days and completed at least 3 cycles. Conversely, nonconcordant chemo was received in 23% (10%–33%) of patients with stage IA/B, grade 1 disease.

**Conclusions:** At NCCN institutions, adherence to treatment recommendations for adj chemo was 77% in patients with ADV disease, 78% in those with HR-ES disease, and 77% in those with LR-ES disease.

Use of guideline-concordant chemo was nearly double what has been reported previously, but there is still room for improvement because nearly 20% of patients were either undertreated or overtreated at NCCN institutions.

**Objectives:** We investigated 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 stages III and IV) who were treated at 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 three groups: no gross residual group (n = 109, 21.5%), optimal group (n = 206, 40.6%), and suboptimal group (n = 192, 37.9%). Delayed ISC was associated with increased HRs for overall survival only in the optimal group. In subsequent analyses performed in the optimal group, we found ISC to be a continuous variable (HR, 1.016; 95% CI, 1.005–1.031; P = 0.007). History of consultation by the department of general surgery (HR, 2.744; 95% CI, 1.345–5.599; P = 0.006) and platinum resistance (HR, 7.175; 95% CI, 4.112–12.52; P = 0.006) were significantly associated with poor overall survival. On multivariate analysis, ISC remained a significant poor prognostic factor (HR, 1.018; 95% CI, 1.003–1.033; P = 0.022). The cutoff value of HR significantly increased on the 17th day of ISC (HR, 2.744; 95% CI, 1.345–5.599; P = 0.006) in the multivariate analysis.

**Conclusions:** Based on the collected data, delayed adjuvant chemotherapy subsequent to surgery most likely would result in a negative impact on overall survival in advanced epithelial ovarian cancer patients who have optimal cytoreduction.
97 — Featured Poster Session
A comparative analysis in management of ovarian cancer between a major tertiary cancer center and non-oncologic institutions in Medellín, Colombia
C.J. Rendón1, L.M. Echeverría2, R. Pareja3, M. Araujo4, M.A. Madariaga5, S.M. Lucchini5,6, P.T. Ramirez7, 8Instituto de Cancerología — Las Américas, Medellín, Colombia, 9Centro Medico Docente la Trinidad, Caracas, Venezuela, 4Hospital de San José, Bogotá, Colombia, 4Hospital Nacional de Clínicas, Bogotá, Argentina, 7The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objectives: Outcomes of patients with advanced ovarian cancer differ based on hospital volume and surgeon expertise. The goal of this study was to determine whether outcomes varied among different hospital settings.

Methods: A retrospective review of all patients with stage I–IV invasive epithelial ovarian cancer was performed to determine the impact of treatment at a major tertiary cancer center.

Results: A total of 292 patients were identified, the majority of whom (52%) had stage III disease and serous adenocarcinoma (42%). A total of 71.6% of patients at the tertiary center were treated with standard staging surgery vs. 35.5% of patients from other institutions. The rate of optimal surgery at the tertiary center was 69.6% vs. 28.9% at other institutions. Overall survival (OS) and disease-free survival (DFS) in advanced ovarian cancer were longer in patients treated at the tertiary academic center (44 months–14 months) vs. other institutions (20 months–16 months), respectively.

Conclusions: Management of patients with advanced ovarian cancer at tertiary cancer centers in Colombia is associated with higher rates of optimal cytoreduction and improved oncologic outcomes. Even in developing countries, we have demonstrated that outcomes are much better in specialized centers.

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98—Featured Poster Session
Surgical factors do not impact survival in high-grade serous ovarian carcinoma patients treated with neoadjuvant chemotherapy
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Objectives: Advanced high-grade serous ovarian carcinoma (HGSC) is treated with a combination of surgery and chemotherapy. We sought to investigate the survival of patients treated with neoadjuvant chemotherapy (NAC) compared to primary cytoreductive surgery (PCS).

Methods: Patients with stage III and IV HGSC diagnosed between 2003 and 2011 were included in this retrospective cohort study; 398 patients met inclusion criteria. Data were obtained from patient records. Patients were divided into two groups treated with either neoadjuvant chemotherapy followed by interval cytoreductive surgery (NAC group, n = 192) or primary cytoreductive surgery followed by adjuvant chemotherapy (PCS group, n = 206). The NAC and PCS groups were stratified by: 1) age; 2) the timing of interval surgery in relation to the number of neoadjuvant chemotherapy cycles (3, 4, or ≥5); 3) surgical cytoreduction status; and 4) platinum sensitivity. Log-rank statistical tests were performed and Kaplan–Meier survival curves were generated.

Results: The NAC group of patients had significantly worse overall survival compared to the PCS group (31.6 vs. 61.3 months; P < 0.001). Survival of the NAC group was independent of age and the timing of interval surgery in relation to chemotheraphy cycles. In addition, optimal surgical cytoreduction had no impact on the overall survival in the NAC group (P < 0.001). Among platinum-sensitive patients, the NAC group had worse survival (P < 0.001). Importantly, optimal cytoreduction (P < 0.001) and platinum-sensitivity (P < 0.001) were independent predictors of improved survival in the PCS group.

Conclusions: Ovarian cancer patients with both thrombocytosis and leukocytosis have an increased risk of postoperative complications. Even after controlling for patient and surgical factors, patients with both thrombocytosis and leukocytosis had twice the rate of major complications and a fourfold increase in postoperative death.

doi:10.1016/j.ygyno.2015.01.101

99 — Featured Poster Session
Preoperative thrombocytosis and leukocytosis among ovarian cancer patients are associated with postoperative death
E.L. Barber, J.F. Bogess, L. Van Le, K.H. Kim, V.L. Bae-Jump, W.R. Brewster, J.T. Soper, P.A. Gehrig, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Objectives: Although thrombocytosis and leukocytosis have each been associated with poor prognosis in ovarian cancer patients, their relationship with postoperative outcomes is unknown. We examined whether patients with thrombocytosis or leukocytosis are at increased risk of postoperative morbidity or mortality.

Methods: Patients undergoing primary surgery for ovarian cancer from 2005–2012 were identified from the American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP). Thrombocytosis was defined as platelets ≥450,000/mm³ and leukocytosis as white blood cells >10,000/mm³. We examined 30-day postoperative complication and mortality rates. Major complications included myocardial infarction, thromboembolism, sepsis, deep surgical site infection, and prolonged intubation. Minor complications included urinary tract infection, superficial wound infection, and transfusion. Student’s t-test, chi square test, and binary logistic regression were used.

Results: We identified 1075 patients. The incidence of thrombocytosis was 9.6%, leukocytosis was 17.9%, and both conditions concomitantly were 4.9%. In univariate analysis, leukocytosis was associated with major (16.5% vs. 10.3%, P = 0.01) and minor complications (37.5% vs. 28.1%, P = 0.01) but not postoperative death (6.0% vs. 1.3%, P = 0.08). Thrombocytosis was also associated with major (19.4% vs. 10.7%, P = 0.01) and minor complications (44.7% vs. 28.4%, P = 0.01), but not postoperative death (2.9% vs. 1.5%, P = 0.30). Patients with both thrombocytosis and leukocytosis had increased rates of major complication (22.6% vs. 10.9%, P = 0.01) and mortality (5.7% vs. 1.4%, P = 0.02). In a multivariate model controlling for surgical complexity, age, American Society of Anesthesiologists score, and medical comorbidities, the association between major complication and thrombocytosis (P < 0.01) and major and leukocytosis (P = 0.01) persisted. In the same model, thrombocytosis and leukocytosis together were associated with major complication (P < 0.01), minor complication (P < 0.01), and postoperative death (P = 0.02).

Conclusions: Ovarian cancer patients with preoperative thrombocytosis or leukocytosis have an increased risk of postoperative complications. Even after controlling for patient and surgical factors, patients with both thrombocytosis and leukocytosis had twice the rate of major complications and a fourfold increase in postoperative death.

doi:10.1016/j.ygyno.2015.01.100
100 — Featured Poster Session
Distinct immune characteristics in women with deleterious germline *BRCA1/2* mutations (gBRCAm)-associated high-grade serous ovarian cancer (HGSOC)

**Objectives:** Women with gBRCAm HGSOC have tumor genomic instability, a feature that may increase antigen quantity and exposure, leading to activation of the immune response. We hypothesized that HGSOC patients with gBRCAm have differences in the relative proportions of peripheral blood lymphocyte subpopulations. We also investigated whether treatment with the poly ADP ribose polymerase (PARP) inhibitor olaparib yields changes in immune subset markers in women with HGSOC.

**Methods:** We collected peripheral blood mononuclear cells (PBMCs) prior to therapy and on day 2 of olaparib alone from women on two olaparib studies (NCT01445418 and NCT01237067). PBMCs were viable frozen until analysis. All immune subset analyses were performed by multiparametric flow cytometry. Immune subsets, including regulatory T cells (CD4 + CD25highFoxp3+), exhausted CD8+ T-cells, and myeloid-derived suppressor cells (MDSCs; Lineage−, HLA-DR−, CD11b+, CD33+), were analyzed. Functional marker expression, including cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), T-cell immuno-globulin and mucin protein 3 (TIM-3), and programmed death-1 (PD-1), were evaluated. Data were analyzed using FlowJo software.

**Results:** Pretreatment PBMCs were collected from 41 recurrent HGSOC patients whose median age was 65 years (range, 49–71 years): 16 gBRCAm and 25 BRCAwt. Among them, 22 patients had paired samples pretherapy and on day 2 of olaparib treatment (11 gBRCAm/11 BRCAwt). Quantities of MDSCs were significantly lower in gBRCAm-HGSOC patients compared to BRCAwt-HGSOC patients (*P* = 0.0086). There was significantly higher expression of CTLA-4 on CD8+ T cells in gBRCAm samples (*P* = 0.0074). Other immune functional markers and percent of Tregs among CD4+ T cells did not differ between the two groups and did not change after olaparib treatment.

**Conclusions:** Our data suggest that women with gBRCAm-HGSOC may have a distinct immune signature in PBMCs, in which lower MDSC levels may be associated with enhanced antitumor immune response. Further work is ongoing to extend and validate these findings.

doi:10.1016/j.jygyno.2015.01.102

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101 — Featured Poster Session
The acceptability and perception of the morbidity and mortality of complex surgical procedures in primary debulking of ovarian cancer: A survey of American and Canadian gynecologic oncologists

**Objectives:** Primary debulking in advanced ovarian cancer may involve complex surgical procedures associated with significant morbidity and potential mortality. This survey was designed to assess gynecologic oncologists’ perceptions of acceptability, morbidity, and mortality of these procedures.

**Methods:** We conducted a cross-sectional survey of gynecologic oncologists in the United States and Canada to collect demographic characteristics and current practice patterns. The primary outcomes were the acceptability of performing complex surgical procedures (distal pancreatectomy and splenectomy [DP S] and subtotal colectomy [STC] with permanent ileostomy or ileorectal anastomosis) and the perceptions of the mortality, short- and long-term morbidity, and expected quality of life from the procedures.

**Results:** A total of 138 gynecologic oncologists participated, of whom 99 (71.7%) defined their practice as part of an academic institution. Seventy-two (52.2%) respondents have been in practice for >10 years. With the goal of achieving no macroscopic residual disease, 77.4% felt that DP S was an acceptable procedure as part of primary surgical debulking, and 52/128 (40.6%) estimated the mortality risk of DP S to be <1%, which is lower than that reported in the literature. Similarly, 43.8% and 74.2% of respondents underestimated the risks of short- and long-term morbidity, respectively, compared to reported rates. STC with permanent ileostomy or ileorectal anastomosis was found to be acceptable by 49.2% of respondents. Of those who did not recommend this procedure, 59.5% cited impaired quality of life with permanent ileostomy or ileorectal anastomosis as the reason to omit this procedure. The perceptions of the risk of significant short- and long-term morbidity from STC varied widely.

**Conclusions:** For primary debulking of ovarian cancer, the majority of respondents considered performing relatively aggressive surgical procedures to achieve complete macroscopic resection of disease in the appropriate candidate. The perceived morbidity from DP S was underestimated, and the perceived impairment in quality of life from STC varied. In these cases, a multidisciplinary approach should be considered to ensure appropriate preoperative counseling as well as establish individualized acceptability of the risks and goals of care.

doi:10.1016/j.jygyno.2015.01.103

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102 — Featured Poster Session
The impact of percent reduction in CA-125 levels on prediction of the extent of interval cytoreduction and outcome in patients with advanced-stage cancer of müllerian origin treated with neoadjuvant chemotherapy
H. Mahdi, K. Maurer, B. Nutter, P.G. Rose. Cleveland Clinic, Cleveland, OH, USA

**Objectives:** To investigate the role of percent reduction in CA-125 after neoadjuvant chemotherapy (NACT) in predicting the extent of the interval cytoreductive surgery (IDS) and outcome in patients with advanced-stage müllerian carcinoma.

**Methods:** Patients who received NACT for advanced-stage müllerian carcinoma in 2000 to 2013 were identified. All patients received platinum-based chemotherapy. Progression free-survival (PFS) was calculated from date of diagnosis to date of progression/recurrence or last follow-up (censored). Overall survival (OS) was calculated from date of diagnosis to date of death or last follow-up (censored). Kaplan–Meier survival curves and Cox regression proportional hazard methods were used. Percent reduction in CA-125 was categorized into two groups: ≥90% (CA ≥90%) and <90% (CA <90%) reduction from prechemotherapy to preoperative CA-125 value.

**Results:** Of the 114 patients identified, 73% (83/114) were CA ≥90% and CA <90% group was associated with enhanced antitumor immune response. Further work is ongoing to extend and validate these findings.

doi:10.1016/j.jygyno.2015.01.102
Conclusions: For patients receiving NAC, a >90% reduction in CA-125 was associated with complete IDS, favorable pathologic treatment effect, and decreased need for bowel resection. A preoperative CA-125 < 20 U/mL suggests improved PFS. These findings are helpful for surgical and treatment planning as well as patient counseling.

doi:10.1016/j.ygyno.2015.01.104

103 — Featured Poster Session
Does time interval between surgery and intraperitoneal chemotherapy administration in advanced ovarian cancer carry a prognostic impact?
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Objectives: Intraperitoneal (IP) chemotherapy in optimally cytoreduced patients with stage III ovarian cancer is associated with a 127.6-month median overall survival. To obtain complete cytoreduction, radical surgical procedures are often required, which may result in prolonged postoperative recovery and delayed initiation of adjuvant chemotherapy. The aim of this study was to evaluate the impact of the time from surgery to IP chemotherapy initiation (TSIC) on progression-free survival (PFS) and overall survival (OS).

Methods: Ancillary review of patients enrolled in Gynecologic Oncology Group (GOG) 172 who received IP chemotherapy was performed. Baseline characteristics were abstracted and patients were stratified according to TSIC. OS and PFS were estimated using the Kaplan–Meier method. The Cox proportional hazards model was used to evaluate independent prognostic factors and to estimate their effect on PFS and OS. A linear model was used to evaluate time from surgery to chemotherapy as a function of baseline variables. TSIC was also analyzed as a categorical variable split near its median.

Results: Data from 200 patients treated with IP chemotherapy was reviewed. The median time from surgery to chemotherapy was 26 days (interquartile range: 19–36 days). Time to chemotherapy was not associated with PFS (P = 0.086) or OS (P = 0.470). In a linear model relating TSIC to other clinicopathologic variables, gross residual disease was significantly associated with shorter TSIC (β = −0.263; 95% CI −0.416–0.109; P < 0.001). Using TSIC as a categorical variable, there was no significant difference in PFS or OS between patients who received the first cycle of IP chemotherapy prior to 25 days of surgery and those who received it after 25 days (PFS: P = 0.224; OS: P = 0.524).

Conclusions: In this ancillary data study of GOG 172, the time from surgery to initiation of IP chemotherapy did not significantly affect PFS or OS. Prolonged recovery from radical surgical procedures required to achieve complete cytoreduction should not preclude the use of IP chemotherapy.

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104 — Featured Poster Session
Improvement in rates of cytoreduction to no residual for stages IIIB–IV ovarian, fallopian tube and primary peritoneal cancer: A change in surgical approach and individualized surgeon feedback
S.J. Lee, R.S. Suidan, M. Quincy, Y. Sonoda, D.A. Levine, M.M. Leitao, G.J. Gardner, E. Jewell, O. Zivanovic, D.S. Chi, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: To examine the rates of cytoreduction at primary surgery for ovarian, tubal, and peritoneal carcinoma.

Methods: All patients with ovarian, tubal, and peritoneal carcinomas at our institution from 1/1/2001 through 12/31/2013 were identified. Only patients who had undergone primary cytoreductive surgery with stage IIIb–IV disease were included. Cases classified as stage IIIC solely by lymph node metastases were excluded. Cytoreductive outcomes were classified as no residual, optimal (residual < 1 cm), suboptimal (residual > 1 cm), and unresectable. Three time periods were selected for comparison corresponding to changes in quality improvement: 2001–2004, incorporation of extensive upper abdominal surgery (group 1); 2005–2010, immediate period after institutional analysis revealed significant survival improvement between no residual and optimal cytoreduction (group 2); and 2011–2013, implementation of anonymous individualized surgeon feedback regarding rates of cytoreduction (group 3). Clinicopathologic data were collected from the medical record. Appropriate statistical tests were used.

Results: In all, 926 patients underwent primary cytoreductive surgery for stage III–IV ovarian, tubal, and peritoneal carcinoma. Median age of the entire cohort was 61 years (range, 19–96 years); body mass index was 25.7 (range, 15.9–58.5) and American Society of Anesthesiologists class 2 (range, 1–4). Primary site of disease was ovary in 695 cases (75%), fallopian tube in 144 cases (16%), and peritoneum in 87 cases (9%). The majority had stage IIIC disease (77%) and serous histology (91%). Over the three time periods, there was a significant improvement in rates of cytoreduction to no residual: 28% (63/224) for group 1, 42% (181/432) for group 2, and 55% (148/270) for group 3 (P < 0.001) (Fig. 1). There were no significant differences in rates of carcinomatosis or upper abdominal disease among the three groups.

Conclusions: The use of extensive upper abdominal surgery and the implementation of an anonymous feedback system of individual surgeon’s cytoreduction rates significantly improved the rate of cytoreduction to no residual.

doi:10.1016/j.ygyno.2015.01.106

105 —Featured Poster Session
Comparison of dose-dense and every-3-week taxane in the neoadjuvant treatment of ovarian, fallopian tube, and primary peritoneal cancer
E.M. Hinchcliff, I. Wilkinson-Ryan, A.A. Gockley, K.M. Esselein, A.R. Hagemann, M. Auer, Y. Tao, D.G. Mutch, K.C. Fuh, N.S. Horowitz, Brigham and Women’s Hospital/Harvard University, Boston, MA, USA,
Objectives: To compare surgical outcomes and survival between women treated with neoadjuvant platinum and weekly (DD) or every 3-week (q3wk) taxane for ovarian, fallopian tube, or primary peritoneal cancer.

Methods: Women treated with neoadjuvant chemotherapy for ovarian, fallopian tube, and primary peritoneal cancer were identified retrospectively at two high-volume academic centers between 1/2011 and 6/2014. Non-parametric Wilcoxon rank sum, chi square, and Fisher exact test were used to compare demographic, surgical, and treatment data. Kaplan–Meier methods and log-rank tests were used to compare overall (OS) and progression-free survival (PFS). Results: Of 217 patients who were included, 61 were treated with DD and 156 with q3wk taxane. There was no difference in median age (65 years; range, 34–85 years), body mass index (26; range, 16–50), disease stage (43% IV, 56% III, 0.5% IIC, and 1.4% unknown), or histology (92% serous). After controlling for number of neoadjuvant cycles, there was a trend toward increased interval cytoreduction to no gross residual disease in patients treated with DD taxane (70% vs. 58%, odds ratio [OR] 1.8, 95% CI 0.92–3.6, P = 0.08). There was no difference in estimated blood loss (250 mL; range, 25–2500 mL), duration of surgery (193 min; range, 74–553 min), or day of discharge (4 days; range, 2–39 days). CA-125 decreased by ≥ 50% in 70% of patients, with no difference between groups. There was a trend toward a higher rate of dose reduction in the DD group compared with the q3wk group (19% vs. 9%, P = 0.07), with no difference in the rate of dose delays (10% DD vs. 7% q3wk, P = 0.65) or use of growth factors (31% DD vs. 41% q3wk, P = 0.78). There was no difference in 2-year PFS (20% vs. 14%, P = 0.53) or OS (73% vs. 89%, P = 0.26) between patients receiving DD or q3wk taxane, respectively.

Conclusions: Women treated with neoadjuvant carboplatin and DD taxane had a trend toward higher rates of no gross residual disease at interval cytoreductive surgery without an increase in toxicity. Despite this, there was no significant improvement in survival, although follow-up time is limited.

doi:10.1016/j.ygyno.2015.01.107
**Post intensive care unit syndrome in women with gynecologic cancer**
C.C. Gunderson1,2, R. Ruskin2, A. Walter2, K. Ding5, 6, K.N. Moore2, 3, 6
1, 2, 6The University of Oklahoma, Oklahoma City, OK, USA, 5Memorial Sloan Kettering Cancer Center, New York, NY, USA

**Objectives:** Eighty percent of intensive care unit (ICU) survivors experience cognitive dysfunction, posttraumatic stress symptoms, depression, and/or prolonged muscle weakness after recovery from acute illness, known as post-ICU syndrome (PICS). PICS has largely been described in septic patients, but baseline psychiatric disorders and need for mechanical ventilation are also likely contributors. Limited data exist regarding PICS in gynecologic oncology patients. This pilot study sought to determine the prevalence of known PICS risk factors among gynecologic oncology patients requiring ICU care.

**Methods:** An institutional review board-approved retrospective review was performed encompassing gynecologic oncology patients requiring ICU care at a single academic center during 1/2008 through 12/2012. Science Analysis Service version 9.3 was used for statistical analyses.

**Results:** A total of 111 patients required ICU care for a median of 3 days (range, 1–30 days). Most were Caucasian (85%), married (59%), and had stage III/IV disease (80%). Three percent did not have a cancer diagnosis and were managed on the gynecologic oncology service because of complexity of care. Psychiatric characteristics included 32% with baseline anxiety or depression, 22% taking a selective serotonin reuptake inhibitor before admission, and 18% taking other psychiatric medications. The most common indication (47%) for ICU admission was planned postoperative management. Thirty-seven percent of patients required mechanical ventilation for a median of 1 day (range, 1–24 days) and 23% required vasopressors while in the ICU. Sixteen percent required physical restraints, 10% had a continuous sitter, 11% required new scheduled psychiatric medications while in the ICU, and 9% were discharged with a newly prescribed antidepressant. Eighteen percent had consultations with psychiatry or social work, and 10% had unprecedented discussion of advanced directives while in the ICU. Seven patients died, and 20% had a non-traditional discharge disposition (e.g., skilled nursing facility, rehabilitation unit).

**Conclusions:** Given the preponderance of psychiatric disorders and mechanical ventilation during ICU care in gynecologic oncology patients, prospective evaluation of risk factors for PICS is warranted. Long-term cognitive disability is known to hasten mortality. Thus, preventive strategies for PICS may prolong survival and increase quality of life in this patient population.

doi:10.1016/j.ygyno.2015.01.109

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**108 — Featured Poster Session**

Post intensive care unit syndrome in women with gynecologic cancer

**Abstracts / Gynecologic Oncology 137 (2015) 2–91**

**109 — Featured Poster Session**

Cost-effectiveness analysis of conventional laparoscopic versus robotically assisted laparoscopic adnexal surgery for benign indications performed by gynecologic oncologists


**Objectives:** To compare the direct costs of conventional laparoscopy (LSC) and robotically assisted laparoscopic surgery (RA-LSC) for benign adnexal indications.

**Methods:** All patients undergoing either LSC or RA-LSC adnexal surgery for benign indications between 1/1/2012 and 6/1/2014 by gynecologic oncologists at our institution were identified. Patient demographics, final pathologic diagnosis, and procedures performed were recorded. The direct costs of all resources used were evaluated (e.g., equipment costs, operating room [OR] facility fees, PACU fees, anesthesia fees, pharmacy fees). Amortized robotic costs (AC) were calculated using the cost of robotic platforms and service contracts divided by institutional surgical volume. This included the acquisition of multiple platforms as well as service contracts amortized over 5 years. Nonamortized costs (NAC) were calculated excluding capital equipment costs. Operative cases performed in combination with non-gynecology services were excluded because this would impact operative time. Median costs were compared using Wilcoxon rank sum. For categorical variables, the Fisher exact test was used.

**Results:** Five hundred forty-seven patients (278 LSC, 269 RA-LSC) were included in this analysis. Age and body mass index did not differ between the study groups. Cost of care for patients undergoing surgery for risk-reducing bilateral salpingo-oophorectomy or removal of adnexal masses, including endometriomas, teratomas, and other benign adnexal cysts, was more expensive when using the robotic platform (Table). Total AC for LSC was $6504.50 (interquartile range [IQR] $5950.75; $7420.75) vs. $9074 (IQR $8446; $10,325) for RA-LSC (P = 0.007). Total NAC for LSC was $6504.50 (IQR $5950.75; $7420.75) vs. $7269 (IQR $6548; $8462) for RA-LSC (P = 0.001). chor. Total NAC for LSC was $6504.50 (IQR $5950.75; $7420.75) vs. $7269 (IQR $6548; $8462) for RA-LSC (P = 0.001). OR facility fees (LSC $1311; RA-LSC $2038, P < 0.001) and OR supplies (LSC $1311; RA-LSC $2038, P < 0.001) were significantly more expensive with the robotic platform.

**Conclusions:** When adnexal surgery is performed for benign indications, LSC is less costly than RA-LSC. Costs associated with operative time and OR equipment are significantly higher when using the robotic-platform in these cases.

**Table**

<table>
<thead>
<tr>
<th>Surgical indication</th>
<th>Median NAC LSC (IQR)</th>
<th>Median NAC RA-LSC (IQR)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk reducing BSO</td>
<td>$6462 ($2414.5)</td>
<td>$7171 ($1806)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Benign adnexal mass</td>
<td>$6504.5 ($1470)</td>
<td>$7269 ($1914)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Abstracts / Gynecologic Oncology 137 (2015) 2–91**

**110 — Featured Poster Session**

Prevalence of cervical cancer screening among women in Nepal: A nationwide population-based survey

A. Ranjit1, S. Gupta2, R. Shrestha3, S. Shrestha4, A.L. Kushner2, B.C. Nwomeh5, R.S. Green2, 6
1Johns Hopkins School of Medicine, Baltimore, MD, USA, 2University of California, San Francisco, San Francisco, CA, USA, 3Nepal Medical College Teaching Hospital, Nepal, 4Nepal Medical College Teaching Hospital, Kathmandu, Nepal, 5Gynecologic Oncology Group Tissue Bank, Biopathology Center, Research Institute at Nationwide Children’s Hospital, Columbus, OH, USA

**Objectives:** World Health Organization data from Nepal documented 10,000 new cases of invasive cervical cancer and between 26,000 and 45,000 women with a precancerous lesion in 2008. The Nepali...
national cervical cancer screening guidelines recommend all women aged 30 to 60 years be screened for cervical cancer. This study evaluated the effectiveness of the screening guideline by documenting the prevalence of cervical cancer screening and awareness.

**Methods:** During a nationwide household survey using a modified Surgeons OverSeas Assessment of Surgical need (SOSAS), female participants were asked if they were aware of what a Papanicolaou (Pap) test was and if they had ever had one. Standard demographics were assessed to look for associations. Included were all women of 21 to 65 years because these are the recommended screening ages from the American Society for Colposcopy and Cervical Pathology.

**Results:** A total of 1350 households were visited and 2695 individuals were interviewed. The response rate was 97%. A total of 1259 (46.72%) female individuals were interviewed. Out of the total females, 829 (65.84%) were between ages 21 and 65 years and eligible for the current calculations. Eighty-seven percent (n = 710) of these women had no knowledge of the Pap test. Of the 829 women aged 21 to 65 years, only 39 (4.7%) had ever had a Pap test done. On univariate analysis with ever having a Pap test as an outcome, literacy (odds ratio [OR]: 3.87; CI: 1.60–9.34; P = 0.003), employment (OR: 2.19; CI: 1.15–4.19; P = 0.017), and rural area of residence (OR: 0.43; CI: 0.22–0.82; P = 0.011) were significantly associated with the outcome. Even after adjusting for other variables, literacy and area of residence were significantly associated with having had a Pap test. Women who were literate were three times more likely (OR: 3.26; CI: 1.25–8.51; P = 0.016) and women in rural areas were 52% less likely (OR: 0.48; CI: 0.24–0.96; P = 0.038) to have had a Pap test.

**Conclusions:** Nepali women rarely practice cervical cancer screening using the nationally recommended Pap test. Compliance with the Nepali national cervical cancer screening guidelines is lowest among the least literate and rural women. To boost screening rates, educational campaigns and rural outreach will be needed.

**doi:** 10.1016/j.ygyno.2015.01.112

**112 — Featured Poster Session**

**Racial differences in reasons for failure to receive ovarian cancer treatment**

M.A. Otoo1, A. Beckmeyer-Borowko1, K.C. Brewer4, C.E. Peterson4, F. Davis1, K. Hoskins1, C.E. Joslin4, A. Buskwo4, D.M. Boruta2, J.O. Schorge1, A. Rauh-Haina2

**Objectives:** Non-Hispanic blacks (NHB) have poorer ovarian cancer survival than non-Hispanic whites (NHW), due in part to differences in treatment. The objective of this analysis was to characterize racial differences in reasons for failure to receive surgery and chemotherapy in women diagnosed with epithelial ovarian cancer in the United States and Puerto Rico between 1998 and 2011.

**Methods:** NHW and NHB cases from National Cancer Database (NCDB) (n = 169,379) were analyzed to assess differences in the receipt of surgery or chemotherapy by stage. Stage was analyzed categorically (stages I, II, III, and IV). Reasons for not receiving surgery and chemotherapy were analyzed using the North American Association of Central Cancer Registries (NAACCR) items (Table 1). Stage-specific tests of proportions were conducted to examine black–white differences for each reason for non-receipt of treatment.

**Results:** Compared to NHW, significantly more NHB failed to undergo surgery (26.5% vs. 16.4%, P < 0.0001) and failed to receive chemotherapy (5.5% vs. 3.6%, P < 0.0001). A greater proportion of NHB than NHW failed to undergo surgery for reasons of non-indication, whereas a greater number of NHB did not receive surgery due to patient or guardian refusal (Stage I: 24% vs. 8%; Stage II: 13% vs. 7%; Stage III: 8% vs. 5%; Stage IV: 6% vs. 4%). For chemotherapy, a greater proportion of NHB failed to receive chemotherapy due to contraindicated patient factors (Stage I: 23% vs. 34%; Stage II: 37% vs. 21%; Stage III: 34% vs. 27%; Stage IV: 34% vs. 32%), while significantly fewer failed to receive chemotherapy due to patient refusal (Stage I: 49% vs. 64%; Stage II: 39% vs. 67%; Stage III: 39% vs. 51%; Stage IV: 46% vs. 52%).

**Conclusions:** Results indicate that in a large sample of women with ovarian cancer, representing about 70% of all diagnoses, there are significant differences in the reasons on why NHB and NHW do not receive surgical and chemotherapeutic treatment. Reasons for racial differences in non-receipt of treatment should be examined further to better understand racial disparities in treatment and survival from ovarian cancer.
### Table 1
Demographics of subjects who did not receive treatment.

<table>
<thead>
<tr>
<th></th>
<th>No surgery, n = 29062</th>
<th>No chemo, n = 49246</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NHW (n = 25471, 16.4%)</td>
<td>NHB (n = 3591, 26.5%)</td>
</tr>
<tr>
<td></td>
<td>NHW (n = 44700, 28.7%)</td>
<td>NHB (n = 4546, 33.5%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median)</td>
<td>73.81 (76)</td>
<td>68.95 (70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66.04 (68)</td>
</tr>
<tr>
<td></td>
<td>63.91 (65)</td>
<td></td>
</tr>
<tr>
<td><strong>Facility type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community cancer program</td>
<td>3656 14.4%</td>
<td>386 10.8%</td>
</tr>
<tr>
<td>Comprehensive community cancer program</td>
<td>15033 59.0%</td>
<td>1617 45.0%</td>
</tr>
<tr>
<td>Academic/research program</td>
<td>5902 23.2%</td>
<td>1444 40.2%</td>
</tr>
<tr>
<td>Other specified types of cancer programs</td>
<td>880 3.5%</td>
<td>144 4.0%</td>
</tr>
<tr>
<td><strong>Facility location</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New England</td>
<td>1822 7.2%</td>
<td>67 1.9%</td>
</tr>
<tr>
<td>Middle Atlantic</td>
<td>4145 16.3%</td>
<td>775 22.4%</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>5066 19.9%</td>
<td>1200 33.4%</td>
</tr>
<tr>
<td>East North Central</td>
<td>4419 17.4%</td>
<td>578 17.4%</td>
</tr>
<tr>
<td>East South Central</td>
<td>1693 6.7%</td>
<td>358 11.4%</td>
</tr>
<tr>
<td>West North Central</td>
<td>1688 6.6%</td>
<td>95 2.7%</td>
</tr>
<tr>
<td>West South Central</td>
<td>1790 7.0%</td>
<td>408 11.4%</td>
</tr>
<tr>
<td>Mountain</td>
<td>1136 4.5%</td>
<td>20 0.6%</td>
</tr>
<tr>
<td>Pacific</td>
<td>3732 14.7%</td>
<td>240 6.7%</td>
</tr>
<tr>
<td><strong>Primary payor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not Insured</td>
<td>647 2.6%</td>
<td>220 6.4%</td>
</tr>
<tr>
<td>Private Insurance</td>
<td>5417 21.9%</td>
<td>775 22.4%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>806 3.3%</td>
<td>359 10.4%</td>
</tr>
<tr>
<td>Medicare</td>
<td>17838 72.2%</td>
<td>2110 60.9%</td>
</tr>
<tr>
<td><strong>Income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$30,000</td>
<td>2794 11.6%</td>
<td>1381 40.2%</td>
</tr>
<tr>
<td>$30,000–$34,999</td>
<td>4638 19.3%</td>
<td>768 22.4%</td>
</tr>
<tr>
<td>$35,000–$45,999</td>
<td>7088 29.5%</td>
<td>702 20.5%</td>
</tr>
<tr>
<td>$46,000+</td>
<td>9530 39.6%</td>
<td>581 16.9%</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;= 12 years</td>
<td>3269 13.6%</td>
<td>1494 43.5%</td>
</tr>
<tr>
<td>13–18 years</td>
<td>5417 21.9%</td>
<td>775 22.4%</td>
</tr>
<tr>
<td>19–25 years</td>
<td>6271 26.1%</td>
<td>442 12.9%</td>
</tr>
<tr>
<td>&gt;25 years</td>
<td>8891 37.0%</td>
<td>380 11.1%</td>
</tr>
<tr>
<td><strong>Year of diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008–2012</td>
<td>7980 31.3%</td>
<td>1239 34.5%</td>
</tr>
<tr>
<td>1998–2002</td>
<td>8632 33.9%</td>
<td>1137 31.7%</td>
</tr>
<tr>
<td>2003–2007</td>
<td>8859 34.8%</td>
<td>1215 33.8%</td>
</tr>
<tr>
<td><strong>Charlson–Deyo score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11778 69.9%</td>
<td>1617 65.9%</td>
</tr>
<tr>
<td>1</td>
<td>3469 20.6%</td>
<td>590 24.0%</td>
</tr>
<tr>
<td>2</td>
<td>1592 9.5%</td>
<td>247 10.1%</td>
</tr>
<tr>
<td><strong>Urban/rural</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>22548 94.4%</td>
<td>3342 97.2%</td>
</tr>
<tr>
<td>Rural</td>
<td>1341 5.6%</td>
<td>97 2.8%</td>
</tr>
<tr>
<td><strong>Year of diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008–2012</td>
<td>7980 31.3%</td>
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<td>8632 33.9%</td>
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</tr>
<tr>
<td>2003–2007</td>
<td>8859 34.8%</td>
<td>1215 33.8%</td>
</tr>
<tr>
<td><strong>Reason for no treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not part of planned first course treatment</td>
<td>20537 80.6%</td>
<td>2790 77.7%</td>
</tr>
<tr>
<td>Contraindicated due to patient factors</td>
<td>2487 9.8%</td>
<td>354 9.9%</td>
</tr>
<tr>
<td>Patient died prior to treatment</td>
<td>291 1.1%</td>
<td>55 1.5%</td>
</tr>
<tr>
<td>Recommended but not performed; no reason recorded</td>
<td>802 3.2%</td>
<td>109 3.6%</td>
</tr>
<tr>
<td>Refused by patient, family or guardian</td>
<td>1354 5.3%</td>
<td>283 7.9%</td>
</tr>
</tbody>
</table>

### Table 2
Differences in the reasons for failure to receive surgery and chemotherapy by race and stage.

<table>
<thead>
<tr>
<th>Reason for no surgery</th>
<th>Overall</th>
<th>Stage 1</th>
<th>Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NHW</td>
<td>NHB</td>
<td>NHW</td>
</tr>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td>P-value</td>
<td>P-value</td>
</tr>
<tr>
<td><strong>Reason for no surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not part of planned first course treatment</td>
<td>16632(81.8%)</td>
<td>2311(79.2%)</td>
<td>16048(81.1%)</td>
</tr>
<tr>
<td>Contraindicated due to patient factors</td>
<td>1973(9.7%)</td>
<td>282(9.7%)</td>
<td>1950(9.7%)</td>
</tr>
<tr>
<td>Patient died prior to surgery</td>
<td>221(1.1%)</td>
<td>42(1.4%)</td>
<td>217(1.1%)</td>
</tr>
<tr>
<td>Recommended but not performed; no reason recorded</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refused by patient, family or guardian</td>
<td>1354(5.3%)</td>
<td>53(1.9%)</td>
<td>1301(5.4%)</td>
</tr>
</tbody>
</table>
The benefits of timely palliative care referral
J.E. Stine, K.M. Doll, S.R. Pierce, S.A. Sullivan, P.A. Gehrig, L. Hanson, K.H. Kim. University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Objectives: To determine the differences in outcomes between patients who have had timely (>60 days from death) vs. late palliative care consultation.

Methods: Using data from a comprehensive hospital palliative care (PC) registry, we conducted a retrospective analysis of all gynecologic oncology patients who received inpatient PC consultation from 2009 to 2013. Clinical data included disease site and stage, reason for PC consultation, hospice choice, number of invasive procedures performed, and subsequent emergency department visits and admissions. Demographic data included age, race, and dates of death, which were recovered from the Social Security Death Index.

Results: A total of 202 patients were identified who received PC. The majority were Caucasian (131/202; 65%) or African American (58/202; 29%). Cancer types included 79 (39%) patients with uterine, 73 (36%) with ovarian, 40 (20%) with cervical, and 10 (5%) with vulvar or vaginal cancers. The most common reasons for consultation to PC were pain control 90/202 (45%) and discussion of goals of care 63/202 (31%). The reason for PC was significantly associated with likelihood of hospice enrollment: goals of care (47/63; 75%), uncontrolled pain (32/90; 36%), and nausea (3/14; 21%) (P < 0.0001). Timely PC consult (>60 days from death) resulted in significantly greater time spent on hospice 118 vs. 19 days (P < 0.0001) (Table). Hospice enrollment was subsequently associated with decreased emergency room visits: 0/91 (0%) vs. 37/103 (36%) (P < 0.0001); hospital readmissions: 8/80 (10%) vs. 87/122 (71%) (P < 0.0001); and invasive procedures: 51/94 (54%) vs. 49/83 (78%) (P = 0.030).

Table 2 (continued)

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHW</td>
<td>NHB</td>
</tr>
<tr>
<td>Overall</td>
<td>113</td>
</tr>
<tr>
<td>Recommended but not performed; no reason recorded</td>
<td>581 (2.9)</td>
</tr>
<tr>
<td>Refused by patient, family or guardian</td>
<td>930 (4.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reason for no chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not part of planned first course treatment</td>
</tr>
<tr>
<td>Contraindicated due to patient factors</td>
</tr>
<tr>
<td>Patient died prior to chemotherapy</td>
</tr>
<tr>
<td>Recommended but not performed; no reason recorded</td>
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<tr>
<td>Refused by patient, family or guardian</td>
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<table>
<thead>
<tr>
<th>Stage 3</th>
<th>Stage 4</th>
<th>Stage missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHW</td>
<td>NHB</td>
<td>P-value</td>
</tr>
<tr>
<td>Overall</td>
<td>113</td>
<td>27</td>
</tr>
<tr>
<td>Recommended but not performed; no reason recorded</td>
<td>581 (2.9)</td>
<td>80 (2.7)</td>
</tr>
<tr>
<td>Refused by patient, family or guardian</td>
<td>930 (4.6)</td>
<td>202 (6.9)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Reason for no surgery</th>
</tr>
</thead>
<tbody>
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doi:10.1016/j.ygyno.2015.01.114
Conclusions: Timely consultation to palliative care resulted in patients spending more time under hospice care. Hospice patients experienced fewer emergency department visits, hospital admissions, and invasive procedures. These data should encourage oncologists to initiate early PC consultation to optimize outcomes.

doi:10.1016/j.ygyno.2015.01.115

114 — Featured Poster Session
Long-term outcomes in BRCA1/2 carriers who undergo risk-reducing salpingo-oophorectomy
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Objectives: There are no standard guidelines for management of long-term health outcomes following risk-reducing salpingo-oophorectomy (RRSO). Our objective was to characterize osteoporosis, cardiovascular, and cancer risks in BRCA carriers following RRSO.

Methods: Women who tested positive for a BRCA1/2 mutation from 1995 to 2012 and underwent RRSO were identified from a large community-based integrated health system in northern California. Exclusion criterion included loss of membership or death within 1 year of testing or prior to ovarian cancer. A retrospective chart review using the electronic medical record was performed to collect data on rates of osteopenia, osteoporosis, cardiovascular disease, and new cancer diagnoses.

Results: A total of 225 women were identified as testing positive for a deleterious BRCA1/2 mutation and having undergone RRSO. They were followed for a median of 53 months from testing. Of these women, 99 (44.0%) had at least one dual-energy x-ray absorptiometry (DXA) scan following testing. The median time from RRSO to a DXA scan diagnosing osteopenia/osteoporosis was 29 months (Q1–Q3 11–52). During follow-up, 32 women (32.3%) had normal DXA results, 55 (55.6%) had osteopenia, and 12 (12.1%) had osteoporosis. Twelve women (5.3%) had an atrumatic fracture after RRSO. Following RRSO, eight women (six BRCA1 and two BRCA2 carriers) developed breast cancer and four women developed high-grade serous cancer (two BRCA1 and two BRCA2 carriers). Sixteen percent of women had a new diagnosis of hyperlipidemia following RRSO compared to 9% of women following BRCA testing who did not undergo RRSO ($P = 0.20$). Median time to diagnosis after surgery was 25 months (Q1–Q3 18–56). One woman was diagnosed with coronary artery disease (CAD) 6 years out from RRSO with no other risk factors for CAD. A myocardial infarction occurred in one patient with multiple cardiac risk factors 4 months after RRSO.

Conclusions: This study describes the health consequences that BRCA carriers face following RRSO, but prospective studies of large cohorts are needed to better characterize long-term outcomes.

doi:10.1016/j.ygyno.2015.01.116

115 — Featured Poster Session
Sexual and marital dysfunction in women with gynecologic cancer: Results of a multi-institutional, cross-sectional trial
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Objectives: Marital and sexual functions remain important components of survivorship in women with gynecologic cancer. To date, only a few small-scale studies have examined these issues across all gynecologic malignancies and minimal data exist regarding marital function. We sought to assess the impact of cancer treatment and marital attachment on sexual function following treatment for women with gynecologic cancer.

Methods: We conducted a multi-institutional, cross-sectional study of women with gynecologic cancer across four geographic areas in the United States. A 181-item survey using validated instruments to assess sexual and marital dysfunction was employed. Sexual dysfunction was measured by change in the Female Sexual Function Index (FSFI) score. A significant decline in sexual function was determined using a Reliable Change Index Statistic (RCIS). Marital relationships were assessed for status, discord, and an Intimate Bond Measure (IBM) measuring partner care and control. T-tests and chi square were used to compare women with sexual dysfunction to those without impairment.

Results: A total of 189 women completed the survey (mean age, 55.5 ± 11.9 years). Cancer diagnoses included uterine/endometrial (39%), ovarian (40%), cervical (11%), and vulvar (10%). Treatments included surgery (93%), chemotherapy (65%), and radiation (30%). Among all women, sexual function declined from 60% to 41% ($P < 0.001$) and sexual activity decreased from 5.9 ± 6.7 to 2.3 ± 4.1 times/month following treatment ($P < 0.001$), regardless of treatment type. Decrease in sexual activity was greater among women with sexual dysfunction (5.6 ± 4.1 vs. 2.7 ± 4.9, $P = 0.003$). Women with sexual dysfunction after treatment were more likely to be <50 years old (47.7% vs. 21.3%, $P = 0.002$), premenopausal (31.8% vs. 16.3%, $P = 0.044$), received chemotherapy (81.8% vs. 52.5%, $P = 0.001$), and to have had marital counseling (18.2% vs. 5.0%, $P = 0.018$). IBM scores, relationship length, and cancer site diagnosis or stage were not associated with sexual dysfunction.

Conclusions: Patients treated for gynecologic cancer are at significant risk for impaired sexual function irrespective of treatment modality. Younger patients and those receiving chemotherapy seem to be at particularly high risk, and prediagnosis relationship status did not appear to mitigate these risks.

doi:10.1016/j.ygyno.2015.01.117
116 — Featured Poster Session
Provision of “primary palliative care” by gynecologic oncologists
Ruskina, M. Rowlanda, K.N. Mooreb, J.L. Walkerb, L.M. Landrumb, M. Matzoa, bThe University of Oklahoma, Stephens Cancer Center, Oklahoma City, OK, USA, bThe University of Oklahoma, Oklahoma City, OK, USA

Objectives: Due to concerns that the demand for palliative care will soon outstrip the supply of providers, Quill and Abernethy have advocated for a care model in which members from every medical field provide “primary palliative care” for their patients while complex cases are referred to individuals with extra training for “specialty palliative care” (N Engl J Med. 2013). The objective of this study was to describe the extent to which gynecologic oncologists (GOs) are providing “primary palliative care,” such as symptom management and advance care planning.

Methods: Patients in our outpatient academic gynecologic oncology clinic complete a symptom assessment questionnaire at each visit. Gynecologic cancer patients who attended the clinic over a 30-day period were included in our cohort. Data related to demographics, disease, and medications were extracted from the medical record. Descriptive statistics and univariate tests were used to characterize symptom management provided by gynecologic oncologists.

Results: A total of 338 patients met inclusion criteria. The prevalence of moderate or severe symptoms (≥4/10) was 28% for pain, 15% for sadness, 43% for fatigue, and 23% for sleep problems. Patients with moderate-to-severe symptomatology with a medication prescribed for that indication included 82% for pain, 35% for depression, and 20% for insomnia. Only one patient out of 140 with fatigue ≥4/10 had a medication prescribed. GOs prescribed 63% of these pain medications, 11% of those for depression, and 27% of those for insomnia, while primary care providers prescribing the majority of the remaining medications. GOs were more likely to prescribe medications for pain than for depression or insomnia (P < 0.001). With respect to advance care planning, 4% of patients had advance directives and 24% had named a health care proxy. The rate of referral to the outpatient supportive care clinic was 8%.

Conclusions: Gynecologic cancer patients have a high symptom burden and advance care planning needs that are inadequately managed through current practices. While management of pain and emesis have been emphasized in oncologic care and have improved, other conditions such as depression, insomnia, and fatigue remain undertreated. Gynecologic oncologists and palliative care providers need to strategize to collectively meet the needs of our patients.

doi:10.1016/j.ygyno.2015.01.119

118 — Featured Poster Session
Referral of obese endometrial cancer survivors to a bariatric specialist: Weight loss attempts initiated and barriers to change
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Objectives: Due to concerns that the demand for palliative care will soon outstrip the supply of providers, Quill and Abernethy have advocated for a care model in which members from every medical field provide “primary palliative care” for their patients while complex cases are referred to individuals with extra training for “specialty palliative care” (N Engl J Med. 2013). The objective of this study was to describe the extent to which gynecologic oncologists (GOs) are providing “primary palliative care,” such as symptom management and advance care planning.

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doi:10.1016/j.ygyno.2015.01.119

117 — Featured Poster Session
Postoperative morbidity and mortality following modern pelvic exenteration
E.L. Barber, J.F. Boggs, P.A. Gehrig, J.T. Soper, N.L. Neubauer, aUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, bNorthwestern University Feinberg School of Medicine, Chicago, IL, USA

Objectives: Total pelvic exenteration (TPE) is a relatively uncommon procedure that can be associated with significant morbidity. Given advances in surgical techniques and postoperative care, morbidity may have decreased over time. We examined 30-day morbidity and mortality from TPE for gynecologic malignancy.

Methods: Women who underwent TPE for a gynecologic malignancy from 2006 to 2012 were abstracted from the American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP) database. Preoperative variables for patients with and without postoperative complications were compared. Pearson’s chi square test and Student’s t-test were used for analysis.

Results: We identified 168 patients whose median age was 58 years (range, 26–89 years) and of whom 11.3% were non-white race. Median length of stay was 11.5 days (range, 4–97 days) and median operative time was 391 min (range, 155–968 min). The rate of postoperative complication was 75.6%, with 36.3% experiencing major and 66.7% minor complications. The mortality rate was 1.2%. Major complications were myocardial infarction (1.8%), thromboembolism (5.4%), sepsis (14.3%), renal failure (1.8%), and deep surgical site infection (14.9%). Minor complications were urinary tract infection (16.1%), blood transfusion (59.5%), and superficial wound infection (11.3%). Additional reconstructive procedures performed included myocutaneous flap (33.8%), neovagina (5.4%), and urinary conduit (23.0%). Reconstructive procedures were associated with an increased risk of minor (82.9% vs. 59.0%, P = 0.02) and a trend toward major complications (48.6% vs. 28.2%, P = 0.07). Preoperative albumin < 3.5 g/dL (P = 0.001), hematocrit < 30% (P = 0.05), American Society of Anesthesiologists (ASA) score > 3 (P = 0.03), and longer operative time (P < 0.001) were associated with complications. Non-white race was only associated with major complication (P = 0.03). Age, diabetes, smoking, and hypertension were not associated with complication.

Conclusions: TPE remains associated with significant postoperative morbidity, but mortality has decreased over time. Operative time and, to a lesser extent, reconstructive procedures were associated with increased morbidity. Preoperative albumin and hematocrit were independently associated with complication and preoperative correction may improve morbidity.

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therapy ($P = 0.0836$) rather than later in their care. Subsequent weights were available for 70 women at a mean of 95.6 (95% CI 83.9–107.1) days. SGWL, seeing a bariatric expert, and having had bariatric surgery were associated with mean weight losses of 4.65 lb (95% CI 1.9–7.4), 3.76 lb (95% CI 0.8–7.44), and 13.3 lb (95% CI 5.33–21.34).

**Conclusions:** Offering a BR is highly acceptable, and results in most women initiating WLA and even attempting SGWL attempts suggest effectiveness. Barriers to follow up with a BR can be difficult to change and include postoperative events as well as geographic and socioeconomic factors. Discussing weight loss early in the course of cancer care may maximize WLA.

doi:10.1016/j.ygyno.2015.01.120

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**Featured Poster Session**

**Measurement and validation of frailty as a predictor of outcomes in women undergoing major gynecologic surgery**

E. George, W.M. Burke, J.Y. Hou, A.I. Tergas, E. Prendergast, L. Chen, A. Neugut, C. Ananth, D. Hershman, J.D. Wright, Columbia University, New York, NY, USA, NYP/Columbia University Medical Center, New York, NY, USA, Columbia University College of Physicians and Surgeons, New York, NY, USA

**Objectives:** Frailty is the loss of physical or mental reserve that impairs function, often in the absence of a defined comorbidity. While frailty likely influences operative outcomes, a reproducible measurement of frailty has not been described for gynecologic surgery. We performed a population-based analysis to determine if a modified frailty index (mFI) correlates with morbidity and mortality in patients undergoing hysterectomy.

**Methods:** Patients who underwent hysterectomy from 2008 to 2012 and who were recorded in the National Surgical Quality Improvement Program (NSQIP) were analyzed. An mFI was calculated using 11 variables of the Canadian Study of Health and Aging Frailty Index that were matched to variables in NSQIP. Multivariable regression models were developed to assess the association between the mFI and wound infection, severe complications, and mortality. Model fit statistics (c-statistics) were used to evaluate the ability of the mFI to distinguish outcomes.

**Results:** A total of 66,105 patients were identified. Wound complications increased from 2.4% in patients with an mFI of 0 to 4.8% in those with an mFI of >0.5 ($P < 0.0001$). Similarly, severe complications increased from 1.0% to 7.3% ($P < 0.0001$), overall complications rose from 3.7% to 14.5% ($P < 0.0001$), and mortality increased from 0.06% to 3.2% ($P < 0.0001$) for patients with an mFI of 0 compared to those with an mFI of >0.5. Versus chance, c-statistics suggested that the mFI increases the ability to detect wound complications by 11.4%, severe complications by 22.0%, and overall complications by 11.0%. The predictive ability of the mFI was greater than that of either age alone or functional status based on the ability to perform activities of daily living.

**Conclusions:** The mFI is easily reproducible from routinely collected clinical data and is predictive of outcomes in patients undergoing gynecologic surgery. Frailty may be useful in the preoperative risk assessment of women undergoing gynecologic surgery.

doi:10.1016/j.ygyno.2015.01.121

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**Featured Poster Session**

**Sarcopenia as a predictor of surgical morbidity in advanced ovarian cancer patients**

A. Kumar, M. Moynagh, B.A. Cliby, M. McGree, P. Young, J.N. Bakkum-Gamez, C.L. Langstraat, S.C. Dowdy, A. Jatoi, A. Mariani

**Objectives:** Nutritional and functional status are often compromised in women with newly diagnosed advanced epithelial ovarian cancer (EOC), which can lead to increased perioperative morbidity and oncologic mortality. Sarcopenia is the wasting of muscle mass and has been associated with adverse outcomes in a variety of malignancies. To help develop preoperative models for optimal triage of EOC patients, we investigated the role of sarcopenia in predicting surgical morbidity and overall survival in advanced EOC.

**Methods:** We reviewed medical records of women with stages III–IV EOC who underwent primary debulking surgery (PDS) with curative intent between 1/1/2006 and 12/31/2011. Sarcopenia was assessed by measurement of the total skeletal muscle area (SMA) at the level of L3 on preoperative axial computed tomography (CT) scans. Postoperative complications within 30 days were graded according to the modified 4-point Accordion classification.

**Results:** Of the 387 women with stages III–IV, 199 women had evaluable CT scans. Mean SMA was 104.5 cm$^2$ (SD: 18.0 cm$^2$). Patients ≥70 years old had lower SMA than patients <70 years old (94.8 cm$^2$ vs. 109.0 cm$^2$, $P < 0.001$). In univariate analysis, grade 3–4 complications were associated with older age ($P = 0.049$), preoperative albumin <3 g/dL ($P = 0.045$), and decreasing SMA ($P = 0.015$). In a multivariate model, considering sarcopenia and after adjusting for albumin, SMA still increased the risk of grade 3–4 complications by 23% per 10 cm$^2$ decrease in SMA ($P = 0.058$). Overall survival was inversely associated with traditional variables, including age ($P < 0.001$), stage ($P = 0.014$), and residual disease ($P = 0.002$) but not SMA.

**Conclusions:** Sarcopenia, as measured by SMA on preoperative CT scan, may be an important and objectively measurable predictor of postoperative morbidity and may guide treatment counseling in women with newly diagnosed advanced-stage EOC.

doi:10.1016/j.ygyno.2015.01.122

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**Featured Poster Session**

**National representation of surgical outcomes and complications of pelvic exenterations for gynecologic cancers in the 21st century**

N.A. Latif, K. Williams, E.M. Ko, University of Pennsylvania, Philadelphia, PA, USA

**Objectives:** To evaluate surgical outcomes and complication rates of pelvic exenterations (PEX) performed for gynecologic cancers in current clinical practice in the United States.

**Methods:** Using the prospectively collected National Surgical Quality Improvement Program (NSQIP) database, we reviewed all cases of PEX performed for gynecologic malignancy between 2007 and 2012. Demographics, comorbidities, functional status, body mass index (BMI), preoperative laboratory values, type of surgeons involved (gynecologic oncologist, urologist, colorectal, plastic), operative time (hours), and outcome data within 30 days of surgery were collected. Descriptive, univariate, and bivariate tests and multivariate regression models were used. Institutional review board exemption was obtained.

**Results:** We identified 112 PEX procedures. The mean age of patients was 57 years (range, 26–83 years) and 82% were Caucasian. More than half were obese (38%) or overweight (25%). The indications for PEX included: cervical cancer (23%), ovarian cancer (12.5%), vulvar and vaginal cancer (12.2%), and uterine cancer (5%). Mean operative time was 7.5 h (range, 1.6–17.5 h). Gynecologic oncologists performed 63% (39/62) of the major concomitant urologic, colorectal, and plastic procedures. Median hospital length of stay was 14 days (range, 4–91 days). Operative time was significantly associated with...
prolonged stay, adjusting for age, BMI, American Society of Anesthesiologists class, serum albumin, and reoperation (odds ratio: 1.4, 95% CI: 1.2–1.7, \( p < 0.001 \)). Major complications occurred in 24% of cases and included unplanned return to the operating room (16%), abscess (6%), septic shock (5%), wound dehiscence (4%), deep venous thrombosis (3%), pulmonary embolism (3%), and 30-day mortality (2%). Seventy-one percent of patients were discharged home and 29% were discharged to skilled nursing facilities (SNFs). The readmission rate was 8%.

Conclusions: In this contemporary review of surgical outcomes for pelvic exenterations in the United States, the 30-day mortality was 2%, major complication rate was 25%, and prolonged hospitalization rate was 40%, similar to those reported in the international literature. Future efforts are needed to identify those at higher risk of surgical complications, prolonged hospital stay, need for SNF, and mechanisms to optimize their multidisciplinary care.

doi:10.1016/j.ygyno.2015.01.123

122 — Featured Poster Session
Prolonged steep Trendelenburg positioning increases the risk of postoperative morbidity in patients undergoing robotic surgery for presumed gynecologic malignancy

Objectives: Although robotic surgery has advanced minimally invasive therapeutic options for women with gynecologic cancers, its use often requires steep Trendelenburg positioning (≥30°). The aim of this study was to determine the risk of postoperative complications in gynecologic oncology patients undergoing robotic surgery in prolonged steep Trendelenburg position (PSTP).

Methods: A review of all gynecologic oncology robotic surgeries from a single academic institution between October 2009 and July 2014 was conducted. Time in PSTP was extrapolated from the total console time. PSTP was defined as ≥180 min. Demographics, intraoperative course, and postoperative complications were analyzed. T-tests, chi square, and Fischer’s exact tests were used to compare outcomes in PSTP and non-PSTP cases.

Results: A total of 305 cases were reviewed; 20 were excluded for conversion to laparotomy (n = 285). Mean age was 54.7 ± 12.4 years and body mass index was 31.6 ± 8.4. Hysterectomy ± bilateral salpingo-oophorectomy was performed in 232 (81.4%) patients and staging lymphadenectomy in 105 (36.8%). Malignancy was confirmed in 180 cases (63.2%), 92.2% of which were endometrial cancer. Postoperative complication rates were similar for those with and without malignancy. Mean console time was 197.5 min (range, 76–381 min). The majority of prolonged procedures were performed in 2009–2010. There were 49 cases of PSTP and 236 non-PSTP. The most common PSTP complications were urinary retention (20.4%) and urinary tract infection (10.2%). Major PSTP complications included subcutaneous emphysema (6.1%) and pulmonary edema (2%). Overall rates for any complication, major and minor, were significantly higher for PSTP patients (57.1% vs. 38.3%, \( p = 0.049 \)). PSTP patients also had higher rates of subcutaneous emphysema (6.1% vs. 0.4%, \( p = 0.002 \)) and non-lymphadenectomy-related peripheral nerve injury (10.2% vs. 0.8%, \( P < 0.001 \)). Lymphadenectomy was performed in 38 (77.6%) PSTP patients. All nerve injuries resolved spontaneously and primarily involved the lateral femoral cutaneous and brachial plexus nerves.

Conclusions: This study suggests that PSTP is more likely to occur at the beginning of a robotics program and is associated with a higher incidence of postoperative morbidity. Measures should be taken to reduce robotic surgery operative times whenever feasible.

doi:10.1016/j.ygyno.2015.01.124

123 — Featured Poster Session
Incidental uterine malignancy following laparoscopic supracervical hysterectomy in a national cohort
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Objectives: To determine the rate of incidental uterine malignancy after laparoscopic supracervical hysterectomy procedures (LASH) and any associated risk factors within the National Surgical Quality Improvement Program database.

Methods: We evaluated all LASH procedures using the prospectively collected National Surgical Quality Improvement Program (NSQIP) database from 2007 to 2012. We reviewed International Classification of Diseases 9, Current Procedural Terminology codes, and any associated or concurrent procedures to identify patients undergoing LASH for nonmalignant conditions. Patient demographics, comorbidities, 30-day postoperative outcomes and complications, and postoperative diagnosis were abstracted. Data were analyzed using descriptive tests and univariate and multivariate logistic regression.

Results: We identified 4508 women who underwent LASH. The most common indication for surgery was leiomyoma (34%). Mean age was 46 years (range, 20–90 years), 73% of patients identified themselves as Caucasian. 42% of patients were obese, and 30% of patients were overweight. Postoperatively, 36 patients (0.79%) were found to have incidental uterine malignancy. Mean age (46 vs. 61 years, \( P < 0.001 \)) and body mass index (BMI) (30 vs. 35, \( P < 0.001 \)) were higher in patients who were diagnosed with incidental uterine cancer postoperatively. Multivariate logistic regression revealed age (odds ratio [OR] = 1.12, 95% CI 1.00–1.15, \( P < 0.001 \)), BMI (OR = 1.7, 95% CI 1.03–1.11, \( P = 0.001 \)), and American Society of Anesthesiologists (ASA) class (OR = 2.79, 95% CI 1.72–4.52, \( P < 0.001 \)) were associated with increased risk of incidental uterine cancer diagnosis whereas race (OR = 1.05, 95% CI 0.83–1.32, \( P = 0.66 \)) and diabetic status (OR = 0.62, 95% CI 0.26–1.46, \( P = 0.27 \)) were not.

Conclusions: The rate of incidental uterine malignancy was 0.79% in this national cohort. Increasing age, BMI, and ASA class should be taken in consideration in assessing the risk of incidental uterine cancer in patients undergoing laparoscopic supracervical hysterectomy.

doi:10.1016/j.ygyno.2015.01.125

124 — Featured Poster Session
The process of transforming pelvic exenteration to a “true” minimally invasive procedure utilizing the robotic platform
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Objectives: The purpose of this case series was to describe our process and experience with converting all candidates for pelvic exenteration to a minimally invasive approach using the robotic platform. The series is now sufficiently mature to report on outcomes.

Methods: Between 31 May 2007 and 15 May 2014 in two institutions, we took 19 consecutive patients to the operating room with the intention of performing a robotic-assisted exenteration.

Results: We offered all patients a robotic-assisted attempt at pelvic exenteration. The mean age was 64.3 years (range, 48–82 years) and mean body mass index was 30.5 (range, 17.5 to 52.1). Sixteen of 19 patients had received prior pelvic radiation. Twelve of 19 patients had successful completion of the procedure with the robotic platform. The last four patients had successful placement of an intracorporeal ileal conduit for urinary tract diversion. Urinary tract morbidity was the most common adverse effect, including three
upper tract infections and one ureteral leak due to devascularization necrosis. Three patients experienced prolonged adynamic ileus and one patient had a mechanical small bowel obstruction. No patients experienced venous thromboembolism and there were no significant wound infections or perioperative deaths. In three patients, we successfully decreased the “radicality” of the procedure specifically because of the precision and dexterity of the robotic technique.

Conclusions: We have shown the feasibility of pelvic exenteration using robotic technology. Gynecologic oncologists who perform the procedure in an open manner must learn to “translate” the maneuvers to a closed space for a minimally invasive surgical approach. It is important for us to share our experience to help other surgeons learn how to potentially decrease the surgical morbidity of this procedure.

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125 — Featured Poster Session
National Age Standardized Rate (ASR) of ovarian cancer (OC) correlates with Human Development Index (HDI): Analysis of data from 165 countries

Objectives: To describe how HDI relates to national OC incidence, accounting for reproductive and lifestyle factors associated with OC.

Methods: The United Nations states that HDI is “a summary measure of average achievement in key dimensions of human development: a long and healthy life, being knowledgeable and a decent standard of living. The HDI is the geometric mean of normalized indices for each of the three dimensions.” Although HDI is primarily a socioeconomic parameter, it has been associated with cancer incidence and mortality in certain geographic regions. The ASR for OC in 2012, fertility rate in women (FR), fraction of citizens with “insufficient activity,” obesity rate in women, contraceptive prevalence, and proportion of citizens with unmet family planning needs were obtained for 183 countries from the World Health Organization database. The HDI value for 2012 was obtained from the United Nations Development Programme. All variables were available for 165 countries/territories, which comprised the study group for analysis. The countries/territories with incomplete data were omitted from analysis. Pearson’s coefficients (PCC) were determined for univariate correlations. Linear regression was performed using ASR of OC as the dependent variable and factors significant in univariate analysis as the independent variables. Significance was defined as \( P < 0.05 \).

Results: In univariate analysis, ASR of OC was significantly correlated to HDI (PCC = 0.50), FR (PCC = −0.25), contraceptive prevalence (PCC = 0.286), and rate of insufficient activity (PCC = 0.351). Linear regression demonstrates that HDI and total fertility rate among women were the only factors studied that were significantly associated with OC rate.

Conclusions: The direct association of HDI and the inverse association of FR with OC incidence suggests that an increasing risk of OC may be expected to accompany a nation’s progress in economy, education, and longevity, but risk may be modified by reproductive factors. Understanding the pathophysiology of this observation may help project national health care needs and guide public health and cancer prevention and control efforts.

doi:10.1016/j.ygyno.2015.01.127

126 — Featured Poster Session
Birthplace does not modify the already elevated risk of ovarian clear cell carcinoma (CC) among Asian/Pacific Islander (API) women in the United States
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Objectives: Complex sociologic and environmental factors are known to affect cancer risks among minority groups. This study sought to determine if API women in the United States (US) are at elevated risk of ovarian CC and to investigate if place of birth modifies this risk.

Methods: The 18 registries of the Surveillance, Epidemiology, and End Results (SEER) database were queried to identify all women registered with epithelial ovarian cancer (EOC) from 1973 to 2011. Relative risk (RR) of CC to non-CC was compared between API and women of other races. The odds ratio (OR) of CC in foreign-born API compared to US-born API was calculated.

Results: Of 106,518 women with EOC in the dataset, 6253 (5.9%) were API, and 692 (11%) API had CC and 5561 (88.9%) had non-CC. Among 100,265 non-API women, 4277 (4.3%) had CC. The RR of CC among API was 2.6 (95% CI = 2.4 to 2.8). Of the 4606 API with place of birth recorded, 1365 (29.6%) were US-born and 3241 (70.4%) were foreign-born. The odds of a foreign-born API with CC were not significantly different compared to a US-born API (OR 1.2, 95% CI = 0.9 to 1.4). The study has >85% power (\( \beta = 0.15 \)) to detect a 50% difference in odds with two sided \( \alpha = 0.05 \).

Conclusions: In the US, API women have an elevated risk of CC. Place of birth does not appear to significantly modify the association, suggesting that the increased risk of CC in API women may not be associated with acculturation or environmental exposure. These findings differ from the epidemiology of gastric cancer among API populations, whose risk is inversely related to time in the US. Future research exploring the complex relationships between ethnicity and risk of malignancy will be important as we make progress in international cancer prevention and control initiatives.

doi:10.1016/j.ygyno.2015.01.128

127 — Featured Poster Session
International study of primary mucinous ovarian carcinomas managed at tertiary medical centers
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Objectives: The objective of this study was to combine demographic and follow-up data on primary mucinous ovarian carcinoma (PMOC) as part of an international collaboration to study rare tumors.

Methods: We identified all cases of PMOC using institutional datasets of patients treated within our United States institution (US) from 1994 to 2013 and at a collaborative institution in Denmark (DK) spanning 2005 to 2013. We excluded cases with pure borderline pathology. Clinicopathologic data were abstracted from medical records and institutional datasets were combined for analysis. Appropriate statistical tests were performed using the Statistical Package for the Social Sciences.

Results: We identified 135 cases of PMOC, of which 42 (31%) were US and 93 (69%) were DK cases. Forty-two (31%) of 135 cases underwent secondary pathology review at our US institution. Median
age for the combined cohorts was 58 years (range, 21–90 years), and median body mass index was 24 (range, 17–42). Surgical staging procedures were performed, including oophorectomy in 135/135 (100%) cases, hysterectomy in 120/134 (89%), omentectomy in 114/135 (84%), appendectomy in 108/135 (80%), and lymph node evaluation in 61/134 (45%). Disease characteristics were as follows: stage I, 102/134 (76%) cases; unilateral tumors, 116/135 (86%); and grade I/II disease, 98/104 (94%). Fifty-seven (42%) of 135 cases received some form of adjuvant therapy. Of the 61 cases that underwent lymph node evaluation, 3 (4.9%) had lymph node metastasis on final pathology. Three-year overall survival (OS) was 75% (±4.1%) in the total cohort. Three-year OS was 91% (±3.0%) for stage I/II cases compared with 19% (±7.7%) for stage III/IV cases (P < 0.001). Three-year OS was 90% (±6.3%) for microinvasive tumors compared with 71% (±4.6%) for invasive tumors (P = 0.02).

Conclusions: In our combined international cohort of patients, PMOC presented in mid-life as an early-stage unilateral mass with an infrequent incidence of lymph node metastasis. Overall survival at 3 years was affected by stage of disease and presence of invasive tumor. Multi-institutional, international collaboration is critical to better study rare tumors.

doi:10.1016/j.ygyno.2015.01.129

129 — Featured Poster Session
Revisiting the methods to calculate carboplatin dose in women with gynecologic cancers
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Objectives: Determining the best estimate of renal function is important when dosing renally eliminated chemotherapeutic agents such as carboplatin, a drug commonly used in the treatment of gynecologic malignancies. The Cockcroft-Gault (CG), Jelliffe (J), and Wright (W) formulas are frequently used to estimate creatinine clearance (CrCl) in lieu of 24-hour urine collection to calculate dose. However, it is not clear whether these formulas are predictive of renal function in women with cancer. Recent publications suggest that present formulas underestimate the carboplatin dose in obese women with gynecologic cancers. Our aim was to determine the level of concordance of calculated CrCl using the most common formulas with measured CrCl. A secondary objective was to evaluate an association between cumulative bone marrow toxicities and method used to calculate CrCl.

Methods: A total of 336 patients were included in this retrospective study, of which 166 had a 24-hour urine collection to measure CrCl before the first cycle of carboplatin chemotherapy. The measured CrCl was compared to the estimated CrCl using the three formulas, and the concordance correlation coefficient (CCC), a reproducibility index, was used to evaluate the degree of precision and accuracy of each formula as well as the strength of agreement. A chi square test was used to compare toxicity among CrCl.

Results: The CCC for the W formula was the highest at 0.6392 compared to CG and J, which were 0.6353 and 0.628, respectively. Strength of agreement for all three formulas was poor. Interestingly, regardless of body mass index (BMI), patients whose carboplatin dose was based on the measured CrCl were more likely to experience grade 3–4 leukopenia (30.1% vs. 20.6%, P = 0.0445) and grade 3 thrombocytopenia (8.4% vs. 2.5%, P = 0.029) compared to calculated CrCl using the CG formula.

Conclusions: Of the three formulas, the Wright formula shows the highest reproducibility, although substantial agreement between estimated and measured CrCl is lacking. Furthermore, given the finding that less toxicity was seen in patients whose doses were based on estimated CrCl, these patients may be receiving a less effective carboplatin dose regardless of BMI. New formulas to estimate CrCl need to be designed that are specific to women.

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130 — Featured Poster Session
Evaluation of the NSQIP surgical risk calculator to predict complications in gynecologic oncology patients undergoing laparotomy
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Objectives: To evaluate the ability of the National Surgical Quality Improvement Program (NSQIP) surgical risk calculator to accurately predict postoperative complications in gynecologic oncology patients undergoing laparotomy.

Conclusions: In recurrent ovarian cancer patients treated with bevacizumab, those who had either SD or PR had comparable survival outcomes. Delay of progression through disease stabilization after biologic treatment warrants consideration as a surrogate endpoint for clinical efficacy.
Methods: A retrospective chart review of all patients who underwent laparotomy on the gynecologic oncology service at a single academic hospital from January 2011 to December 2013 was conducted. Baseline demographic and clinical characteristics included in the NSQIP surgical risk calculator were summarized and entered into the NSQIP surgical risk calculator (http://riskcalculator.facs.org). The risk of any complication, serious complication, death, and other specific complications (urinary tract infection, venous thromboembolism, cardiac, renal, pneumonia, surgical site infection [SSI], return to operating room, discharge to a rehabilitation facility) was correlated with actual patient outcomes using logistic regression. The c-statistic and Brier score were used to calculate the prediction capability of the risk calculator for each complication.

Results: Of the 556 patients included, the majority were <65 years old (70.7%), independent (91.2%), American Society of Anesthesiologists classes 1–2 (66.2%), had disseminated cancer (56.1%), and were overweight or obese (72.3%). Higher calculated risk scores were associated with an increased risk of the actual complication occurring for all events (P < 0.05). The calculator performed best for predicting death (c-statistic = 0.899, Brier = 0.007) and cardiac complications (c-statistic = 0.895, Brier = 0.009). However, the calculator did not accurately predict most complications, including overall complication risk (c-statistic = 0.642, Brier = 0.210), serious complication risk (c-statistic = 0.665, Brier = 0.145), and SSI risk (c-statistic = 0.632, Brier = 0.124). (See Table 1.) Overall, the calculator performed worse for the gynecologic oncology population than reported in the general surgery population (Bilimoria. J Am Coll Surg. 2013).

Conclusions: The NSQIP surgical risk calculator adequately predicts postoperative death and cardiac complications but does not appear to be a reliable predictor of most surgical risks for the gynecologic oncology population. A better prediction model is needed for this patient population.

Table 1

<table>
<thead>
<tr>
<th>Complication</th>
<th>Events, n (%)</th>
<th>Odds Ratio (95% CI), p-value</th>
<th>c-statistic</th>
<th>Brier score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4 (0.7)</td>
<td>1.16 (1.03–1.28), p = 0.004</td>
<td>0.899</td>
<td>0.007</td>
</tr>
<tr>
<td>Any serious comp</td>
<td>108 (19.5)</td>
<td>1.11 (1.07–1.15), p &lt; 0.0001</td>
<td>0.665</td>
<td>0.145</td>
</tr>
<tr>
<td>Any complication</td>
<td>185 (33.4)</td>
<td>1.06 (1.04–1.08), p &lt; 0.0001</td>
<td>0.642</td>
<td>0.210</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>19 (3.4)</td>
<td>1.06 (1.03–1.71), p &gt; 0.0001</td>
<td>0.587</td>
<td>0.033</td>
</tr>
<tr>
<td>Cardiac</td>
<td>5 (0.9)</td>
<td>1.51 (0.80–2.84), p = 0.204</td>
<td>0.895</td>
<td>0.009</td>
</tr>
<tr>
<td>SSI</td>
<td>84 (15.1)</td>
<td>1.15 (1.07–1.23), p &gt; 0.0001</td>
<td>0.632</td>
<td>0.124</td>
</tr>
<tr>
<td>UTI</td>
<td>43 (7.8)</td>
<td>1.17 (1.09–1.26), p &lt; 0.0001</td>
<td>0.623</td>
<td>0.068</td>
</tr>
<tr>
<td>VTE</td>
<td>11 (2.0)</td>
<td>1.47 (1.08–2.00), p = 0.015</td>
<td>0.695</td>
<td>0.019</td>
</tr>
<tr>
<td>Renal failure</td>
<td>15 (2.7)</td>
<td>1.74 (1.04–2.89), p = 0.034</td>
<td>0.716</td>
<td>0.027</td>
</tr>
</tbody>
</table>

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132 — Featured Poster Session

Therapeutic benefit of lymphadenectomy in low grade epithelial ovarian carcinoma: A national cancer database study

Objectives: Low-grade epithelial ovarian carcinoma (EOC) has a distinct biologic behavior with an indolent growth pattern and relative insensitivity to chemotherapy compared to high-grade EOC. Surgical cytoreduction is the mainstay of treatment, but the therapeutic benefit of lymph node dissection (LND) has not previously been assessed. The aim of this study was to determine the impact of LND on survival in patients with node-negative low-grade EOC.

Methods: Patients with grade 1 EOC of any histologic subtype and clinical stage N0 or pathologic NX or NO were identified from the National Cancer Database from 1998 to 2011. LND was defined as either lymph node sampling or dissection. Patients were divided into those who did and did not undergo LND (LND-Yes and LND-No, respectively). Univariate analysis was performed using Student’s t-test, Pearson’s chi square, and Fisher’s exact tests. The Kaplan–Meier method was used to calculate overall survival (OS) and compared using the log-rank test.

Results: There were 12,732 patients identified with low-grade EOC. When comparing LND-Yes to the LND-NO groups, patients were younger (53 vs. 57 years, P < 0.0001), less often of black race (4.8% vs. 6.7%, P < 0.0001), and had a lower Charlson–Deyo comorbidity score (85% vs. 79% with a score of zero, P < 0.0001). Fewer patients in the LND-Yes group received adjuvant chemotherapy (42.2% vs. 44.7%, P = 0.009). The median OS was not reached in the LND-Yes group and was 135 months for the LND-No group. This difference

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131 — Featured Poster Session

Observed-to-expected ratio for adherence to treatment guidelines as a quality of care indicator for ovarian cancer
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Objectives: To develop an observed-to-expected ratio (O/E) for adherence to National Comprehensive Cancer Network (NCCN) ovarian cancer treatment guidelines as a risk-adjusted hospital measure of quality care correlated with disease-specific survival.

Methods: Consecutive patients with stages I–IV epithelial ovarian cancer were identified from the California Cancer Registry (1/1/96–12/31/06). An O/E for guideline adherence was calculated for each hospital using a fit logistic regression model and distributed into quartiles (Q) stratified by hospital annual case volume: low-O/E (Q1, <5 cases/year); intermediate-O/E (Q2–3, ≥5 cases/year; high-O/E (Q4, ≥5 cases/year). A multivariable logistic regression model was used to characterize the independent effect of hospital O/E on ovarian cancer-specific survival.

Results: Overall, 18,491 patients were treated at 405 hospitals, and 37.3% received guideline-acceptable care. Low-O/E hospitals (n = 285) treated 4661 patients (25.2%) with a mean O/E = 0.77 ± 0.55 and median survival of 38.9 months (95% CI = 36.2–42.0 months). Intermediate-O/E hospitals (n = 85) treated 8715 patients (47.1%) with a mean O/E = 0.87 ± 0.17 and a median survival of 50.5 months (95% CI = 48.4–52.8 months). High-O/E hospitals (n = 35) treated 5115 patients (27.7%) with a mean O/E = 1.34 ± 0.14 and median survival of 53.8 months (95% CI = 50.2–58.2 months). After controlling for other variables, treatment at a high-O/E hospital was associated with an independent and statistically significant improvement in ovarian cancer-specific survival compared to intermediate-O/E (HR = 1.06, 95% CI = 1.01–1.11) and low-O/E (HR = 1.16, 95% CI = 1.10–1.23) hospitals.

Conclusions: Calculation of a hospital-specific O/E for NCCN treatment guideline adherence, combined with a minimum case volume criterion, as a measure of ovarian cancer quality of care is feasible and is an independent predictor of survival.

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was significant on multivariable analysis controlling for age, race, Charlson-Deyo score, and receipt of adjuvant chemotherapy. When stratified by stage, the median OS for LND-Yes and LND-No was not reached for stage I, was 173.5 vs. 142.2 months for stage II, was 129.1 vs. 54.2 months for stage III, and was 70 vs. 29.9 months for stage IV. The improvement in median OS was significant for each stage ($P < 0.0001$).

**Conclusions:** Patients with low-grade EOC and negative nodes appear to have a survival benefit from LND regardless of stage, suggesting a therapeutic benefit in patients with early- as well as advanced-stage disease.

![Fig. 1. Overall survival of patients with low grade ovarian carcinoma with and without lymph node assessment.](image)

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**133 — Featured Poster Session**

**Rescreening for genetic mutations using multi-gene panel testing in patients who previously underwent noninformative genetic screening**

S.H. Kim, M.K. Frey, R. Yee Bassett, J. Martineau, S.V. Blank. New York University School of Medicine, New York, NY, USA

**Objectives:** The recent identification of multiple cancer-related genes and pathways and the availability of next-generation sequencing has resulted in a shift away from single-gene testing toward multi-gene panel testing for familial cancer syndromes. However, the role of rescreening individuals without prior multi-gene panel testing has yet to be evaluated. We sought to evaluate the use of rescreening and results of multi-gene panels in this rescreened population.

**Methods:** We reviewed all patients who had previously undergone genetic screening for familial cancer syndromes and then underwent a specific multi-gene panel testing platform at a single institution between 6/2013 and 6/2014.

**Results:** Forty-two patients with prior non-multi-gene panel testing underwent multi-gene panel screening. The mean age at time of repeat screening was 55 years. Thirty-three patients (79%) had personal histories of cancer and 40 patients (95%) had family histories of cancer. On primary testing, no deleterious mutations were identified and five patients (12%) were found to have variants of uncertain significance (VUS). On repeat multi-gene panel testing, one patient was discovered to have a deleterious *BRCA2* mutation and 17 patients were found to have VUS (40%). The five patients found to have VUS on primary testing were again found to have VUS on repeat testing, although one patient was discovered to have a VUS in a different gene (patient #5, *MLH1* vs. *BRIP1*). Twenty-five patients (59.5%) were referred to genetics by medical oncology, 12 (28.6%) by surgical oncology, 4 (9.5%) by gynecologic oncology, and 1 (2.4%) by urology.

**Conclusions:** Rescreening 42 previously tested patients with multi-gene panels resulted in the discovery of one pathologic *BRCA2* mutation and VUS in 12 additional patients, for a 31% rate of change in mutation characterization. Our data suggest that genetic rescreening with multi-gene panel assays in patients with noninformative prior screening results can provide additional diagnoses that may be clinically important. As more is learned about mutations now classified as VUS, the additional information gleaned from multi-gene panel testing may prove to be increasingly relevant.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Personal history of cancer</th>
<th># Relatives with cancer</th>
<th>Primary testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Uterine</td>
<td>2</td>
<td>Negative</td>
</tr>
<tr>
<td>11</td>
<td>None</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>12</td>
<td>Breast</td>
<td>1</td>
<td>Negative</td>
</tr>
<tr>
<td>13</td>
<td>Breast</td>
<td>2</td>
<td>Negative</td>
</tr>
<tr>
<td>14</td>
<td>Breast, Leukemia</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>15</td>
<td>Breast</td>
<td>1</td>
<td>Negative</td>
</tr>
<tr>
<td>16</td>
<td>Breast</td>
<td>1</td>
<td>Negative</td>
</tr>
<tr>
<td>17</td>
<td>Breast</td>
<td>2</td>
<td>Negative</td>
</tr>
<tr>
<td>18</td>
<td>Breast, Colore</td>
<td>2</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Patient Repeat multi-gene panel testing**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Repeat multi-gene panel testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mutation <em>BRCA2</em> c.1969+1G-A</td>
</tr>
<tr>
<td>2</td>
<td>VUS <em>BRCA2</em> c.1765A-C, p.E589Q</td>
</tr>
<tr>
<td>3</td>
<td>VUS <em>BRCA2</em> c.8542G-C, p.E2848Q</td>
</tr>
<tr>
<td>4</td>
<td>VUS <em>BRCA2</em> c.9206G-C, p.C3069F</td>
</tr>
<tr>
<td>5</td>
<td>VUS <em>BRCA2</em> c.3715T-C, p.S1239P</td>
</tr>
<tr>
<td>6</td>
<td>VUS <em>CDH1</em> c.2572G-C, p.D858H</td>
</tr>
<tr>
<td>7</td>
<td>VUS <em>MLH1</em> c.52C-T, p.R18C</td>
</tr>
<tr>
<td>8</td>
<td>VUS <em>PALB2</em> c.1364A-G, p.N455S</td>
</tr>
<tr>
<td>9</td>
<td>VUS <em>MUTYH</em> c.821G-A, p.R274Q</td>
</tr>
<tr>
<td>10</td>
<td>VUS <em>CHEK2</em> c.320-5T-A</td>
</tr>
<tr>
<td>11</td>
<td>VUS <em>CHEK2</em> c.320-5T-A</td>
</tr>
<tr>
<td>12</td>
<td>VUS <em>CHEK2</em> c.7C-T, p.R3W</td>
</tr>
<tr>
<td>13</td>
<td>VUS <em>MSH2</em> c.216C-G</td>
</tr>
<tr>
<td>14</td>
<td>VUS <em>MSH6</em> c.1049C-T, p.A350V</td>
</tr>
<tr>
<td>15</td>
<td>VUS <em>MSH6</em> c.1069G-A, p.C566R</td>
</tr>
<tr>
<td>16</td>
<td>VUS <em>NF1</em> c.4417G-A, p.D1473N</td>
</tr>
<tr>
<td>17</td>
<td>VUS <em>RAD50</em> c.2647C-T, p.R883C</td>
</tr>
<tr>
<td>18</td>
<td>VUS <em>TP53</em> c.217G-A, p.V73M</td>
</tr>
<tr>
<td>19</td>
<td>VUS <em>ATM</em> c.2608A-G, p.N870D</td>
</tr>
<tr>
<td>20</td>
<td>VUS <em>ATM</em> c.3993C-T, p.S754</td>
</tr>
<tr>
<td>21</td>
<td>VUS <em>BRCA2</em> c.5020A-G, p.S1674R</td>
</tr>
<tr>
<td>22</td>
<td>VUS <em>BRIP1</em> c.5505G-C, p.D184Y</td>
</tr>
</tbody>
</table>

doi:10.1016/j.ygyno.2015.01.135
134 — Featured Poster Session
The FAK of uterine cancer: PTEN expression predicts response of uterine cancer to focal adhesion kinase inhibition
R.A. Previs1, D. Thanapprapasra2, W. Hu3, R. Rupaimoole4, J. Huang5, H.J. Dalton6, R. Ali7, G.N. Armaize-Pena8, J.M. Hansen9, B. Zand9, R.L. Coleman9, A.K. Sood9. 1The University of Texas MD Anderson Cancer Center, Houston, TX, USA, 2Wayne State University, Detroit, MI, USA

Objectives: PTEN is known to be frequently mutated in uterine cancer and dephosphorylated focal adhesion kinase (FAK). We examined the impact of PTEN alterations on the response to treatment with a novel FAK inhibitor, GSK2256098.

Methods: In vitro and in vivo therapeutic experiments were carried out using PTEN mutated and PTEN wild-type models of uterine cancer. GSK2256098 was used alone or in combination with clinically relevant chemotherapy to evaluate whether patients could benefit in frontline or recurrent settings from FAK inhibition.

Results: In vitro treatment with GSK2256098 resulted in greater inhibition of expression of pFAK397 in PTEN-mutated (Ishikawa) than in PTEN wild-type (HeC1A) cells. Ishikawa cells treated with GSK2256098 had lower pFAK397 expression and decreased viability than treated HeC1A cells, but both were sensitive to FAK inhibition. After transfection with a wild-type PTEN construct, the Ishikawa cells treated with GSK2256098 no longer had decreased pFAK397 expression. Decreased cell viability and enhanced sensitivity was observed in Ishikawa cells compared to HeC1A cells after treatment with GSK2256098 combined with paclitaxel and topotecan. Responses to treatment with GSK2256098 and cisplatin were similar. In the Ishikawa orthotopic mouse model, treatment with GSK2256098 resulted in lower tumor weights, fewer tumor nodules, and fewer metastases than mice inoculated with HeC1A. Additive effects were seen in mice treated with GSK2256098 and paclitaxel. Immunohistochemistry using CD31, bFMI, and TUNEL staining demonstrated that tumors from mice inoculated with Ishikawa cells and treated with GSK2256098 had lower microvessel density, less cellular proliferation, and increased apoptosis than in tumors from mice inoculated with HeC1A. From the large cohort of evaluable patients, increased FAK and pFAK expression levels were inversely related to pFAK expression levels.

Conclusions: These preclinical data demonstrate that PTEN-mutated uterine cancer responds better to FAK inhibition than does PTEN wild-type uterine cancer. Therefore, PTEN represents a potential biomarker for FAK-targeted therapy during clinical development.

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135 — Featured Poster Session
Molecular predictors of response to EphA2 targeted therapy in uterine cancer
A.K. Sood1, J. Huang, W. Hu, R.A. Previs, H.J. Dalton, J.M. Hansen, Y. Sun, A.M. Nick, R. Broadus, R.L. Coleman. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objectives: EphA2 is recognized as a key target for uterine cancer therapy. Dasatinib targets EphA2 pS897, but predictive biomarkers are needed.

Methods: Preclinically, RPPAs were used to identify candidate biomarkers of response that were subsequently functionally validated. Moreover, we tested the validity of the biomarkers in a prospective clinical trial (dasatinib plus paclitaxel and carboplatin) using circulating tumor cells (CTCs) collected pre- and posttreatment. In addition, select markers (EphA2 S897, CAV1, CRAF/RAF dimers) were evaluated in pretreatment tumor samples using immunohistochemistry or proximity ligation assays (PLA).

Results: Protein analyses revealed that the following markers were related to dasatinib response in preclinical assessment: CRAF, pCRAF5338, pMAPKT202/Y204, pS6S240/244, p70S6K389, and pAKTS473. In vitro studies further showed that high levels of CAV-1 and EphA2 phosphorylation at S897 were key determinants of dasatinib response in uterine carcinoma. A novel mechanism for response was discovered whereby the high CAV-1 at the plasma membrane disrupts the BRAF/CRAF heterodimer and, thus, inhibits the MAPK pathway during dasatinib treatment. In pretreatment clinical samples, high CAV-1 and EphA2 pS897 were key determinants of dasatinib response in patients. Furthermore, PLA assay demonstrated that uterine cancer patients who responded to EphA2-targeted therapy had high coexpression of EphA2-S897 and CAV1 and low expression of CRAF/BRAF dimers in tumors. In addition, high EphA2-S897 on CTCs collected pretreatment was related to response.

Conclusions: These data provide a new understanding of EphA2 targeting by dasatinib and identify key biomarkers for personalized therapy. These findings have implications for ongoing dasatinib-based clinical trials.

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136 — Featured Poster Session
The landscape of somatic hypermutation in gynecologic cancer
J.S. Chapman1, M. Chang1, S. Asthana1, L.M. Chen1, N. Schultz2, B. Taylor3, 4UCSF Helen Diller Comprehensive Cancer Center, San Francisco, CA, USA, 2University of California, San Francisco, San Francisco, CA, USA, 3Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: Somatic hypermutation is present in the tumor genomes of a subset of human cancers. Nevertheless, the extent as well as the biological and clinical impact of hypermutation in gynecologic cancer is unknown. In an age of precision oncology, there is a pressing need to understand the catastrophic mutational burden of sporadically hypermutated tumors to reveal the drivers of cancer biology and identify candidate actionable lesions.

Methods: We assembled a curated repository of cancer genome data consisting of the sequenced tumor exomes and whole genomes of 10,694 patients representing 43 tumor types from 95 unique cohorts. We used integrative genomic analyses of publicly available mutational and DNA copy number data to identify hypermutated cancers and to infer underlying mutational processes driving hypermutation.

Results: We identified 311 hypermutated tumors in 20 diverse tumor types representing ~3% of all cancers. Of these, 47% of patient tumors possessed somatic hypermutation that could not be explained by an established exogenous mutagen, environmental exposure, or known defect in DNA repair. Pelvic tumors represented 30% of all hypermutated cases and hypermutation was present in 27% of all sequenced cases of uterine and cervix cancers. While defects in DNA polymerase epsilon (POLE) and/or in mismatch repair drives hypermutation in most cases, an APOBEC mutational signature was the dominant mutational process in several uterine and one cervical cancer case. Non-hotspot mutations in the POLE exonuclease domain were observed to produce a POLE mutation signature. Despite the identification of hypermutation in disparate tumor types, ovarian serous carcinomas did not have this phenotype (P < 0.0001). We used allelic abundance data to help determine the temporal sequence of somatic events in endometrial cancers with multiple defects potentially contributing to the observed hypermutation.

Conclusions: Somatic hypermutation is common in pelvic cancer and APOBEC is a novel mutational process that may explain the mutation burden in some cases. We can exploit big data to explore uncommon cancer phenotypes such as somatic hypermutation.
137 — Featured Poster Session
The metastatic role of AXL, a receptor tyrosine kinase, in a genetically engineered mouse model of metastatic, endometrioid ovarian cancer
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Objectives: To evaluate the role of AXL in a genetically engineered mouse model of ovarian cancer metastasis.

Methods: Immunohistochemical staining of ovarian cancer tissue microarrays of advanced-stage, high-grade epithelial ovarian cancer specimens for AXL expression was performed and correlated with overall survival. A metastatic endometrioid ovarian cancer model was generated through an intrabursal AdCre-infected LSL-K-rasG12D/+Ptenfl/fl mouse model. LSL-K-rasG12D/+Ptenfl/fl Axl+/+ and LSL-K-rasG12D/+Ptenfl/fl Axl−/− were used to evaluate the role of AXL.

Results: Of the 80 patient-derived primary ovarian tumor specimens, 76% (61) of advanced-stage, high-grade epithelial ovarian cancer specimens had AXL expression. When correlated with overall survival, patients with tumors that had no AXL expression had a median survival of 52.9 months vs. 26.7 months for those with 3+ AXL expression (P = 0.03). The majority of intrabursal AdCre-infected LSL-K-rasG12D/+Ptenfl/fl Axl+/+ mice had primary (78%) and metastatic tumor formation (86%) whereas the majority of LSL-K-rasG12D/+Ptenfl/fl Axl−/− mice had primary tumor formation (64%) but few had metastatic tumors (28%) (P < 0.05). There was no difference in primary tumor weight between the two groups: 120 mg for Axl+/+ vs. 110 mg for Axl−/−. Metastatic tumors were microscopic and, therefore, unable to be resected and weighed prior to identification by hematoxylin-and-eosin staining. Western blotting of primary and metastatic tumors from LSL-K-rasG12D/+Ptenfl/fl Axl+/+ showed high AXL expression compared to no AXL staining in the ovaries of normal mice.

Conclusions: AXL expression in advanced-stage epithelial ovarian cancer correlated with lower overall survival. Primary ovarian and metastatic tumors in this intrabursal AdCre-infected LSL-K-rasG12D/+Ptenfl/fl mouse model expressed AXL. Deletion of the receptor tyrosine kinase, AXL, in this conditional genetically engineered mouse model of endometrioid ovarian cancer resulted in inhibition of metastatic tumor formation. AXL is a critical factor driving metastasis in this immunocompetent murine model of metastatic ovarian cancer.

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139 — Featured Poster Session
Evaluation of insulin-like growth factor 2 as a biomarker in uterine carcinosarcoma
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Objectives: The purpose of this study was to evaluate insulin-like growth factor (IGF)2 as a biomarker in women with uterine carcinosarcoma (CS).

Methods: After institutional review board approval, formalin-fixed paraffin-embedded tumor sections were prepared from 103 patients who underwent primary surgical resection of uterine CS. IGF2 immunohistochemistry was performed using previously validated methodology. A pathologist blinded to all clinical data evaluated the IGF2 staining in each compartment (epithelial cytoplasmic, epithelial nuclear, stromal cytoplasmic, stromal nuclear), and the IGF2 expression was summarized as an H-score calculated as the product of staining intensity and percentage of cells with positive staining. Statistical comparison of mean IGF2 expression scores between two groups was performed using a two-tailed t-test, while comparison of means among greater than two groups was performed by one-way ANOVA. Comparison of survival curves was computed by log-rank test.

Results: The median age was 66 years (range, 32–90 years). Race breakdown was 66 black patients, 36 white, and 1 other. Among 73 surgically staged patients, 34% were FIGO stage I, 8% were stage II, 32% were stage III, and 26% were stage IV. Cytoplasmic IGF2 expression was significantly higher in both the malignant epithelial (P < 0.05) and malignant stromal (P < 0.05) cells in patients with advanced-stage CS (FIGO III/IV) compared with early-stage CS (FIGO I/II) patients, while nuclear IGF2 expression was similar. This validates our prior data in an independent cohort. Cytoplasmic IGF2 expression in the malignant epithelial cells was significantly higher among patients who recurred compared with patients who remained disease-free (P = 0.02). Cytoplasmic IGF2 expression in the malignant epithelial cells was also significantly higher in patients who died compared with those who survived (P = 0.001). Among patients with high cytoplasmic epithelial IGF2 expression (greater than or equal to the median H-score for the entire cohort), the a 16S rRNA V4 region amplicon library, which was sequenced using Illumina MiSeq. Raw sequence data were analyzed using the QIME program. Taxonomy was assigned to 16S sequences using RDP Classifier against the Greengenes 16S rRNA database.

Results: Thirty-eight samples were collected, and after quality control measures, a mean of 69,502 sequences with 250 base-paired end reads were identified. Eight samples had inadequate numbers of sequences, leaving 30 specimens (14 benign and 16 malignant) for detailed analysis. The most abundant phyla were Proteobacteria (48%), followed by Firmicutes (31%) and Bacteroidetes (11%). The proportion of Proteobacteria was higher in the malignant samples (60%) than the benign samples (34%) (P < 0.01). The proportion of Firmicutes was less in malignant samples (20%) compared to the benign samples (43%) (P < 0.01). Based on unweighted UniFrac, the malignant samples cluster differently from the benign samples, suggesting differences in the microbiota between groups.

Conclusions: The peritoneum, fimbriae, and fallopian tube epithelium contain an extensive array of microbes. Differences in the microbe populations between malignant and benign samples suggest the need for further study to understand the interplay between these bacteria and malignancy.

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138 — Featured Poster Session
Microbial diversity in the fimbriae, fallopian tube and peritoneum in women with benign disease and advanced pelvic malignancies
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Objectives: To describe the bacterial community (microbiota) of the peritoneum, fallopian tube, and fimbriae in women with benign and malignant disease.

Methods: Samples from the peritoneal cavity, fimbriae, and fallopian tubes at the time of exploratory laparotomy or laparoscopy for benign and malignant conditions were collected. Microbial DNA was prepared and polymerase chain reaction primers were used to create bacterial communities.

Results: Thirty-eight samples were collected, and after quality control measures, a mean of 69,502 sequences with 250 base-paired end reads were identified. Eight samples had inadequate numbers of sequences, leaving 30 specimens (14 benign and 16 malignant) for detailed analysis. The most abundant phyla were Proteobacteria (48%), followed by Firmicutes (31%) and Bacteroidetes (11%). The proportion of Proteobacteria was higher in the malignant samples (60%) than the benign samples (34%) (P < 0.01). The proportion of Firmicutes was less in malignant samples (20%) compared to the benign samples (43%) (P < 0.01). Based on unweighted UniFrac, the malignant samples cluster differently from the benign samples, suggesting differences in the microbiota between groups.

Conclusions: The peritoneum, fimbriae, and fallopian tube epithelium contain an extensive array of microbes. Differences in the microbe populations between malignant and benign samples suggest the need for further study to understand the interplay between these bacteria and malignancy.

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median progression-free survival was 8.9 months vs. 23.2 months in patients with low IG2 expression (P < 0.01). Patients with high IG2 expression also had a significantly worse overall survival of 11.4 months vs. 30.3 months in patients with low IG2 (P < 0.05).

Conclusions: High cytoplasmic expression of IG2 in the malignant epithelial cells of uterine CS predicts disease recurrence/progression and death in women with this disease. The potential for targeted therapy is under investigation using patient-derived xenografts.

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140 — Featured Poster Session
Neratinib, an irreversible ErbB receptor tyrosine kinase inhibitor, shows efficacy in the treatment of HER2 amplified carcinosarcoma in vitro and in vivo
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Objectives: Carcinosarcoma (CS) is a deadly gynecologic malignancy with few effective treatment options. The study of new therapies is difficult because of the rarity of the CS. The HER2/neu oncogene is reported overexpressed and/or amplified in up to 25% of CS of the female genital tract. The objective of this study was to determine the efficacy of neratinib, an irreversible ErbB receptor tyrosine kinase inhibitor, in the treatment of HER2-amplified CS in vitro and in an in vivo mouse model.

Methods: Six primary CS cell lines were evaluated for HER2 gene amplification by fluorescence in situ hybridization and receptor expression by immunohistochemistry and flow cytometry. The efficacy of neratinib in the treatment of HER2-amplified carcinosarcoma was determined in vitro against primary CS cell lines, with differential expression of HER2/neu. Data regarding median inhibition concentration (IC50), cell cycle distribution, and cell signaling changes were assessed by flow cytometry. The efficacy of neratinib in treating mice harboring HER2-amplified carcinosarcoma xenografts was also determined.

Results: HER2 protein overexpression and gene amplification were detected in one of six (16.6%) of the primary CS cell lines studied. Of the six CS cell lines, SARAR6K (i.e., HER2-amplified) was significantly more sensitive to neratinib than the five non-HER2/neu-amplified CS cell lines (mean ± SEM IC50: 0.020 ± 0.002 μM vs. 0.164 ± 0.019 μM, P = 0.0039). Neratinib treatment caused a significant buildup in G0/G1 phase of the cell cycle, arrest in the autophosphorylation of HER2/neu, and activation of S6. Neratinib was efficacious in treating mice harboring HER2-amplified CS xenografts (P = 0.0039).

Conclusions: Neratinib is highly effective in inhibiting HER2-amplified CS proliferation-associated signaling, cell cycle progression, and tumor growth in vitro and arresting HER2/neu-amplified xenograft growth in vivo. Neratinib may represent a novel treatment option for the subset of HER2-positive CS patients with disease refractory to chemotherapy. Clinical trials are warranted.

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142 — Featured Poster Session
How important is the pathologic margin distance in vulvar cancer?

Objectives: Even after the introduction of triple incision surgery, radical vulvectomy and removal of all external genitalia remained as the standard treatment until the description of radical local excision. Moreover, while wide local resection became a good option for primary tumor treatment, the extent of the tumor-free resection margins after wide local excision remains controversial and under constant debate. A tumor-free resection pathologic margin of at least 8 mm is still considered state of the art in vulvar squamous cell carcinoma (VSCC). Our aim was to evaluate the prognostic value of pathologic margin in VSCC.

Methods: We analyzed a series of 157 patients treated for VSCC from January 1980 to November 2007 at AC Camargo Cancer Center. We excluded patients with distant recurrence or neoadjuvant treatment. Twelve (7.6%) patients received wide local resection and the others had radical vulvectomies. Because our primary objective was to correlate local recurrence and pathologic free margin, we included 34 (21.7%) patients who did not have inguinal lymphadenectomy.
The patients were divided in three groups according to pathologic free margin (PFM): <3 mm (n = 8), ≥3 and <8 mm (n = 35), and ≥8 mm (n = 79).

**Results:** Median age was 70 years (range, 28–91 years). Median tumor size was 4.2 cm (range, 0.3–15 cm) and median depth of invasion was 8 mm (range, 1–32 mm). The median PFM distance was 10 mm (range, 1–65 mm). Forty-seven (38.2%) patients had lymph node (LN) metastasis, with median 18.5 LNs resected (range, 1–51 LNs) and median of 2 positive LNs (range, 1–8 LNs). After a median follow-up of 40.1 months, 55 (35.5%) cases recurred: 33 (60%) had local and 22 (40%) groin recurrence. Local recurrence occurred in 20% (2/8) of patients with PFM of <3 mm, 20.5% (9/45) with ≥3 and <8 mm, and 21.8% (22/79) with ≥8 mm (P = 0.97). PFM also did not correlate to local recurrence when analyzed as a continuous variable (P = 0.10). The 5-year cancer-specific survival was 71% and 5-year local recurrence disease-free survival was 78.1%. Margin distance did not negatively affect local disease-free survival (P = 0.94).

**Conclusions:** Our results suggest no correlation between local recurrence and pathologic margin distance. Furthermore, a more conservative surgical approach may be considered in some special situations, such as margins near the urethra or anus.

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apollipoprotein L6 (4.2-fold), and c-myc binding protein (4.1-fold). DAVID functional annotation analysis revealed significant enrichment in "protein transport" (P = 5.5E-5), "antigen processing and presentation of exogenous peptide antigen" (P = 1.3E-3), and "pyrimidine ribonucleotide biosynthetic process" (P = 3.6E-2).

Conclusions: Differential patterns of gene expression were found with elevated BMI in high-grade serous OC tumors in the TCGA database. Many of the differentially expressed genes were related to lipid metabolism and the apollipoprotein pathway. This suggests that obesity may contribute to OC pathogenesis through differential expression of metabolically relevant genes.

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145 - Featured Poster Session
Platinum and taxane-induced ovarian toxicity: Mechanism of damage and evaluation of gonadoprotective agents
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Objectives: Reproductive-age women with early-stage ovarian cancer are candidates for fertility-sparing surgery, but may require chemotherapy (CT). Platinum-based CT is gonadotoxic and can result in loss of primordial follicles (PMF) and decrease ovarian reserve. Our objective was to evaluate the mechanisms of CT damage and potential gonadoprotective adjuvant treatments.

Methods: C57BL/6 mice were divided into eight groups (n = 18 per group) and treated with vehicle (control), CT (carboplatin 80 mg/kg intraperitoneally [IP] and paclitaxel 20 mg/kg IP), or CT concurrent with one of six potential protective agents that inhibit apoptosis (imatinib, fingolimod), vascular remodeling (bevacizumab, Neupogen), or follicle development (everolimus, leuprolide). Immunohistochemistry (IHC) was performed to evaluate and quantify apoptosis (caspase-3), DNA damage (γH2AX), and microvessel density (MVD, PECAM/CD31). Outcome measures for ovarian reserve included differential follicle counts and serum anti-müllerian hormone (AMH) levels. Groups were compared using analysis of variance with pairwise comparisons.

Results: CT-treated mice had more PMFs with DNA-damaged oocytes than controls (67.6% vs. 1.4%, P = 0.002) and apoptotic oocytes (65% vs. 0%, P < 0.0001), but granulosa cell death and damage did not differ between groups. This could not be reduced by any experimental agent. Compared to controls (3.33 ± 0.55 microvessels/μm²), a 58.8% reduction in MVD was observed in the CT-treated group (1.96 ± 0.94 microvessels/μm²). With the exception of Lupron and everolimus, all the protective agents rescued MVD. CT-treated mice had a 93.5% reduction in PMF (53 ± 133.6) compared to controls (830 ± 387.5; P < 0.0001) and lower AMH levels of 89.3 ± 36.1 compared to 58.5 ± 21.4 (P = 0.008). No protective agent had a significant protective effect on PMF counts or AMH levels.

Conclusions: Platinum and taxane-based combination CT dramatically reduced PMF through DNA damage and apoptosis of the PMF oocytes and a reduction in MVD. This effect could not be reversed with any of the agents evaluated. Future study will evaluate the breeding outcomes and alternate agents to reduce the gonadotoxic effect of ovarian cancer combination CT.

Supported by Magee-Womens Research Institute & Foundation and gifts from Julie and Michael McMullen and Sylvia Bernassoli.
Objective:** The use of 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase inhibitor in women with ovarian cancer (OC) has been shown to improve survival, yet the molecular mechanisms underlying this clinical finding are unknown. We sought to evaluate the effects of simvastatin on cell proliferation in ovarian cancer (OC) cell lines and on tumor growth in a genetically engineered serous OC mouse model.

**Methods:** Two human OC cell lines (SKOV3 and HEY) were used. Cell proliferation was assessed by MTT assay. Cell cycle progression was evaluated by Caleometer. Apoptosis was evaluated by Annexin V-FITC assay. HMG-CoA activity was assessed by enzyme-linked immunosorbent assay. The effects of simvastatin on phosphorylated (phos)-S6 and phos-p42/44 were documented by Western immunoblotting. For the in vivo studies, we used the Kpb++/+ serum OC mouse model. This is a more aggressive derivative of the K18-gT121+/+; p53fl/fl; Brcalfl/fl (Kpb) genetically engineered OC mouse model. The Kpb++/+ mice were treated with placebo or simvastatin (intraperitoneal injection, 10 mg/kg/day) following tumor onset for 4 weeks. Immunohistochemical analysis was performed on the ovarian tumors after treatment with placebo or simvastatin for Ki-67, HMG-CoA reductase, phos-S6, and phos-p42/44 expression. Individual slides were digitized using Aperio ScanScope and analyzed using Aperio ImageScope software.

**Results:** Simvastatin inhibited cell proliferation in a dose-dependent manner in both ovarian cancer cell lines within 48 to 72 h of exposure (median inhibition concentration [IC50] range of 8–16 nm, P < 0.001–0.05). Treatment with simvastatin resulted in G1 cell cycle arrest, induction of apoptosis, and reduction in the enzymatic activity of HMG-CoA reductase. Western immunoblot analysis demonstrated that simvastatin decreased phosphorylation of S6 and p42/44 within 18 h of exposure. As compared to placebo, simvastatin inhibited tumor weight in the Kpb++/+ mice by 52% (P < 0.0053). Treatment with simvastatin in the OC tumors decreased Ki-67, HMG-CoA reductase, phos-Akt, and phos-p42/44 staining (P < 0.05).

**Conclusions:** Simvastatin potently suppressed OC cell and tumor growth. These antitumorigenic effects may be partially mediated through inhibition of the mTOR and MAPK pathways. Thus, statins may have a role in the treatment of OC and may be worthy of further exploration in clinical trials.

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**Featured Poster Session**

**Cell-based therapy in ovarian cancer: Improved adenoviral transduction strategy of human mesenchymal stem cells as tumor-homing drug factories**

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**Objectives:** Human mesenchymal stem cells (MSCs) have the potential to serve as cellular delivery vehicles for targeted cancer therapy due to their intrinsic tumor homing capacity. We recently published a novel method to produce a stabilized TRAIL trimer (TR3) in mammalian cells, well suited as an MSC-produced cancer drug. TR3 has been further modified to adhere to the ovarian cancer biomarker MUC16. This modification substantially increases tumor selectivity and bioactivity. To produce TR3-secreting MSCs, we tested several modifications to the adenoviral (Ad) vectors and demonstrated the feasibility of using selected adenovirus vectors for the production of TR3-based therapeutics from MSCs.

**Methods:** MSCs were isolated from the adipose tissue of gynecologic oncology patients and phenotypically identified by flow cytometry using established surface markers. Transduction efficiency of MSCs was assessed by GFP expression using a panel of fiber-modified Ad5-based vectors. Delivery of TR3-based therapeutics with Ad5 vectors was evaluated using flow cytometry, Western blot, and functional killing assays.

**Results:** We established 20 stable MSC lines from patient-derived adipose tissue. All MSC lines were positive for the expected MSC specific markers, including CD49d, CD73, CD90, CD105, and CD166. Compared to Ad5 control, modified Ad5pK7 vectors significantly enhanced the infectivity of MSCs with >95% efficiency (Fig. 1A). TR3 was successfully expressed on the surface of cells following Ad infection, and bioactivity was confirmed in co-culture with TRAIL-sensitive target cells (Fig. 1B and C, 74% specific cell death).

**Conclusions:** Ad5pK7 demonstrated high transduction efficiency of MSCs, establishing the feasibility of using MSCs as potential carriers for anticancer therapeutics. We are planning additional studies to further elucidate the clinical potential for this promising approach.

Fig. 1. Exploring MSCs to serve as cellular carriers for targeted TR3 cancer therapy. (A) MSCs from 4 patients were transduced with either wild-type adenovirus serotype 5 (Ad5) or with fiber-modified Ad5pK7. Transduction efficiency was assessed by monitoring GFP expression. Please note that Ad5pK7 is capable of infecting a broad range of MSC lines with close to 100% efficiency. (B) 1x10^5 CHO-CAR cells were infected with TR3-expressing Ad5-TR3GFPY (MOI 5000). Cells infected with the Ad5-Luciferase and GFP markers (Ad5-Luc_GFP) served as control. 24 hrs post infection, the cells were overlaid with Jurkat cells (5x10^5) for 9 hours in a 24-well format. Functional TR3 activity in this co-culture experiment is shown by appearance of apoptotic bodies (Ad5TR3GFPY). (C) Graphic representation of the viability assay shown in (B), with specific cell death of 75% mediated by expression of TR3 on the CHO-CAR effector cells.

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**Featured Poster Session**

**Progestins inhibit calcitriol-induced CYP24A1 in endometrial and ovarian cancer cells**

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**Objectives:** In ovarian and endometrial epithelial cells, we have shown that combined progesterone (PROG) and calcitriol (1,25-dihydroxycholecalciferol, active vitamin D) reduces proliferation and promotes apoptosis to a greater extent than does each agent alone. Possible mechanisms may include inhibition of 24-hydroxylase, or...
posttranscriptional modifications (splice variants [SV]) of CYP24A1 mRNA, both of which decrease the activity of CYP24A1, the enzyme that renders vitamin D inactive, thereby increasing vitamin D potency. Our objective was to test whether progestins reduce the catalysis of calcitriol to preserve its antiproliferative activity.

**Methods:** We investigated the impact of several progestins on calcitriol-induced CYP24A1 expression in cancer cell lines that express progesterone receptors (PRs) (HEC-1b, OVCAR-3, T47D-WT, A and B [breast lines expressing PR or individual PR isoforms]) or lines that do not express PRs (OVCAR-3 and T47D-Y). The impact of PROG, medroxyprogesterone acetate (MPA), norgestrel (NORG), and norethindrone (NOR) on calcitriol-induced CYP24A1 and CYP24A1-SV expression was tested using reverse transcriptase polymerase chain reaction and Western blotting. Apoptosis was assayed by TUNEL. Statistical significance was at \( P < 0.05 \) by ANOVA.

**Results:** CYP24A1 and CYP24A1-SV expression was enhanced by calcitriol treatment. When treated with progestins, cell lines expressing PRs (HEC-1B, OVCAR-3-PGR, and T47D-WT, A and B) showed marked inhibition of CYP24A1 expression \((P < 0.001)\), along with increased apoptosis \((P < 0.01)\), while cells not expressing PRs (OVCAR-3 and T47D-Y) did not. PROG, MPA, and NORG each inhibited calcitriol-induced CYP24A1 transcript. Calcitriol-induced expression of CYP24A1-SV was also downregulated by PROG and MPA but not by NORG or NOR.

**Conclusions:** We show for the first time that progestins inhibit calcitriol-induced CYP24A1. This effect is PR-dependent and occurs in cells from multiple organ sites. CYP24A1 limits calcitriol's antitumorigenic signaling in cancer cells, and our data provide evidence that progestins may be beneficial in preserving calcitriol activity. The combination of progestins and calcitriol deserves further consideration as a strategy for inhibiting endometrial and ovarian carcinogenesis.

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**151 — Featured Poster Session**

**Dietary isothiocyanates inhibit cancer cell growth by inducing replication stress mediated DNA damage response**


**Objectives:** Dietary isothiocyanates (ITCs) such as allyl isothiocyanate (AITC) and phenyl isothiocyanate (PITC) are abundant in many cruciferous vegetables such as mustard, cabbage, broccoli, and brussels sprouts. These metabolites are safe and highly bioavailable and data suggest that consumption of these plants containing ITCs may support chemoprevention in cancers by offering protection against carcinogens. Considering the need for novel therapeutic agents in ovarian cancer, our objective was to assess the tumor-specific growth inhibitory properties of dietary phytochemicals on ovarian cancer.

**Methods:** The ability of AITC and PITC to inhibit ovarian cancer cell growth was evaluated by dose response curves in isogenic ovarian cancer platinum-sensitive and platinum-resistant cell lines. Metastatic and invasive properties were evaluated using time-lapse scratch assays. Cell cycle kinetics and DNA damage response were evaluated at timed intervals to determine the response to ITC therapy.

**Results:** ITCs demonstrated a significant inhibition of ovarian cancer cell growth and induced apoptosis in a concentration-dependent manner. Dose response curves demonstrated that AITC was more potent in inducing cytotoxicity with a 2.3- to 33-fold reduction in survival in platinum-sensitive cells and a 3.4- to 14.2-fold reduction in platinum-resistant cells. AITC was more effective in antimetastatic effects in both platinum-sensitive and -resistant cancer cells. Timed cell cycle kinetics demonstrated an attenuation of cell cycle progression with S-phase and G2/M accumulation, thus making cells more susceptible to cytotoxic therapy. ITCs induced replication stress-mediated DNA damage response and double-strand breaks, as evidenced by increases in FANCD2, pChk1 (s317), pChk2, cyclin B, and H2AX.

**Conclusions:** ITCs inhibit ovarian cancer cell growth in both platinum-sensitive and -resistant cell lines. AITC was more effective in terms of cytotoxic effects, in vitro migration, and induction of replication stress-mediated DNA damage. These data strongly advocate for further development of this interesting agent as novel anticancer therapy.

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**152 — Featured Poster Session**

**Comprehensive genomic profiling of advanced stage endometrioid endometrial adenocarcinomas (EEAC) reveals differences associated with CTNNB1 mutation status and a high frequency of clinically relevant genomic alterations**


**Objectives:** Comprehensive genomic profiling of advanced stage endometrioid endometrial adenocarcinomas (EEAC) reveals differences associated with CTNNB1 mutation status and a high frequency of clinically relevant genomic alterations.
**Objectives:** To use comprehensive genomic profiling of late-stage endometrial adenocarcinoma (EEAC) to validate the link between CTNNB1 (β-catenin) mutation/Wnt-pathway activation and aggressive behavior despite deceptively low-grade histology and to identify additional associated alterations that could lead to potential targeted therapy selection.

**Methods:** Hybridization capture from 236 cancer-related genes and 19 genes commonly rearranged in cancer (FoundationOne, n = 236) was applied to ≥50 ng of DNA extracted from 326 clinically advanced EEAC formalin-fixed, paraffin-embedded tumor specimens and were sequenced to high, uniform coverage. A total of 98 EEAC cases were selected by the presence (EEAC-CM; n = 46) or absence (EEAC-CWT; n = 52) of CTNNB1 gene mutation for further analysis. All classes of genomic alterations (GA) were assessed, including base substitutions, small insertions and deletions (indels), rearrangements, and copy number alterations.

**Results:** CTNNB1 mutation rate across all endometrial subtypes was 17%, with enrichment in endometrioid (25.9%) and depletion in serous (2.7%) histology. Within the EEAC with primary tumors (n = 49) available for grading, FIGO grades varied (1 = 27%, 2 = 32%, 3 = 41%) across samples despite advanced stage (>95%) irrespective of grading. A total of 291 total GA were identified in the EEAC-CM group (5 GA per tumor) of which 141 were clinically relevant alterations (CRA) (3.1 per tumor) involving 28 different genes. Ninety-three percent (43/46) of EEAC-CM featured at least 1 CRA. A total of 389 alterations were identified in the EEAC-CWT group (7.5 GA per tumor) of which 207 were CRA (4.0 per tumor) involving 41 different genes. Ninety-eight percent (51/52) of EEAC-CWT featuring at least 1 CRA. Both EEAC-CM and EEAC-CWT subsets had high rates of PIK3CA pathway mutations, including PTEN, PIK3CA, PIK3R1, AKT1, NFI, FBXW7, STK11, MTO1 and TSC1 (93%/88%, ARID1A (43%/44%), and JAK1 (15%/17%), but differed dramatically in frequency of KRAS/ NRAS (11%/37%), TP53 (4%/40%), and ESR1 (11%/0%) mutations (P = 0.03).

**Conclusions:** This set of aggressive EEAC confirms previous observations that CTNNB1 mutation predicts a molecularly and clinically distinct subgroup of EEAC. The high frequency of CRA, including the co-occurrence of alterations in multiple signaling pathways, has implications for design of therapy regimens to effectively target all activated pathways.

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**153 — Featured Poster Session**

**Stathmin over-expression correlates with poor prognosis in patients with endometrial cancer**


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**Objectives:** Stathmin (STMN1) expression has been attributed to poor prognosis in a variety of solid tumors. The aim of the study was to relate STMN1 expression with overall survival (OS) and progression-free survival (PFS) and determine if it is an independent prognostic factor in patients with endometrial cancer (EC) using The Cancer Genome Atlas (TCGA) database.

**Methods:** Endometrial cancer patients were identified from the TCGA database. Clinicopathologic parameters, risk group stratification, and STMN1 gene expression (high- and low-expression group) were extracted from the dataset. These variables were then correlated with PFS and OS of all patients with EC and then according to histologic subtype using multi- and univariable analysis via Cox’s proportional hazards ratio.

**Results:** Among 333 patients with endometrial cancer, STMN1 overexpression was associated with PFS in both multi- and univariable analysis. STMN1 expression at >50th percentile significantly correlated (P < 0.05) with poorer 5-year PFS of 63% compared with a PFS of 83% among those with low expression. When patients were stratified to histologic subtype, STMN1 overexpression in serous EC patients was associated with worse PFS during multivariable analysis (P = 0.01). Moreover, STMN1 overexpression at >75th percentile in the serous subgroup showed a significantly worse (P < 0.001) 5-year PFS of 22% compared to a PFS of 67% among those with low expression during univariable analysis. The endometrioid subgroup did not have a significant correlation (P = 0.08) but showed a similar trend, with a 5-year PFS of 70% for those with high expression and 85% for those with low expression. STMN1 expression also correlated with OS, but only during univariable analysis. The effect of STMN1 on serous EC may be related to its opposing action on paclitaxel, a component of the chemotherapeutic regimen used for advanced and recurrent EC, where a significant majority of tumors are of serous histology. Stathmin destabilizes microtubules to promote cell division while paclitaxel promotes microtubule polymerization that leads to mitotic arrest and cell death. Thus, STMN1 could potentially be a surrogate marker for paclitaxel resistance in patients with serous EC.

**Conclusions:** Stathmin is an independent prognostic factor associated with PFS in patients with serous endometrial cancer.

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154 — Featured Poster Session

**Exon-specific p53 mutations drive different models of ovarian cancer risk**

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**Objectives:** The Cancer Genome Atlas (TCGA) reported that p53 is the most frequently mutated oncogene in epithelial ovarian cancer (EOC). Yet, p53 mutations occur over a wide range of exons, and the functional consequences are unknown. The goals of this study were to: 1) Identify the patterns of exon clustering of p53 mutations in EOC, 2) Determine the impact of exon-specific mutations on p53 transcript expression, 3) Test if different p53 mutations result in changes in expression levels of proteins downstream of and interacting with p53 (p53 interactor), and 4) Determine the effect of specific p53 mutations on prognosis.

**Methods:** This was a computational study of level 3 exon sequencing (391 mutations in 385 patients) and level 1 mRNA expression data from the TCGA study. The p53 interactor tested was defined by the KEGG pathway hsa04115.

**Results:** Exon location of p53 mutations significantly correlated with increased, decreased, or neutral expression p53 mRNA (ANOVA P = 0.05). p53 mutations in exon 6 did not have a significant effect on p53 expression. Mutations at exons 4, 9, and 10 were associated with reduced p53 expression and exon 5, 7, and 8 mutations were associated with increased p53 expression. p53 upregulating exons were associated with varying expression levels of downstream p53 interacting genes. p53 downregulating exons were associated with varying expression of p53 interacting genes. Multivariate prognostic models using p53 interacting genes were built for patients classified by exon mutational type. Examining the interaction between expression in patients with upregulated p53 depends on co-expression of cell
cycle and apoptosis genes (median PFS 19.5 vs. 13.5 months, log-rank P = 6.8e−04) and downregulated/neutral p53 depends on co-expression of genes regulating negative feedback of p53 (PFS 26.7 vs. 11.9 months, log-rank P = 4.04e−05).

Conclusions: When aggregated to specific exons, somatic mutations in p53 are associated with increased, neutral, or decreased expression of p53 mRNA in EOC. p53 mutations vary in their effect on the p53 interactome and downstream genes in an exon-specific manner. The impact of p53 mutations on PFS is dependent on the resulting level of p53 expression and its downstream genes. These results have implications for development of strategies to manipulate p53 pathways in ovarian cancer.

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155 - Featured Poster Session
Fuel for the fire: Connecting genomics with metabolomics in ovarian cancer

Objectives: To identify genomic correlates of metabolic dysregulation in ovarian cancer.

Methods: We profiled 101 high-grade serous ovarian cancer (HGSOC) samples and 15 normal ovarian tissue samples, identifying 172 significantly altered metabolites. We classified these metabolites into altered pathways and carried out full-scale gene expression analyses.

Results: We compared expression of measured metabolites for normal ovarian tissues and HGSOC and classified them into super pathways. We created a random forest classifier to generate a prediction model using metabolic profiles from normal tissue vs. tumor within 3% error. From the random forest classification, the top 10% of significantly altered metabolites included gluconate, ADMA, and NAA. Carbohydrate, amino acid, and lipid super pathways were identified as most important, with carbohydrate enrichment as significant (P = 0.03). Metabolites from the pentose phosphate pathway (PPP) and glycolysis were identified with this prediction model and found to be globally downregulated. Gene expression for enzymes in the PPP and glycolysis were compared between HGSOC and normal ovary and not found to be different. Gene expression ratios from the rate-limiting steps in these pathways were evaluated. No differences were identified between gene ratios from normal and tumor tissues (P = 0.22) within our data set, but relative expression was significantly different within TCGA (P = 0.009). A correlation analysis using all of the metabolites and genes was undertaken to identify the top 10 most and least correlated genes. After filtering by connectivity, GPHB1 was identified as the gene with the highest connectivity among altered metabolites. Within TCGA, 74% of ovarian cancers were found to have alterations of GPHB1 (n = 572), and expression did not correlate with copy number changes. High expression of GPHB1 was associated with worse overall survival (P = 0.04).

Conclusions: We developed an unprecedented systems-based approach using altered metabolites and genes to predict a malignant phenotype specific to HGSOC patients. Altered metabolism coupled with genomic analyses identified the most interconnected gene-biochemical networks that could lead to novel biomarkers and therapeutic approaches.

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156 – Featured Poster Session
Withdrawn per author’s request.

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157 – Featured Poster Session
Long-term safety follow-up, dosimetry and immunologic responses in patients enrolled on a phase I trial of intraperitoneal 212Pb labeled trastuzumab
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Objectives: To study the safety, dosimetry, and immunogenicity of intraperitoneal (IP) 212Pb-TCMC-trastuzumab in patients with HER2-expressing ovarian cancer and other malignancies.

Methods: A phase I dose escalation design studied >3 patients per level. 212Pb-TCMC-trastuzumab was delivered IP <4 h after giving 4 mg/kg trastuzumab intravenously to 16 patients with HER2-expressing peritoneal carcinomatosis, 15 of whom had ovarian cancer.

Results: Minimal agent-related toxicity has been observed with five dose escalations (7.4, 9.6, 12.6, 16.3, 21.1 MBq/m2) after a minimum follow-up of 6 months. Most adverse events were related to disease or medications other than the 212Pb-TCMC-trastuzumab. No late toxicity was noted. The lack of substantial toxicity was consistent with the dosimetry assessments performed using pharmacokinetic data obtained in the initial cohort that showed relatively low radiation exposure to normal organs. Whereas hematologic toxicity has been dose-limiting in prior IP radionuclide conjugate studies, the mean platelet counts, total white blood cell counts, and neutrophil counts in this study remained normal after a mean equivalent dose to marrow of 0.18 mSv/MBq. Only two patients had a transient decrease to grade 1 levels. Five of 16 patients developed transient elevation of one or more liver function tests in the initial 6 weeks. Assays to detect an immune response to 212Pb-TCMC-trastuzumab were negative for the 12 patients tested to date.

Conclusions: Little agent-related toxicity was observed after five dose levels of IP 212Pb-TCMC-trastuzumab treatment in patients with peritoneal carcinomatosis. Accrual to higher dose cohorts in this trial is ongoing and updated information will be presented.

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158 – Featured Poster Session
Mesothelin-derived peptide vaccination leads to survival advantage in epithelial ovarian cancer mouse model
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Objectives: To develop a vaccine strategy containing synthetic peptides derived from tumor-associated antigen mesothelin (MSLN) and to determine whether there is a survival advantage after mouse ovarian tumor challenge.

Methods: Ten C57Bl/6 mice per group were vaccinated with one of two 8-amino acid peptides (P1 and P2) derived from mouse MSLN in experimental groups and ovalbumin peptide in a control group. Mice were pretreated with 100 mg/kg cyclophosphamide on day −1 and then immunized by subcutaneous injection of 50 nM peptide with adjuvant on days 0 and 7, followed by a boost with peptide-pulsed dendritic cells on day 14. Five days after vaccine
administration, $4 \times 10^6$ luciferase-YFP infected ID8 mouse ovarian surface epithelium cancer cells were injected intraperitoneally. Bioluminescent imaging (BLI) and tumor weights were used to measure and compare tumor burden. Mice were weighed every other day and were considered dead after a 30% weight gain due to ascites. One-way ANOVA was used to compare BLI signals 6 and 9 weeks after tumor challenge. T-test was used to compare BLI signals and tumor weights between control and pooled MSLN vaccine groups (P1 and P2). Kaplan–Meier method and log-rank test were used to compare survival.

Results: Immunization with MSLN-derived peptides resulted in a CD8 + T-cell response against the specific peptide detected by IFNγ ELISpot assays. The average BLI signal was equivalent in all three groups 2 weeks after the tumor challenge. The BLI signal in the control group was significantly higher than in the P2 group (P = 0.04) after 6 weeks and significantly higher than for both P1 (P = 0.02) and P2 (P = 0.002) groups after 9 weeks. When P1 and P2 groups were pooled into the MSLN vaccine group, the BLI signal was significantly different from control at both 6 (P < 0.05) and 9 (P = 0.02) weeks. The mean tumor weight was higher in the control than in the MSLN vaccine group (324 mg vs. 164 mg, P < 0.001). There was a significant difference in median survival between control and MSLN vaccine groups (Fig. 1, log-rank P = 0.001).

Conclusions: Vaccination with MSLN-derived synthetic peptides leads to a statistically significant lower tumor burden and increased survival in a murine model of epithelial ovarian cancer. Further study of this therapy is warranted to determine if vaccination against MSLN can improve survival in patients with ovarian cancer.

Poster Session A
Saturday, March 28, 2015

160 — Poster Session
Breast cancer is common in women with ovarian malignant mixed Müllerian tumors
R.M. Whynott. University of South Florida, Tampa, FL, USA

Objectives: Ovarian malignant mixed Müllerian tumors are uncommon cancers. The purpose of the study was to determine the rate of metachronous or synchronous breast cancer as well as the rate of truncating germline BRCA1 and/or BRCA2 mutations in a series of women with these uncommon tumors.

Methods: Records were checked to find all women with ovarian malignant mixed Müllerian tumors treated by the gynecologic oncology service. Disease stage, grade, and histology as well as survival and rate of coexistent breast cancer were determined. Tumor and/or peripheral blood was tested for BRCA1 and BRCA2 truncating mutations.

Results: Twenty-four patients with ovarian malignant mixed Müllerian tumors were found. Tumor and paired peripheral blood were available on 19 patients; 4 more patients had only peripheral blood available. Family pedigrees were available on all 24 patients. Fifteen of 24 (62.5%) patients had metachronous or synchronous breast cancers, with 9/15 (60%) having bilateral breast cancer. No BRCA1 or BRCA2 mutations were found (somatic or germline) in this cohort.

Conclusions: Although uncommon, ovarian malignant mixed Müllerian tumors are often found in women with breast cancer. Despite this finding, BRCA1 or BRCA2 germline mutations are not common in this population.

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159 — Featured Poster Session
Role of increased n-acetylaspartate levels in epithelial ovarian cancer

Objectives: The clinical and biological effects of metabolic alterations in ovarian cancer are not well understood. We systematically examined the clinical and biological roles of metabolic alterations in ovarian cancers.

Methods: High-grade serous ovarian cancer (n = 101) and normal human ovarian tissue (n = 15) samples were subjected to comprehensive metabolic profiling with mass spectrometry. Gene expression (n = 261), protein expression (n = 209), and nuclear magnetic resonance for specific metabolite levels (n = 145) in samples from multiple ovarian cancer patient cohorts were assessed. Analyses to detect associations between n-acetylaspartate (NAA) production and clinical outcomes were performed. The biological effects of NAA in vitro and in vivo were also investigated.

Results: We found 172 metabolites whose levels in epithelial ovarian cancer samples were significantly different from those in normal ovary samples. Metabolic profiling revealed that the neuron-specific metabolite NAA had the highest relative median level in ovarian cancer compared with normal ovary. The mean (± standard error of the mean) NAA levels were 63.0 μM (± 6.3 μM) in ovarian cancer and 19.47 μM (± 4.4 μM) in normal ovary samples. Patients with high levels of NAA and its biosynthetic enzyme, aspartate N-acetyltransferase (NAT8L), had worse overall survival than patients with low levels of NAA and NAT8L. For example, from our metabolic profiling data, analysis using a Cox proportional hazards model revealed a significant association between NAA levels dichotomized at the median and disease-specific survival duration (HR, 3.58; 95% CI, 2.51 to 4.66; P = 0.03). This was validated with our NMR data, which also revealed a significant association between NAA levels dichotomized at the median and disease-specific survival duration (odds ratio, 3.67; 95% CI, 2.27 to 5.94; P = 0.001). NAT8L knockdown significantly decreased ovarian cancer cell viability and growth. In orthotopic mouse models (HEYA8, A2780) of ovarian cancer, NAT8L silencing reduced tumor growth significantly.

Conclusions: These findings indicate that the metabolite NAA has a prominent role in promoting tumor growth. NAA represents a novel metabolic pathway for targeted drug development.

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161 — Poster Session
Who was first or who knows how? Surgical management of mammary carcinoma on a gynecologic oncology service
S.J. Kapnick. I. Kapnick Memorial Cancer Consortium, Jupiter, FL, USA
Objectives: Comprehensive management of patients with breast cancer revolves around a surgery surrounded by delivery of multimodal adjuvant therapies and individualized attention to seminal endocrine, reproductive, and quality of life issues. Such variegated clinical mandates — taken in toto — reside within the purview of but one single specialty: gynecologic oncology. Breast oncology fellowships are limited. If feasible, additional avenues for developing the surgical expertise of gynecologic breast oncologists are needed.

Methods: We performed a retrospective analysis of a series of 322 patients with operable in situ microinvasive primary lesions excluded) treated between 1990 and 2009 on a single gynecologic oncology service with sentinel node/axillary dissection accompanying breast-sparing excision or mastectomy. Readmission for re-excision, hematoma, or infection; interval from diagnosis to initiation of radiation therapy (more or less than 6 weeks); patient-only esthetic grading; and intrammary/nodal/regional recurrence via nonactuarial on-site verification of disease status at 5 years from surgery were assessed.

Results: There were no statistically significant differences from United States/United Kingdom literature-based (general surgical) norms in the parameters investigated, with a locoregional recurrence rate of 5.6% (P = 0.20, chi square and Fisher's exact). Interpentad variance (learning curve) was not observed.

Conclusions: Peer-reviewed reportage, including oncologic outcomes, of breast surgery performance by gynecologic oncologists may expand the availability of definitive surgical care by otherwise optimally qualified breast oncologists via proctorships and by improving specialty-based (and biased) credentialing to patients with the most common female reproductve organ cancer.

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162 — Poster Session

Treatment outcomes for patients with locally advanced cervical cancer in a low-resource setting: Experience at a single institution in Tegucigalpa, Honduras

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Objectives: Treatment of locally advanced cervical cancer in low-resource settings involves many challenges, including the lack of brachytherapy and unpredictable availability of chemotherapy drugs. The objective of this study was to determine the treatment outcome following chemoradiation for locally advanced cervical cancers in Honduras.

Methods: This was a retrospective study of patients who were treated with either concurrent chemoradiation (CCRT) or radiation therapy (RT) alone at Hospital San Felipe in Tegucigalpa, Honduras. RT to the pelvis (70 Gy) was given either alone or concurrently with chemotherapy. Extrafascial hysterectomy was performed 6 weeks after completion of neoadjuvant treatment in patients with a complete clinical response.

Results: Between 2008 and 2011, 165 women with locally advanced cervical cancer were reviewed: 25 (15.2%) with stage IB2, 15 (9.1%) with stage IIA, 90 (54.5%) with stage IIB, and 35 (21.2%) with stage IIIB. Squamous cell carcinoma was identified in 135 (82%) cases and adenocarcinoma in 30 (18%) cases. Ninety-five (54.5%) patients received pelvic RT alone and 75 (45.5%) patients received CCRT. Thirty-three percent of CCRT patients received weekly cisplatin, with the remainder receiving either 5-fluorouracil, capecitabine, or gemcitabine with varying schedules. Seventy of 90 (77.8%) patients who received pelvic RT alone had a complete clinical response and underwent hysterectomy; 40 of 75 (53.3%) patients who received CCRT achieved a complete clinical response and underwent hysterectomy (P < 0.01). Of note, the CCRT group that was treated with weekly cisplatin achieved an 80% response rate, while the CCRT group given alternate therapies had only a 41.2% response rate.

Conclusions: Among our patients, those unable to receive standard cisplatin-based CCRT had the worst outcomes. Challenges, including access to timely treatment, are among the barriers to care for these women. In this setting, the patients receiving RT alone showed an excellent response, and treatment should not be delayed in an effort to give CCRT, especially if therapy will not include platinum.

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163 - Poster Session

Factors associated with post-cryotherapy wound healing among HIV-infected women in a low-resource Sub-Saharan African setting

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Objectives: We sought to evaluate markers of visually apparent post-cryotherapy wound healing of the cervix among human immunodeficiency virus (HIV)-positive women participating in a "screen-and-treat" cervical cancer prevention program in a low-resource setting.

Methods: We enrolled 101 cryotherapy-eligible HIV-positive women in Lusaka, Zambia. Participants returned for follow-up at 4, 8, and 12 weeks post-cryotherapy for evaluation of wound healing via visual assessment. We conducted multivariable logistic regression modeling to evaluate factors associated with wound healing, including HIV-related factors (CD4+ counts and antiretroviral therapy status) and markers of local cervicovaginal inflammation (presence of leukocytes and blood in cervicovaginal lavage).

Results: A total of 101 HIV-positive women (median age: 32 years, interquartile range: 28–36 years) with cryotherapy-eligible lesions were enrolled, of whom 91 returned for the 4-week follow-up visit and 81 returned for the 8- and 12-week follow-up visits. Clinical evidence of post-cryotherapy wound healing at 4, 8, and 12 weeks was noted in 33%, 35%, and 65% of participants, respectively (P = 0.01). After adjusting for HIV-related factors and markers of inflammation, clinical wound healing was independently associated with lower age at enrollment, such that women ≥30 years were 80% more likely than women <30 years to have healed 12 weeks post-cryotherapy (adjusted odds ratio 0.20, 95% CI: 0.05-0.76, P = 0.02).

Conclusions: This study provides evidence that even at 12 weeks post-cryotherapy, only two thirds of HIV-positive women have experienced complete healing of their cervical wounds, and this healing is delayed in women ≥30 years. Given the increasing roll out of "screen-and-treat" cervical cancer prevention programs in high HIV prevalence regions, it is scritical to study the increased risks of HIV transmission associated with delayed healing of post-cryotherapy cervical wounds.

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164 — Poster Session

Outcomes for partial metabolic response on posttherapy positron emission tomography for cervical cancer: Role of surgical intervention

S.L. Williams, J. Wilkinson-Ryan, S. Lederhandler, N. Al-Hammadi, A.R. Hagensinn, P.H. Thakorn, M.A. Powell, D.G. Mutch, P.W. Grigsby, J.K. Schwarz. aWashington University School of Medicine, St
Objectives: To describe the management and outcomes of cervical cancer patients with partial metabolic response on postradiation 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) scan.

Methods: We identified women with a partial metabolic response on postradiation FDG-PET from a prospectively maintained database of cervical cancer patients treated with curative intent radiation between 1998 and 2013. Descriptive statistics were used to quantify demographic and treatment data. Kaplan–Meier methods were used to estimate progression-free (PFS) and overall survival (OS).

Results: Sixty-one women with a median age of 50 years (range, 32–88 years) were included. Eighty-five percent of patients had squamous histology; 25% were stage I, 41% stage II, 29% stage III, and 5% stage IV. On pretreatment FDG-PET, 41% of patients had disease confined to the cervix, 48% had FDG-positive pelvic or paraaortic lymph nodes, and 11% had distant extranodal disease. Patients completed a mean radiation dose of 4939 ± 518 cGy to the pelvis with brachytherapy boost to the primary tumor delivered over a median of 49 days (range, 36–90 days), with 92% receiving radiosensitizing chemotherapy. Posttherapy FDG-PET was performed over a median of 91 days (range, 6–152 days) after completion of treatment. Thirty-four women underwent biopsy after their posttherapy FDG-PET; 13 were found to have biopsy-proven persistent disease. Nine patients with localized persistent disease underwent surgery: radical hysterectomy (n = 3), pelvic exenteration (n = 2), or disease-specific resection via lymphadenectomy or simple hysterectomy followed by adjuvant chemotherapy or radiation (n = 4). The remaining four had unresectable disease and received chemotherapy. The median survival following surgery was 28.7 months (range, 9.6–110.1 months) compared to 3.6 months (range, 2.8–5.8 months) with chemotherapy alone. During follow-up (median 27.9 months; range, 3.2–156.6 months), 30 additional patients were diagnosed with recurrence for a total of 43 patients with recurrent or persistent disease (mean PFS 38 ± 5.8 months). Thirty-six patients died (mean OS 67.5 ± 7.5 months) during follow-up.

Conclusions: Women with partial metabolic response on FDG-PET following curative intent radiation have a guarded prognosis, with a potential benefit from early surgical intervention for localized persistent disease.

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165 – Poster Session
Incidence of human papillomavirus, cervical dysplasia and cervical cancer among women in Liberia: Assessing the burden of disease
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Objectives: Cervical cancer (CC) continues to be a major cause of morbidity and mortality among women living in resource-limited countries. In Liberia, incidence and prevalence data for human papillomavirus (HPV) and CC are unknown. The purpose of this study was to establish baseline data regarding HPV, cervical intraepithelial neoplasia (CIN), CC, and known risk factors among Liberia women.

Methods: Institutional review board approval was obtained from both our institution and the University of Liberia, Monrovia. Fourteen volunteer nurses (VN) underwent training as health care providers for this program, as previously described. Women enrolled in the study consented to gynecologic examination by a VN in the presence of physician staff until 60 supervised examinations were performed, after which trained VNs acted independently. Demographic information was collected and included sexual and lifestyle history. Women were included if they were aged 16–85 years, had no previous history of cervical cancer, and were not pregnant. The examination included visual inspection with acetic acid (VIA); Papanicolaou (Pap); and testing for HPV, gonorrhea/chlamydia (GC/C), human immunodeficiency virus (HIV), and syphilis (RPR). VIA findings consistent with low-grade CIN were offered treatment with cryotherapy at the time of VIA or within 48 h. Women with lesions suspicious for high-grade CIN or invasive cervical cancer underwent colposcopy-guided biopsy and were treated according to consultation with a gynecologic oncologist.

Results: A total of 1041 women consented for participation; 154 participants did not meet the inclusion criteria and were excluded. VIA was performed on 887 women, of whom 8% had findings consistent with low-grade dysplasia and were scheduled for cryotherapy. A total of 616 cervical smears were submitted for Pap and HPV testing. Of the 614 evaluable samples, 20.3% were positive for high-risk HPV and 9.25% were reported as abnormal cytology (ranging from atypical squamous cells of unknown significance to high-grade squamous intraepithelial lesion). GC/C was positive in 1.3%. HIV and RPR rates were 2.93% and 1.96%, respectively. Five patients were excluded due to advanced invasive cervical cancer. Comparisons of matched VIA and cervical smear results are currently underway.

Conclusions: These are the first data available on HPV and CC prevalence in Liberia. The information gained from this study should allow for the initiation of public health planning with regard to expanded screening, health education, and HPV vaccination programs.

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166 – Poster Session
Factors influencing acceptability of the HPV vaccine among urban women
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Objectives: To survey urban women to identify risk factors for human papillomavirus (HPV) vaccine refusal and areas for intervention aimed at increasing acceptability.

Methods: Two hundred women age 12–34 years presenting for gynecologic care were surveyed to assess socioeconomic status, gynecologic history, sexual practices, and knowledge and acceptability of the HPV vaccine. Fifteen women subsequently participated in semistructured qualitative interviews to further explore barriers to vaccine uptake. Standard statistical methods were used to analyze dichotomous and continuous variables.

Results: A total of 102 (51%) women reported willingness to accept the HPV vaccine at the time of their visit, but only 82 (41%) reported that they actually initiated vaccination. Series completion rate was 46% (38/82) for those who did initiate the series, yielding an overall rate of 19% (38/200). African Americans were more likely to accept the vaccine than Caucasians (odds ratio [OR] 2.13, 95% CI 1.00–4.51). There was a trend toward increased acceptability among women of lower household incomes (P = 0.06). Factors related to women being more likely to accept vaccination were: private insurance (OR 2.05, 95% CI 1.15–3.36), higher parity (1.20 vs. 0.83, P = 0.04), increasing number of sexually transmitted infections (OR 1.4, 95% CI 1.02–1.90), and increasing number of lifetime Papanicolaou (Pap) tests (P < 0.01). Number of sexual partners and history of abnormal Pap tests did not predict vaccine acceptability. Women unwilling to accept the vaccine were less likely to believe they could stop routine screening after vaccination (P < 0.01) and more likely to believe they could stop routine screening after vaccination (P = 0.04). There was no difference in knowledge
regarding risk of cervical cancer, role for barrier methods regardless of vaccination status, or route of HPV spread. In interviews, those refusing the vaccine were most likely to cite lack of information as the reason. Most women preferred reading or watching educational material.

**Conclusions:** HPV vaccine acceptability among this group of urban women is poor and misinformation is common. Through the survey process, prior reported disadvantages to African Americans may be negated, suggesting a role for targeted educational interventions in increasing acceptability. Further studies are warranted to determine the efficacy of various educational methods.

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**167 – Poster Session**

**Cervical cancer screening in rural Guatemala**

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**Objectives:** The prevalence of human papillomavirus among women in Guatemala approaches 40% and the prevalence of abnormal cervical cytology is 8%. However, the estimated population coverage of cervical cancer screening is <10%, highlighting an important gap in health care. Our objective was to determine which screening methods were used in rural Guatemala and the sensitivity of the methods for cervical cancer detection.

**Methods:** All cervical cancer screening records from hospitals and clinics that offer surveillance in Santiago Atitlan, Guatemala, were reviewed from 1/2012 to 11/2012.

**Results:** In Atitlan, cervical cancer screening is provided by three institutions that differ in method, availability, and cost: a private hospital, a public government-funded community health center, and a health outreach organization via mobile clinics. Of the 202 women who underwent Papanicolaou screening (Pap) at the private hospital, there were no cases of abnormal cytology. Of the 128 women who underwent Pap at the mobile outreach clinics, there was one result of cervical intraepithelial neoplasia 3 and one cervical carcinoma. Of the 41 women who underwent visual inspection with acetic acid (VIA) at the public community health center, there was one abnormal result.

**Conclusions:** Among the 330 women who underwent cervical cancer screening via Pap, only two had abnormal results (0.6%), which is discordant with the reported national rate of abnormal cervical cytology. Our data suggest a low sensitivity for screening with Pap in this region. These findings support other studies suggesting that although Pap testing has effectively decreased cervical cancer rates in developed countries, developing countries may lack the infrastructure required to maintain a successful Pap screening program. Further exploration is necessary to determine the etiology of this low sensitivity, focusing on the quality of laboratories, training of providers, access to supplies, means of transporting specimens, and patient tracking systems.

**Table 1**

<table>
<thead>
<tr>
<th>Institution</th>
<th>Screening</th>
<th>Cost</th>
<th>#Patients screened</th>
<th>#Abnormal results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private hospital</td>
<td>Pap</td>
<td>60 Quetzales ($7.68)</td>
<td>202</td>
<td>0</td>
</tr>
<tr>
<td>Public outreach</td>
<td>Pap</td>
<td>2 Quetzales ($0.26)</td>
<td>128</td>
<td>2</td>
</tr>
<tr>
<td>organization</td>
<td></td>
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**168 – Poster Session**

**Catastrophic intraperitoneal recurrence in patients with early cervical cancer treated with laparoscopic/robotic radical hysterectomy**

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**Objectives:** This study was designed to investigate the pattern of disease recurrence and identify the clinicopathologic prognostic factors for patients with FIGO stage IB and IIA cervical carcinoma treated with abdominal radical hysterectomy (ARH) or laparoscopic/robotic radical hysterectomy (LRH/RRH).

**Methods:** We conducted a retrospective analysis of 239 patients with FIGO stage IB and IIA cervical cancer. All patients had no evidence of parametrial invasion and lymph node metastasis in preoperative examination and underwent ARH or LRH/RRH with retroperitoneal lymphadenectomy between February 2006 and December 2013. Sites of disease recurrence and all possible clinicopathologic factors related to the risk of disease recurrence were determined.

**Results:** Of the 239 patients, 111 (46.4%) and 128 (53.6%) received ARH and minimally invasive surgery (MIS), respectively. We categorized the MIS group into LRH through vaginal colpotomy (LRH-VC; 79 patients) and LRH/RRH through intracorporeal colpotomy (LRH/RRH-IC; 49 patients) according to the colpotomy approaches. Multivariate analysis in MIS group demonstrated that laparoscopic intracorporeal colpotomy (OR = 7.038, 95% CI = 1.059–15.183, P < 0.041) represented a strong prognostic factor related to disease recurrence. Five-year disease-free survival rates were 88.1% in the ARH group and 88.7% in the MIS group (P = 0.940). However, disease recurrence was higher in LRH/RRH-IC group than in LRH-VC group (16.3% vs. 5.1%, P = 0.057), with five patients in LRH/RRH-IC group having intraperitoneal spreads.

**Conclusions:** It remains to be elucidated whether laparoscopic intracorporeal colpotomy under carbon dioxide pneumoperitoneum might be related to disease recurrence, including intraperitoneal spread, in early-stage cervical cancer patients undergoing laparoscopic/robotic radical hysterectomy.

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**169 – Poster Session**

**Quality improvement audit of cervical cancer screening in Mbeya, Tanzania**

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**Objectives:** Cervical cancer is among the leading causes of death among women in the world, especially in developing countries. Due to lack of screening programs and high human immunodeficiency virus (HIV) burden, affected women are often diagnosed with advanced stages of cervical cancer. The long course of progression from dysplasia to cancer offers a significant opportunity for screening and treatment, especially in these at-risk populations. In 2011, the United Republic of Tanzania Ministry of Health and Social Welfare released a plan for prevention and control of cervical cancer. The approach is comprehensive and includes training, documentation of care, and initiation of a human papillomavirus vaccination program.

**Methods:** Over a 2-week period in May 2014, we visited two sites in Mbeya, Tanzania. Our visit consisted of data analysis and performance improvement recommendations of Tanzania’s visual inspection with acetic acid (VIA) program.

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Results: A total of 4413 patients had been screened for cervical cancer at the two sites, and 2163 records were available for review. Of the records we reviewed, 26.3% of patients were HIV-positive and 7.4% had unknown HIV status. Results of VIA and interventions showed increased VIA-positive rate in HIV-positive patients (6.7% vs. 2.9%) and a large number of incomplete records.

Conclusions: Significant progress has been made in Mbeya since the initiation of the cervical cancer screening program. Process improvement measures should include development of an electronic database, future visits with focus on research opportunities, and expansion of the VIA/cervical dysplasia treatment training program.

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170 – Poster Session
Laparoscopic surgical management in early-stage cervical cancer: Analysis of surgical and oncological outcome
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Objectives: Evaluate the morbidity and the oncological outcome of cervical cancer patients treated with laparoscopic radical hysterectomy (LRH).

Methods: We included all patients with early-stage cervical cancer (FIGO stages IA, IB1, IIA1, and IIIB) undergoing LRH from January 1999 to December 2013 in our center. Morbidity was classified according to the Clavien and Dindo classification.

Results: A total of 170 patients were included, of whom 7 patients were stage IA2, 150 were IB1, 2 were IIA, and 7 were IIIB. Mean operation time was 256 min (range, 67–495 min). Fourteen severe perioperative complications (8.2%) occurred, and five (2.9%) patients required conversion to an open procedure. The complications included: bowel injuries (3), hemorrhages (3), ureteral injuries (2), bladder injuries (3), severe adhesions (2), and intolerance of Trendelenburg position (1). Fourteen patients (8.2%) had one severe postoperative complication (grade III or more). Two factors appeared to be independent risk factors for peri- and/or postoperative complication: tumor size (OR 1.128, 95% CI 1.054–1.207) and operative time (OR 1.0116, 95% CI 1.003–1.020). In a median follow-up of 47.7 months, the 5-year overall survival was 94.1% (range, 88.1%–97.3%) and the 5-year disease-free survival was 88.8% (range, 81.0%–92.6%).

Conclusions: The laparoscopic approach has favorable perioperative and postoperative morbidity. With the advantage of minimal invasiveness, laparoscopic treatment by experienced surgeons is an alternative for early-stage cervical cancer with correct long-term survival outcomes. Mini-invasive surgery could be the standard in early cervical cancer.

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172 – Poster Session
Prognostic value of preoperative intratumoral FDG uptake heterogeneity in uterine cervical cancer
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Objectives: Intratumoral fluorodeoxyglucose ([18F]FDG) uptake heterogeneity reflects disease outcome. We investigated the prognostic value of intratumoral heterogeneity (IH) as determined using positron emission tomography (PET)/computed tomography (CT) in patients with uterine cervical cancer.

Methods: Patients with FIGO stage IB to IIA uterine cervical cancer were imaged using [18F]FDG PET/CT before radical surgery. IH, maximum standardized uptake values (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) were measured for each patient. Regression analyses were used to identify clinicopathologic and imaging variables associated with progression-free survival (PFS).

Results: We retrospectively reviewed the clinical data, treatment modalities, and results of 48 eligible patients. Median PFS was 40 months (range, 3 to 43 months), with recurrence in five patients (10.4%). IH at a an SUV of 2.0 correlated with primary tumor size (P < 0.001), SUVmax (P < 0.001), MTV (P < 0.001), TLG (P < 0.001), and PM invasion (P = 0.012). Cox proportional HR revealed that recurrence was significantly associated with SUVmax (P = 0.005), TLG (P = 0.007), IH (P = 0.023), SUVmax (P = 0.030), and FIGO stage (P = 0.037). Multivariate analysis showed that IH (P = 0.020; HR, 7.44; CI, 2.87–19.31; P = 0.005), TLG (P = 0.007), SUVmax (P = 0.005), and FIGO stage (P = 0.022; HR, 2.90; CI, 2.23–3.77; P = 0.005) were independent risk factors for recurrence.

Conclusions: Preoperative IH, as determined using FDG PET/CT, was significantly associated with cervical cancer recurrence and may be a useful quantitative biomarker for disease prognostication before treatment.

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173 — Poster Session
Chemosensitizing effect of aqueous extract of sweet fennel in cisplatin treated HeLa cells
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Objectives: Cisplatin is an important chemotherapeutic agent that is widely used in treatment against several malignancies, but the adverse effects in normal tissues and organs limit its use. The aim of this study was to evaluate the effect of aqueous extract of sweet fennel alone and in combination with cisplatin on a human cervical cancer adenocarcinoma cell line (HeLa cells) in a search for an effective, cost-effective therapy with minimal adverse effects.

Methods: The HeLa cell line was used to study the cytotoxic effect of different concentrations of the aqueous extract of sweet fennel alone and in combination with 50 mcg/mL cisplatin. Drug interaction was quantified by the combination index. Gas chromatography–mass spectrometry (GC–MS) and high-performance liquid chromatography (HPLC) were used to analyze the components of the sweet fennel decoction. MTT assay was used to examine cell viability percentage. Electron microscopy was applied to study the ultrastructure of the cells.

Results: The phenyl propanoids (23%) and phenols (12%) constituted the highest percentage of the aqueous extract. Increasing the concentration of sweet fennel from 50 mcg/mL to 80 mcg/mL decreased the percentage of cell viability of HeLa cells from 86.74% to 78.28%, respectively. Further decrease to 11.31% was demonstrated when 50 mcg/mL of fennel was combined with 50 mcg/mL cisplatin (additive effect). In addition to the signs of apoptosis observed in HeLa cells at 50 mcg/mL of fennel, disruption of both nuclear and cytoplasmic membranes and presence of autophagolysosomes were noticed at a dose of 80 mcg/mL. Combining 50 mcg/mL of cisplatin with 60, 70, and 80 mcg/mL of sweet fennel revealed no significant difference in comparison to cisplatin alone. The combination with 50 mcg/mL of sweet fennel revealed marked vacuolization of the cytoplasm, fragmentation of the nucleus, and complete disruption of the nuclear membrane.

Conclusions: The combination of cisplatin and 50 mcg/mL fennel could enhance inhibition of cervical cancer growth. This combination could be effective in lowering the dose of single or repeated cumulative courses of cisplatin and, hence, decrease its hazardous adverse effects. In vivo studies and the evaluation of different combination doses of cisplatin and sweet fennel are recommended.

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174 — Poster Session
Treatment compliance among medically underserved women receiving chemoradiation for locoregionally advanced cervical cancer
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Objectives: To assess treatment compliance among women undergoing definitive chemoradiation with weekly cisplatin for locoregionally advanced cervical cancer in a regional safety-net health system.

Methods: After obtaining institutional review board approval, clinical demographics were abstracted for all women treated with definitive chemoradiation for cervical cancer (FIGO IB2-IVA) between March 2007 and May 2014. Reasons for treatment delays were categorized as being cisplatin-related, related to comorbid medical conditions, patient-initiated (e.g., declined treatment), or system issues (e.g., scheduling error).

Results: A total of 121 women (mean age 48.6 ± 12.5 years) received chemoradiation for cervical cancer. Tumor histologies included squamous (n = 100, 83%), adenosquamous (n = 14, 12%), poorly differentiated (n = 6, 5%), and adenocarcinoma (n = 1, 1%). A total of 116 (95.9%) women completed definitive radiotherapy as planned (mean duration 56.2 ± 20 days). Of these, 66 (58.4%) completed radiotherapy in ≤56 days. Only 44 women (36.4%) received all six planned cycles of weekly cisplatin. Of the remaining women, 46 (38.0%) received five cycles, 17 (14.0%) received four cycles, and 14 (11.6%) received three cycles or less. Among 122 delayed cycles, reasons cited for chemotherapy delays included cisplatin toxicities (n = 54, 44.3%), medical comorbidities (n = 28, 22.9%), patient-initiated (n = 13, 10.6%), and system issues (n = 8, 6.6%). Two or more issues complicated treatment for seven doses (5.7%). Reasons for delay were not documented for 12 cisplatin doses (9.8%). Twelve of 121 first planned cycles were delayed, of which 5 (41.7%) were due to comorbid conditions and functional status. As treatment progressed, chemotherapy-associated toxicities became increasingly common. Of 77 planned sixth cycles, 39 (50.6%) were held, with 20 (51.2%) held due to cisplatin toxicities.

Conclusions: Medically underserved patients undergoing definitive radiotherapy for cervical cancer experience more delays with weekly cisplatin than demonstrated in clinical trials establishing the need for concurrent chemotherapy. Future efforts to improve outcomes for these women should focus on addressing preventable reasons for delays, such as system issues and patient noncompliance. Chemotherapy regimens associated with less toxicity may also benefit this vulnerable population.

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175 — Poster Session
Upfront laparoscopic surgery in IB2 cervical cancer: Surgical and survival outcomes

Objectives: To assess surgical and survival outcomes of upfront laparoscopic radical surgery patients affected by FIGO stage IB2 cervical cancer.

Methods: In the observed period, all patients with FIGO stage IB2 cervical cancer received upfront laparoscopic surgery, including radical surgery if the lymph nodes were found to be tumor-free. Data collection for these women should focus on addressing preventable reasons for delays, such as system issues and patient noncompliance. Chemotherapy regimens associated with less toxicity may also benefit this vulnerable population.

Conclusions: Surgical upfront treatment is feasible in patients affected by stage IB2 cervical cancer.

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176 — Poster Session
The impact of lymph node density (LND) on outcome in pelvic lymph node-positive cervical cancer patients
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Objectives: To investigate the prognostic value of lymph node density (LND) in patients with lymph node (LN)-positive cervical cancer.

Methods: Through a review of medical records, cervical cancer patients with LN-positive and >10 excised LNs were enrolled. LND was defined as the ratio of positive LNs to the total number of excised LNs. To determine the cutoff value of LND to best discriminate the prognosis, a time-dependent receiver operating characteristic (ROC) curve was used. Survival rate was calculated using the Kaplan–Meier method, and the Cox regression model was used to evaluate the prognostic significance of LND on progression-free survival (PFS).

Results: A total of 140 patients were included. A cutoff of 6.3% LND was selected by time-dependent ROC curve for PFS. The median follow-up time was 51.9 months (range, 3–157 months) and the median LND was 9.6% (range, 1.8%–74%). Of 140 patients, 66.4% (93/140) had the LND ≥6.3%, and the patients with LND ≥6.3% showed significantly higher lymphovascular space invasion and systemic LN recurrence rate than those with LND <6.3% (P = 0.012 and P = 0.046, respectively). In univariate analysis, LND (≥6.3% vs. <6.3%), 5-year PFS rate 81.2% vs. 60.9%, P = 0.016) and histology (squamous cell carcinoma [SCC] vs. non-SCC, 5-year PFS rate 73.7% vs. 35.2%, P < 0.0001) were significantly associated with PFS. In multivariate analysis, LND ≥6.3% (HR 2.6, 95% CI 1.16–5.66, P = 0.02), and histology of non-SCC (HR 4.2, 95% CI 2.20–8.25, P < 0.0001) were independent predictors for poorer PFS.

Conclusions: The results suggest the applicability of LND as a predictor of outcome in cervical cancer patients with nodal metastasis. LND could assist in identifying patients with disease progression for whom more aggressive adjuvant treatment is considered.

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178 – Poster Session

Cervical cancer recurrence risk evaluation based on SUV(max) during initial ^18^F-FDG PET/CT

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Objectives: To determine the prognostic significance of the pretreatment maximum standardized uptake value (SUV(max)) of [18F]fluorodeoxyglucose (FDG) in FDG-potisitron emission tomography (PET)/computed tomography (CT) imaging in patients with stage IB2–IVA cervical cancer. FDG uptake can be a predictive marker of disease recurrence in patients with cervical cancer, but no definitive threshold of the SUV(max) has been demonstrated. The secondary objective was to evaluate the pre- and posttreatment PET scan and determine a percentage reduction in the SUV(max) below which patients were at higher risk for recurrence of disease.

Methods: Retrospective review of stage IB2–IVA cervical cancer patients at Florida Hospital Cancer Institute from January 2009 through December 2012 was performed. Patients with FIGO stages IB2–IVA disease who had a pretreatment PET scan were included in the evaluation. All patients received primary whole pelvic radiation therapy with concurrent radiosensitizing chemotherapy. Thirty-one patients met the criteria. Patients were grouped into those with recurrence of disease and those without evidence of disease at last follow-up. Pre- and posttreatment SUV(max) were compared in relation to each patient’s disease status.

Results: Median patient age was 49 years (range, 26–84 years) and median body mass index was 29 (range, 21–43). Histologic breakdown was: 80% squamous, 16% adenocarcinoma, and 4% other. The median follow-up time was 20.5 months (range, 3 to 72 months). The mean and median SUV(max) in the recurrence-free group were 22 and 19.9, respectively. The mean and median SUV(max) in the recurrence group were 21.2 and 21.3, respectively. Although the difference in pretreatment SUV(max) was not statistically significant between the two groups, we did observe a greater difference in percentage reduction in the disease-free group vs. the recurrence group. The mean difference in SUV(max) was only 13.3 for the patients with disease recurrence, with all showing some residual uptake on posttreatment PET. In contrast, the mean difference in SUV(max) in the disease-free group was 20.1, with >54% of patients demonstrating no residual disease.

Conclusions: Although the SUV(max) on pretreatment PET scan was not indicative of disease recurrence, we did find a correlation when comparing the percent difference in the pre- and posttreatment SUV(max). This finding may guide clinicians in patient selection for sequential chemotherapy.

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Salvage laparoscopic lymphadenectomy combined to chemotherapy and/or radiation therapy for isolated para-aortic nodal recurrence of cervical cancer: Morbidity and outcomes of a case series

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**Objectives:** To present a case series of 12 patients with isolated paraaortic recurrence of cervical cancer treated with salvage laparoscopic lymphadenectomy and chemotherapy and/or radiation therapy.

**Methods:** Twelve consecutive patients with isolated paraaortic recurrence of cervical cancer were selected. Mean age was 43.6 years (range, 21–73 years). Only three patients had symptoms associated with the diagnosis (lumbago); the other nine diagnoses were based on computed tomography scans or magnetic resonance imaging requested routinely during follow-up (Table 1). Due to bulky lymph nodes, three patients received chemotherapy prior to surgery.

**Results:** The surgical procedure was performed via a transperitoneal approach, with three 5-mm ports in the lower quadrants and one 11-mm port at the umbilicus. The lymphadenectomy was systematic, including the retroperitoneal lymphovascular tissues, from the level of the common iliac vessels in both sides until the left renal vein (Video). Mean operative time was 260 min, mean blood loss was 122 mL, and no transfusion was necessary. There was one conversion due to a vascular injury (left common iliac vein). Complete resection of the node was interrupted in this case (R2 resection). All the other 11 patients received a complete macroscopic resection. Mean postoperative hospitalization was 1.5 days (range, 1–4 days). There was no ureteral or nerve injury. Ten patients received postoperative treatment, including chemoradiotherapy or isolated radiotherapy (Table 1). Nine patients recovered after the salvage therapy, with a mean recurrence interval of 10 months (range, 0–31 months). There was a significant correlation between the time interval for the first recurrence and for the second recurrence (Graph 1). Four patients died of disease 8, 11, 14, and 27 months after salvage surgery, respectively. The estimated overall survival in 30 months was 31%. Three patients are alive free of disease, with a maximum follow-up of 21 months.

**Conclusions:** Salvage laparoscopic paraaortic lymphadenectomy is feasible, with acceptable morbidity, and could improve overall survival and disease-free survival. There was a correlation between time to first relapse and time to the second relapse in this small series.

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**181 – Poster Session**

Molecular signaling pathways associated with squamous-cell carcinoma of the cervix cisplatin-resistance


**Objectives:** Women with locally advanced and metastatic squamous cell carcinoma of the cervix (SCC) are frequently treated with cisplatin (CIS). Unfortunately, many patients develop platinum-resistant disease that is associated with poor outcome and for which the molecular basis has yet to be fully delineated. We sought to elucidate the molecular pathways that are associated with the evolution of SCC CIS resistance.

**Methods:** Three groups of two cervical cancer cell lines (ME-180 and ME-180R) were treated with increasing CIS concentrations (Group A: 1–3 μg/mL, Group B: 2–4 μg/mL, Group C: 3–5 μg/mL). Prior to CIS treatment and at each dose level following treatment and cell recovery, RNA was extracted and subjected to genome-wide expression analysis using U133 plus 2.0 Affymetrix Arrays. At baseline and after each treatment/recovery cycle, CIS resistance was quantified (EC50). Microarray data were robust multiaarray average-normalized, and genes associated with SCC CIS EC50 (identified using SAM) were subjected to pathway analysis (MetaCore from GeneGo). Expression of SCC CIS resistance pathways was evaluated for associations with clinical variables in two external databases (GSE7803, n = 41 and GSE56363, n = 21).

**Results:** A total of 409 probe sets (false discovery rate < 0.01) representing 11 pathways (P < 0.001) were associated with SCC development of in vitro CIS resistance. Pathways included PTMS, Activin-A, TGF-EMT, TGF-beta, VEGF-sig, amino-regulation, ESR1-ESR2, GDNF, PAR1-PAR2, NF-kB, and ESR1-SP. In clinical datasets from patients with SCC, 11/11 CIS-resistance pathways were also found to be differentially expressed in clinical samples based upon patient response.

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to CIS (complete vs. incomplete responders). Five of 11 pathways were differentially expressed between normal cervix and cervical intraepithelial neoplasia (CIN), 8 of 11 pathways were differentially expressed between CIN and SCC, and 10 of 11 pathways were differentially expressed between normal cervical tissue and SCC. Conclusions: We identified molecular signaling pathways associated with SCC in vitro and in vivo resistance to CIS. Many of these pathways may also be associated with the transition of normal cervical epithelium to CIN and invasive disease. Identified pathways are now subject to functional analysis, including study of pathway inhibition on SCC CIS resistance and cell proliferation/apoptosis.

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182 — Poster Session
Cervical adenocarcinoma in situ: An institutional retrospective review of surgical management and outcome

Objectives: The aim of this study was to review management of patients with adenocarcinoma in situ of the cervix as well as to identify the difference in progression-free survival and future fertility outcomes based on the type of surgical management.

Methods: A retrospective review of complete records between 1990 and 2014 identified 49 patients with adenocarcinoma in situ on cone biopsy. The median follow-up time was 30 months.

Results: The mean age at diagnosis was 36 years, and the mean parity was 1.2. Initial cervical biopsies showed adenocarcinoma in situ in 36 (73%), squamous dysplasia in 19 (39%), and no pathology in 3 (6%) patients. Subsequently, 47 patients (96%) had cone biopsies. Margins were positive for glandular abnormalities in 30% of cold knife cones (CKC), 71% of loop electrosurgical excision procedures (LEEP), and 10% of laser cones. Out of 34 patients with endocervical curettage, 5 (14%) were positive. The definitive treatment was hysterectomy in 21, repeat cone in 3, and no additional therapy in 23 patients. Residual disease was noted in 30% of treated patients. Among 18 cone biopsies with negative margins followed by subsequent treatment, there was residual disease in eight (44%). Among 11 cones with positive margins followed by subsequent treatment, there was residual disease in seven (64%). There were no instances of recurrence in any of the 49 patients, with median follow-up time of 20 months for the conization group and 39 months for those who underwent hysterectomy. Of those patients who underwent conization, five patients (19%) subsequently became pregnant, with a total of five uncomplicated term deliveries. One was assisted with a history-induced abdominal cerclage after a spontaneous abortion at 15 weeks’ gestation. There were no adverse neonatal outcomes.

Conclusions: Women with adenocarcinoma in situ of the cervix had residual disease in 44% of cases with negative margins in cone biopsies and in 64% of cases with positive endocervical margins. LEEP cones had a higher rate of positive endocervical margins (57%) compared to CKC (20%) and laser cone (10%). Nineteen percent of those patients who sought future fertility have achieved five successful term deliveries with no maternal or neonatal compromise. Hence, conservative management with a high probability of successful pregnancy is possible. Despite previous reports, our experience demonstrated a much lower incidence of recurrence with conservative management.

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183 — Poster Session
Radical hysterectomy: Programmatic change to reduce laparotomy rate while maintaining oncologic outcome for early stage cervical cancer

Objectives: To determine the impact on surgical approach and perioperative and overall survival outcomes for radical hysterectomy performed for cervical cancer since the introduction of a robotics platform at our institution in 2007.

Methods: We identified all patients scheduled to undergo radical hysterectomy for newly diagnosed cervical cancer from 1/1/2007 to 12/31/2013 at our institution. Adenocarcinoma in situ (ACS) to stage IIA invasive carcinoma was included. Patients were excluded for conversion from a planned fertility-sparing trachelectomy or if they received neoadjuvant treatment. Operative time was defined as initial incision to skin closure. Area of parametrial tissue resected was defined as the width times the length of parametrial tissue as measured by pathology. Clinical and operative data were abstracted from the medical record. Perioperative and overall survival outcomes were evaluated. Standard statistical tests were applied.

Results: Of 152 patients, 74 (49%) had a robotic procedure (RBT), 72 (48%) had laparotomy (LAP), and 6 (4%) had laparoscopy (LSC). There were two conversions to laparotomy, both of which were planned RBT cases (2.7%). The majority of cases (119/152 [78%]) had stage IB disease. There was no difference in median age, body mass index, prior pelvic surgery, stage of disease, nodal counts, parametrial size, vaginal cuff size, and surgical margin status among RBT, LAP, and LSC. Median operative time was 266 min (range, 132–562 min) for RBT, 345 min (range, 265–416 min) for LSC, and 204 min (range, 120–381 min) for LAP (P < 0.001). Estimated blood loss was 100 ml (range, 10–1250 ml) for RBT, 200 ml (range, 100–350 ml) for LSC, and 300 ml (range, 0–850 ml) for LAP (P < 0.001). Median length of stay was 1 day (range, 0–4 days) for RBT, 3 days (range, 2–5 days) for LSC, and 3 days (range, 2–9 days) for LAP (P < 0.001). Over the 7-year study period, RBT volume increased while LAP volume decreased (P = 0.001). The rate of LAP was 96% in 2007 compared to 39% in 2013 (P < 0.001). Excluding the two cases of ACIS, the median follow-up was 26.2 months (range, 0.3–75.8 months). Three-year OS was 92.3 ± 4.4% for RBT and 89.1 ± 4.2% for LAP (P = 0.2).

Conclusions: Use of the robotic platform is associated with similar oncologic outcomes compared to laparotomy. A programmatic increase in RBT cases corresponded to a significant decrease in LAP, raising potential implications regarding quality of life and cost.

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184 — Poster Session
QRF1 expression results in oncogenic potential and poor prognosis in cervical cancer
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Objectives: QRF1 is considered as both a tumor suppressor candidate and a potential oncogene. Here, we investigated QRF1 expression in cervical cancer and the clinical significance of QRF1 and its mechanism of action in cervical cancer.

Methods: The functional role QRF1 was investigated by employing lentiviral-mediated overexpression and knockdown in cervical cancer cell lines. Immunohistochemical staining for QRF1 was performed on a cervical cancer tissue microarray consisting of 158 primary cervical
cancers, 280 cervical intraepithelial neoplasias, and 378 matched normal tissues.

**Results:** QRF1 overexpression promoted cell proliferation and tumorigenesis, whereas QRF1 knockdown inhibited these properties in HeLa and CaSki cell lines. On immunohistochemical staining, QRF1 expression increased during the normal-to-tumor transition of cervical carcinoma ($P < 0.001$), and this increased expression was significantly associated with tumor stage ($P = 0.009$) and tumor grade ($P < 0.001$). In multivariate analysis, QRF1 + ($P = 0.031$) and tumor stage ($P = 0.032$) were independent prognostic factors for overall survival.

**Conclusions:** Taken together, our data indicate that QRF1 has a crucial role in cervical cancer progression, and its overexpression is associated with poor prognosis, supporting the hypothesis that QRF1 may be used as a promising novel target for therapeutic interventions.

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**185 – Poster Session**

**Postoperative intensive-modulated radiation therapy (IMRT) with or without concurrent chemotherapy for intermediate- and high-risk cervical cancer patients**

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**Objectives:** In Taiwan, IMRT has been used for cervical cancer treatment since 2001. This study sought to assess local control and toxicity with adjuvant IMRT with or without concurrent chemotherapy and brachytherapy for intermediate- and high-risk cervical cancer patients following hysterectomy and if applicable, retropitoneal lymph node dissection.

**Methods:** From January 2004 to December 2012, 68 patients diagnosed with early-stage cervical cancer underwent hysterectomy ($n = 15$), modified radical hysterectomy ($n = 2$), and radical hysterectomy ($n = 51$). Pelvic lymph node dissection was performed in the modified radical hysterectomy and radical hysterectomy groups ($n = 56$, median 35 nodes removed). Median dose of postoperative pelvic IMRT was 50.4 Gy (range, 4000–7000 Gy). Sixteen patients received concurrent chemotherapy with cisplatin only, and two patients with cisplatin plus 5-fluorouracil. Thirty-three patients received brachytherapy to boost local control, with a median dose of 1000 cGy in two fractions.

**Results:** With a median follow-up of 74 months, nine patients have recurred. All of them received radical hysterectomy. There were three regional recurrences, three regional and distant recurrences, and five distant recurrences. The 5-year overall survival (OS) was 88.9%, with a median OS of 9.1 years (95% CI, 8.5–9.7). The 5-year disease-free survival (DFS) was 88.1%, with a median DFS of 9.0 years (95% CI, 8.3–9.7). There was 19.1% ($n = 13$) grade 3–4 hematologic toxicity, no acute grade 3 or higher gastrointestinal toxicity, and 1.5% ($n = 1$) acute grade 3 genitourinary toxicity. There were no chronic grade 3 or higher gastrointestinal or genitourinary toxicities.

**Conclusions:** Our results demonstrated good local control with postoperative IMRT, with DFS and OS rates of >88% at median follow-up of 74 months. The morbidity profile was minimal, even for cases that received the trimodality (surgery, radiation, and chemotherapy) approach. This study demonstrated the advantages of administering IMRT to early-stage postoperative cervical cancer patients.

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**186 – Poster Session**

**Role of neoadjuvant chemotherapy in the management of advanced ovarian yolk sac tumor**

Y. Jiaxin, K. Shen, D. Cao. Peking Union Medical College Hospital, Beijing, China

**Objectives:** The aim of this study was to identify the role of neoadjuvant chemotherapy (NACT) in the treatment of the patients with advanced-stage ovarian yolk sac tumor (OYST).

**Methods:** The comparative study was based on 53 cases with advanced-stage OYST registered at Peking Union Medical College Hospital from 1995 to 2010. Twenty-one cases were treated with NACT followed by interval debulking surgery (IDS). Thirty-two cases were treated with primary debulking surgery (PDS). Data on patient characteristics, treatment, and survival were analyzed and compared between two groups to assess the outcome of NACT.

**Results:** After NACT, the overall status of the patients improved significantly. Patients receiving NACT had better optimal cytoreduction rate and less perioperative morbidity. Seven patients (13.2%) had relapses. There was a significantly better progression-free survival for patients with ovarian tumor size <20 cm receiving NACT than those who underwent PDS. Residual disease >2 cm was an independent risk factor for relapse.

**Conclusions:** NACT is the better treatment option for some patients with advanced-stage OYST, especially those who have unresectable tumors and poor general condition.

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**187 – Poster Session**

**Deep tissue hyperthermia for recurrent/progressive malignancies**

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**Objectives:** Deep-tissue hyperthermia (DTH) is an evidenced-based level 1 intervention used as an adjuvant with chemotherapy and/or radiation. We report a cohort of patients re-treated with radiotherapy (RT) and DTH after previously failing RT.

**Methods:** This institutional review board-approved prospective study evaluated a cohort of patients treated with DTH and RT from August 2011 to August 2014 at a tertiary care center. All patients referred for RT with progressive disease unsuitable for surgery, refractory to chemotherapy, and/or with a prior radiated field were considered for DTH. DTH temperatures were monitored via bladder, rectum, intragluteal fold, and vagina catheters.

**Results:** DTH (2/wk) and RT (5/wk) were administered to 106 patients according to previously reported protocols from randomized clinical trials. Median age was 71 years (range, 22–75 years), 27% were African-Americans, 60% were Caucasian, 13% were other, and 64% were female. Median number of DTH treatments was 9 (range, 1–10). Mean target therapeutic temperature (TTT) was 40.0 °C, maximum TTT was 41.5 °C, and mean time at TTT was 40 min. Median RT dose was 45 Gy (range, 30–60 Gy). Primary tumors were: 27 gynecologic cancers (25.5% of total DTH), with 8 cervical (29.6% of all gynecologic cancers), 7 ovarian (25.9%), 7 uterine sarcomas (25.9%), and 5 endometrial (18.5%); 28 pancreatic (26.4% of total DTH); 26 colorectal (24.5%); and all others 22.2%. In 2013, new gynecologic cancers were less likely to receive DTH than other cancer types: 8/90 (9%) gynecologic vs. 42/3481 (12%) of all other cancers ($P < 0.001$). In the entire 3-year cohort, 8/9 cervical cancers received DTH, as did 7/17 uterine sarcomas, 5/11 endometrial, and 7/33 ovarian ($P < 0.05$ cervical vs. all other gynecologic cancers). The total number of all cancers treated with DTH increased by 53% from 7.9% (20/2,518) in 2012 to 12.1% (42/3,481) in 2013. There were no grade 3 or 4 toxicities.

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Conclusions: Heavily pretreated patients can receive additional DTH therapy in previously radiated fields. However DTH is used in treating recurrent disease in a minority of patients with various cancers. Gynecologic cancers are not more likely to be treated with DTH than other cancers. However, cervical cancers are more likely to be treated with DTH than other gynecologic cancers. DTH may be considered an uncommon option when few others exist.

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188 – Postersession

Adding a molecular profile test to make use of bevacizumab more affordable in ovarian cancer


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Objectives: Bevacizumab is an antiangiogenic monoclonal antibody that is very expensive but has been found to be most effective when tumors overexpress angiogenic markers such as vascular endothelial growth factor A (VEGF-A).

Methods: A cost-effectiveness analysis was performed using a molecular profiling test (cost $1,500). An estimated 64% of women with ovarian carcinoma have tumors that express VEGF-A. Based on the profile results, a standardized patient would receive intravenous carboplatin AUC 6 and paclitaxel 175 mg/m² q 3 weeks or intravenous carboplatin AUC 6, paclitaxel 175 mg/m², and bevacizumab 15 mg/kg q 3 weeks (with maintenance) for the adjuvant treatment of ovarian carcinoma. Actual and estimated costs of treatment and the potential costs of complications were included. One-way sensitivity analysis was performed for the desired variables in the model. Costs were from Centers for Medicare and Medicaid Services and published figures.

Results: Patients were stratified to receive or not receive bevacizumab based on molecular profile results. If molecule profile results were not used, the average cost per life-year saved for a full course of chemotherapy (and potential complications) was estimated to be $13,775 for the regimen without bevacizumab and $182,469 for the bevacizumab-containing regimen. If the chemotherapy regimens were stratified according to the molecular profile results, the average cost of chemotherapy (and potential complications) was greatly reduced to $108,193.

Conclusions: If all patients with advanced ovarian cancer are given bevacizumab, the average cost of therapy is $182,469. If a $150 molecular profile test is added to the treatment regimen and only patients whose tumors express VEGF-A are given bevacizumab, the average cost of chemotherapy is reduced to $108,193/patient.

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189 – Poster Session

The impact of body mass index on intraperitoneal chemotherapy outcomes

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Objectives: Obesity is a growing epidemic in the United States and has been shown to affect treatment-related morbidity and survival in gynecologic cancers [Modestit]. Gynecologic Oncology Group 172 demonstrated an improved median overall survival (OS) with intraperitoneal (IP) chemotherapy [Armstrong]. The aim of this study was to investigate the impact of body mass index (BMI) on treatment with IP chemotherapy and subsequent clinical outcomes.

Methods: Patients with optimally cytoreduced stage IIIC ovarian cancer treated at Brigham and Women’s Hospital and Massachusetts General Hospital were retrospectively identified using an institutional review board-approved database. Demographic, pathologic, and clinical data were abstracted from the longitudinal medical record. Survival estimates were calculated using the Kaplan–Meier method. Primary outcomes included completion of IP chemotherapy and cycle-related complications.

Results: A total of 259 patients were treated between 2005 and 2010, with 92 (35.5%) completed at least one cycle of IP therapy. Among patients treated with IP chemotherapy, there was no difference in tumor site, histology, surgical complexity, or degree of optimal cytoreduction between patients who were normal weight (BMI < 25), overweight (BMI 25–29.9), or obese (BMI > 30). There was no difference in the number of IP cycles completed or the completion of total intended cycles, with 67.5% of normal weight, 70.0% of overweight, and 59.1% of obese women completing six cycles ($P = 0.697$). There was also no significant difference in IP chemotherapy complications based on BMI ($P = 0.303$). Among all patients with class II obesity, only three (15.8%) were treated with IP chemotherapy compared with 16 (84.2%) who were treated with intravenous (IV) therapy ($P = 0.06$) (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Route of chemotherapy based on body mass index.</th>
<th>BMI (~&lt;35)</th>
<th>BMI (~&gt;35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IP chemotherapy</td>
<td>89 (37.1%)</td>
<td>3 (15.8%)</td>
<td>0.06</td>
</tr>
<tr>
<td>IV chemotherapy</td>
<td>151 (62.9%)</td>
<td>16 (84.2%)</td>
<td></td>
</tr>
</tbody>
</table>

IP = intraperitoneal, IV = intravenous, BMI = body mass index.

Conclusions: There was no difference in completion of IP chemotherapy or IP-related complications with respect to BMI. This translated into no significant difference in OS based on BMI. In class II obesity, there was a trend toward increased treatment with IV therapy over IP. These data suggest that IP chemotherapy is feasible in obese patients without incurring increased morbidity but may be selected out by provider bias.

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190 – Poster Session

Trends in FDA approval of oncology drugs: Have we made progress?


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Objectives: To determine the characteristics of oncology drug approvals by the United States Food and Drug Administration (FDA) over the last 20 years.

Methods: Data on drugs approved by the FDA for cancer treatment were extracted from the FDA website from 1995 to 2012. Characteristics of drugs, including type of agent, indication, phase of clinical trial, and clinical benefit, were used in our analysis. For trials that used progression-free survival (PFS) as an endpoint, a relative clinical benefit was determined by calculating the difference in PFS between standard therapy and novel therapy. ANOVA and chi square tests were performed to determine statistical significance.
Results: A total of 37 oncology drugs were approved; 24 were cytotoxic and 13 were biologic agents. Five drugs were approved for breast cancer, five for kidney, four for skin cancer, four for prostate, three for lymphoma, two for leukemia, two for myeloma, two for lung cancer, one for brain cancer, and one for gastric cancer. The number of oncology drugs approved that used PFS as an endpoint varied from 50% to 58% to 40% over the study period (P = 0.78). The median relative benefit of these drugs was 39%, 100%, and 56% over the years 1995–2000, 2001–2006, and 2007–2012, respectively (P = 0.26).

Conclusions: Over the last 20 years, the relative benefit of FDA-approved cancer drugs has not changed. The importance of relative clinical benefit in evaluating new drugs warrants further investigation.

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191 – Poster Session
Antitumor activity of the ribonucleotide reductase inhibitor Triapine alone or in combination with paclitaxel
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Objectives: Triapine is being evaluated as an anticancer agent in National Cancer Institute-funded phase I/II clinical trials. We have elucidated the sequential events in which inhibition of ribonucleotide reductase, the primary action of Triapine, is ultimately conveyed to DNA double-strand breaks after prolonged DNA replication stress. Extensive cell kill by Triapine requires a long exposure period (16 h) at concentrations of 0.6 to 0.8 μM. The aim of the present study was to determine whether Triapine is an effective combination partner of current therapeutics, including carboplatin, paclitaxel, doxorubicin, etoposide, and X-rays, in cell culture as well as in preclinical tumor models.

Methods: Triapine is largely insoluble in aqueous media. Thus, Triapine isethionic salt, soluble in water, was used throughout. The epithelial ovarian cancer (EOC) cell lines SKOV-3 and OV90 were obtained from American Type Culture Collection. Cell-kill in culture was determined using clonogenic assays and combination indices were calculated using a CalcuSyn software. Antitumor activity in vivo was assessed by tumor growth of the murine M109 lung carcinoma (1 × 10⁶ cells) implanted subcutaneously into CD2F1 mice.

Results: In SKOV-3 and OV90 cells, the combination of graded concentrations of Triapine with those of paclitaxel, doxorubicin, etoposide, or X-rays resulted in additive cell kill. In M109 lung tumor, once-a-day injection of Triapine at 40 mg/kg produced insignificant tumor growth delay. In contrast, twice-a-day (8 h apart) injection of Triapine at 10 mg/kg was as effective as paclitaxel at 10 mg/kg/day in producing tumor growth delay. Combining Triapine with paclitaxel resulted in extensive tumor growth delay in an additive manner with minimum host toxicity.

Conclusions: The salt form of Triapine eliminated the use of organic solvent in animal studies. Antitumor activity of Triapine was schedule-dependent; Triapine alone in the twice-a-day regimen was as effective as paclitaxel, while the once-a-day regimen was ineffective. The hallmark of combination chemotherapy is an exploitation of multiple and discrete tumor sites of vulnerability to achieve a higher probability of cure and to avert emergence of drug resistance. This study demonstrating the efficacy of Triapine in combination with paclitaxel suggests that Triapine has a place in the therapeutic armamentarium against EOC.

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192 – Poster Session
Phase II trial of bevacizumab with carboplatin and dose-dense paclitaxel as first-line treatment in patients with advanced ovarian cancer
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Objectives: To assess the tolerability and efficacy of bevacizumab with carboplatin and weekly paclitaxel as first-line adjuvant therapy for advanced-stage epithelial ovarian, peritoneal, and fallopian tube cancers.

Methods: After institutional review board approval, this single-institution phase II study enrolled patients with stage III or IV epithelial ovarian, peritoneal, or fallopian tube cancer after primary cytoreductive surgery to treatment with carboplatin (AUC 5), weekly paclitaxel (80 mg/m²), and bevacizumab (15 mg/kg) every 3 weeks for at least 6 cycles. The primary endpoint was treatment success, defined as the ability to tolerate at least 4 cycles of combination therapy regardless of delay or dose modification, with a target treatment success rate of more than 60%. Secondary endpoints included progression-free survival (PFS) and response rate.

Results: Thirty-three patients were enrolled in the study, and 30 evaluable patients received at least one cycle of combination treatment. Median age was 57 years (range, 31–76 years) and median follow-up was 20.5 months (range, 7.8–51.5 months). The stage distribution was: IIIIB (n = 3), IIIC (n = 26), and IV (n = 1). Four patients (13%) had low-grade and 26 (87%) had high-grade tumors. Following cytoreduction, 16 patients (53%) had no gross residual disease (RO), 9 (30%) had <1 cm residual, and 5 (17%) had >1 cm residual. Twenty-three patients (73%) were able to complete at least 4 cycles of therapy per protocol, and the posterior probability that the treatment success rate is >60% was 0.97. Seventy percent of patients were able to complete ≥6 cycles of therapy. Although 73% of patients experienced at least one treatment delay, 60% required no growth factor support. Fifteen patients (50%) developed recurrence, and four patients (13%) had progressive disease. Median PFS was 22.4 months in optimal (RO) compared to 16.9 months for optimal –1 cm (HR 1.71, 95% CI 0.58–4.98, P = 0.03) and 16.9 months for suboptimal –1 cm (HR 3.75, 95% CI 1.05–13.34, P = 0.04).

Conclusions: Adjuvant bevacizumab with dose-dense chemotherapy is associated with an acceptable toxicity profile and 77% likelihood of completing 4 cycles of therapy on protocol.

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193 – Poster Session
Comprehensive health-related quality-of-life profiling using a novel idiographic goal-oriented metric in patients with advanced malignancies: A pilot study
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Objectives: Data are sparse regarding optimal health-related quality of life (HRQOL) assessment for patients receiving chemotherapy for high-risk gynecologic cancers and for those enrolled in phase I clinical trials. We piloted a dual HRQOL assessment incorporating a validated metric, the QOL Questionnaire 30 (QLQ-30), as well as a novel "idiographic" questionnaire with the aim of identifying the feasibility of implementation and to analyze HRQOL profile differences between two groups.

Methods: Twenty-five women with high-risk gynecologic malignancies (defined as <30% 5-year survival) and 10 active patients enrolled...
in phase I clinical trials were consecutively recruited. Patients’ answers to the QLQ-30 and idiographic QOL assessment were recorded and decoded. Raw scores of the QLQ-30 were standardized using linear transformation. Statistical analysis was performed using R v.3.0.2.

**Table 1**

<table>
<thead>
<tr>
<th>Idiographic goal content</th>
<th>Phase 1 responses (%; n = 87)</th>
<th>High risk responses (%; n = 260)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivational themes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achievement</td>
<td>20 (23%)</td>
<td>85 (33%)</td>
<td></td>
</tr>
<tr>
<td>Solving problems</td>
<td>9 (10%)</td>
<td>31 (12%)</td>
<td></td>
</tr>
<tr>
<td>Prevent or avoid problems</td>
<td>9 (10%)</td>
<td>22 (8%)</td>
<td></td>
</tr>
<tr>
<td>Maintenance/keeping things as they are now</td>
<td>14 (16%)</td>
<td>27 (10%)</td>
<td></td>
</tr>
<tr>
<td>Letting go of responsibilities</td>
<td>5 (6%)</td>
<td>20 (8%)</td>
<td></td>
</tr>
<tr>
<td>Accepting</td>
<td>9 (10%)</td>
<td>15 (6%)</td>
<td></td>
</tr>
<tr>
<td>Reaching an event/milestone</td>
<td>16 (18%)</td>
<td>8 (3%)</td>
<td></td>
</tr>
<tr>
<td>Cancer-specific goals</td>
<td>31 (36%)</td>
<td>56 (23%)</td>
<td>0.062</td>
</tr>
<tr>
<td>Provider and treatment related concerns</td>
<td>10 (11%)</td>
<td>13 (5%)</td>
<td></td>
</tr>
<tr>
<td>Health issues — not cancer</td>
<td>8 (9%)</td>
<td>11 (4%)</td>
<td></td>
</tr>
<tr>
<td>Existential/end of life concerns</td>
<td>6 (7%)</td>
<td>14 (6%)</td>
<td></td>
</tr>
<tr>
<td>Independent functioning</td>
<td>2 (2%)</td>
<td>26 (11%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Sexual functioning</td>
<td>0</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Mental health and mood</td>
<td>1 (1%)</td>
<td>12 (5%)</td>
<td></td>
</tr>
<tr>
<td>Self image and personality</td>
<td>2 (2%)</td>
<td>11 (4%)</td>
<td></td>
</tr>
<tr>
<td>Drugs and alcohol use</td>
<td>0</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Financial concerns</td>
<td>6 (7%)</td>
<td>9 (4%)</td>
<td></td>
</tr>
<tr>
<td>Work and unemployment</td>
<td>2 (2%)</td>
<td>13 (5%)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>0</td>
<td>8 (3%)</td>
<td></td>
</tr>
<tr>
<td>Interpersonal relationships</td>
<td>11 (13%)</td>
<td>30 (12%)</td>
<td></td>
</tr>
<tr>
<td>Living situation, housing</td>
<td>5 (6%)</td>
<td>8 (3%)</td>
<td></td>
</tr>
<tr>
<td>Societal and altruistic concerns</td>
<td>1 (1%)</td>
<td>5 (2%)</td>
<td></td>
</tr>
<tr>
<td>Community involvement</td>
<td>0</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Accomplishing chores</td>
<td>5 (6%)</td>
<td>7 (3%)</td>
<td></td>
</tr>
<tr>
<td>Spiritual and religious concerns</td>
<td>2 (2%)</td>
<td>7 (3%)</td>
<td></td>
</tr>
<tr>
<td>Leisure activities</td>
<td>0</td>
<td>11 (4%)</td>
<td></td>
</tr>
<tr>
<td>Travel</td>
<td>5 (6%)</td>
<td>12 (5%)</td>
<td></td>
</tr>
<tr>
<td>Fantasy</td>
<td>3 (1%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td><strong>EORTC QLQ-c30 scores (mean)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall quality of Life</td>
<td>7</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>Global health score</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Functional scores</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function score</td>
<td>81</td>
<td>61</td>
<td>0.015</td>
</tr>
<tr>
<td>Role function score</td>
<td>80</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Cognition function</td>
<td>20</td>
<td>79</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Emotional function</td>
<td>83</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Social function</td>
<td>70</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td><strong>Symptom scores</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>33</td>
<td>19</td>
<td>0.072</td>
</tr>
<tr>
<td>Pain</td>
<td>20</td>
<td>43</td>
<td>0.067</td>
</tr>
<tr>
<td>Fatigue</td>
<td>43</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>37</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>23</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>18</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>33</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Financial concern</td>
<td>33</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

**Results:** Table 1 compares the comprehensive HRQOL profile using both idiographic and QLQ-c30 metrics. Idiographic assessment resulted in 87 goal statements in 17 categories from patients in phase I trials (8.7 goals/patient) vs. 260 goals in 20 categories from patients with high-risk gynecologic malignancies (10.4 goals/patient). Significantly more phase I patients had the goal of reaching an event/milestone (18% vs. 3%, P = 0.0008). Aside from cancer-related (P = 0.062) and independent function-related themes (P = 0.018), the goal contents were remarkably similar between the two groups. There were no differences in goal attainment or satisfaction with attainment. The overall global health score did not differ using QLQ-30. Phase I patients scored significantly higher in physical function (P = 0.015) and lower in cognitive function (P < 0.001). Symptom burdens were similar in the two groups. Scores for pain and dyspnea approached significance (P = 0.067 and P = 0.072, respectively).

**Conclusions:** Implementation of qualitative and quantitative metrics using the idiographic and QLQ-c30 survey is feasible and useful in increasing understanding of HRQOL in patients with poor diagnoses undergoing chemotherapy. Patients in phase I clinical trials do not report a significantly worsening HRQOL than those receiving chemotherapy. Further research is needed to address novel concerns revealed by the comprehensive profile and to correlate QOL indicators with treatment outcome.

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**194 -- Poster Session**

**Uncertainty in self-reported responses to a symptoms questionnaire relevant to gynecologic oncology**


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**Objectives:** Questionnaires on patient health are often administered to help identify issues or complaints. Our objective was to evaluate the confidence that women report when completing a symptom questionnaire and to determine if there is evidence for a learning curve.

**Methods:** A questionnaire containing the constellation of symptoms relevant to gynecologic oncology developed by Goff (Cancer, 2007) was administered to 24,526 women in the Kentucky Ovarian Screening Program over multiple visits so that 70,734 symptoms reports were obtained. A self-administered evaluation of reporting confidence was added to the Goff questionnaire as a Confidence Score (CS): no confidence = 0, minimally sure = 1, more than minimally sure = 2, pretty sure = 3, sure = 4, and absolutely sure = 5. Chi square, ANOVA, and multivariate analyses were performed.

**Results:** A total of 17,623 women completed the symptoms questionnaire >1 time and >9500 women completed it >4 times for >43,000 serially completed questionnaires. Complete lack of confidence (CS = 0) in symptoms reporting was observed in 21.1% of all responses and increased concurrently (from 16.7% to 26%) as a function of questionnaires completed, showing the absence of an active learning curve. Age-related decreases in reported confidence were significant when comparing premenopausal to postmenopausal women (P < 0.0001). Women reporting at least one symptom expressed more confidence in their responses (41,984/52,379 = 80.2%) than women reporting no symptoms (11,882/18,355 = 64.7%), P < 0.0001. Confidence in reporting symptoms was unrelated to hormone replacement therapy use or an abnormal ultrasound finding (P = 0.30 and P = 0.89, respectively).

**Conclusions:** More than 20% of all study participants relayed a complete lack of confidence in their symptom reporting for ovarian cancer. Confidence in reporting did not improve over time, increased with age, and was lowest when no symptoms were reported. Health care providers should be aware that symptom questionnaire responses are associated with significant inherent uncertainty.

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195 — Poster Session
A quality initiative to improve compliance with perioperative anticoagulation
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Objectives: Venous thromboembolism (VTE) is a leading cause of morbidity and mortality in gynecologic oncology surgical patients. It is, therefore, imperative to follow guidelines for perioperative prevention. Many centers use neuraxial analgesia (NA), a practice that may affect the timing of prophylactic anticoagulant administration. In 2013, compliance with preoperative anticoagulant administration at our institution was noted to be 41% in NA patients undergoing laparotomy. We undertook a quality initiative (QI) aimed at increasing compliance.

Methods: A multidisciplinary working group comprising stakeholders in the surgical pathway was formed with the goal of increasing compliance to at least 80% in NA cases and maintaining a minimum of 90% in non-NA cases. Compliance was defined as receipt of a prophylactic dose of anticoagulant within 1 h after NA or before skin incision regardless of anesthesia type. Following discovery, design, and trial implementation phases, a QI intervention bundle was deployed that included targeted education sessions, specific perioperative physician order tools, and improved documentation of anticoagulant administration. Institutional review board approval was obtained and retrospective data collection performed between 7/1/14 and 9/4/14 for interim analysis. Those having surgery in the year before the QI were used for comparison. The primary outcome was rate of compliance. The secondary outcome was timing of anticoagulation. Student’s t-test and Fisher’s Exact were used.

Results: There were 36 women treated under the QI and 182 historical cases (HC). Fifty percent of QI cases (n = 18) had NA compared with 34% of HC (n = 63), P = 0.09. Overall compliance improved, with 94% QI vs. 73% HC, P = 0.004. This difference was marked in cases with NA (94% QI vs. 40% HC, P < 0.001). Compliance remained stable in non-NA cases (94% QI vs. 91% HC, P = 1.0). The mean number of minutes between drug administration and skin incision was −55 (standard deviation [SD] 61) in QI cases compared with −19 (SD 52) in HC cases and this difference was significant P = 0.0024.

Conclusions: Relatively simple quality initiatives aimed at improving routine processes within the surgical pathway are feasible and attract participation from staff. Such ongoing efforts are likely to translate into higher levels of patient safety and greater workplace satisfaction.

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196 — Poster Session
Opioid risk screening in gynecologic oncology patients: A pilot study
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Objectives: Opioids are increasingly used for management of pain in gynecologic oncology patients. Nationally, there has been a considerable rise in rates of opioid misuse and abuse. We suspect that women treated for gynecologic malignancies are as prone to substance abuse as the general population and should be screened accordingly, although data regarding this practice are limited. This study sought to determine the propensity for opioid abuse and evaluate risk factors.

Methods: Institutional review board approval was obtained and retrospective data collection performed. Data were abstracted on women actively taking or receiving a new prescription for opioids who presented to either the gynecologic oncology or palliative care clinic between May and September 2014 and who had documented opioid risk screening using the Opioid Risk Tool (ORT). This five-item tool takes <1 min to administer and categorizes patients as low (0–3), moderate (4–7), or high risk (>7). Age, race, cancer status, and scores from the ORT were gathered. The primary outcome was ORT score. Statistical analyses included Fisher’s exact and Kruskal–Wallis.

Results: A total of 53 women met inclusion criteria. Mean age was 54 years (range, 25–89 years) and 75% were Caucasian (n = 40). Nearly half were either uninsured or received Medicaid (45%); the remainder were split between Medicare (26%) and private coverage (28%). Most had a cancer diagnosis (n = 40, 75%). The mean ORT score was 2.1 (range, 0–10). Overall, 79% fell into the low-risk category, 13% in the moderate-risk category, and 7.5% in the high-risk category. Twenty-three percent of women admitted to a personal history of illegal drug, prescription drug, or alcohol abuse that had not previously been detected by routine history-taking. Race, cancer status, and insurance type did not significantly influence ORT score (P = 0.85, P = 0.12, and P = 0.27, respectively). Age significantly affected ORT score, with younger patients being at higher risk (P = 0.02).

Conclusions: The propensity for opioid misuse in gynecologic oncology patients exists, and baseline risk may be higher than previously thought. Given the prevalence of opioid use in managing cancer-related pain and the absence of reliable pre-screening indicators, apart from age, universal screening with tools such as the ORT should be employed as an element of risk assessment to minimize risk while optimizing pain control.

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Results: Study entry was offered to 22 women, with 19 consenting participants. Mean age was 52 years and 79% were Caucasian. The presentation significantly improved satisfaction with the care provider, with a mean change of 1.4 (standard deviation [SD] 2.1), \( P = 0.005 \). Ten of 19 women (53%) indicated maximal satisfaction on both instruments before and after viewing the presentation, with an insignificant mean change in CSQ-8 score 0.3 (SD 1.4), \( P = 0.13 \). Mean baseline FACT-G7 was 17.6 (SD 5.5), and this score was not correlated with any of the pre or postpresentation satisfaction measures. Need for timely completion of the nurse education and laboratory portions of the preoperative visit limited the ability to consistently offer study entry.

Conclusions: Baseline satisfaction with informed consent before surgery is high. The use of supplemental multimedia is feasible but may be of more benefit at points of care beyond the preoperative encounter.

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198 – Poster Session
A comparison of epidural analgesia and patient controlled intravenous analgesia on postoperative pain control and recovery parameters in women undergoing laparotomy for gynecologic malignancy
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Objectives: Postoperative pain is a common fear of patients before surgery and adequate pain control is frequently used as a quality measure in surgical care delivery. The question of whether epidural analgesia (EA) provides better pain control than patient-controlled parenteral opioid analgesia (PCA) remains controversial. We sought to determine the effect of EA compared to PCA on postoperative recovery parameters and pain scores.

Methods: A retrospective analysis of patients with gynecologic malignancy who had a laparotomy at the University of New Mexico from 2011 to 2013 was performed. Clinical and demographic variables were collected. Descriptive statistics were used to summarize patient characteristics. Linear mixed modeling was used to calculate the least squares mean postoperative pain scores after adjusting for PCA/EA use, demographic characteristics, and repeated measures.

Results: A total of 159 patients met study criteria: 80 received EA and 79 received PCA. Hispanics and Native Americans represented 51% of the patients. Ovarian cancer was the most common cancer type (48%). Demographic, preoperative, and intraoperative factors were similar between groups. Patients in the EA group had both a significantly longer length of stay and longer time to Foley catheter removal, first ambulation, and flatus (all \( P \leq 0.01 \)). The median length of stay was 5 vs. 3 days in the EA vs. PCA group (\( P < 0.01 \)). The number of patients with postoperative complications was significantly higher in the EA group (\( P < 0.01 \)). The EA group reported lower pain scores compared to the PCA group over postoperative days 0, 1, and 2 (\( P = 0.04 \)). After controlling for postoperative day, the mean pain score (using the Numeric Rating Scale) for the PCA group was 3.4 (95% CI: 3.0–3.8) compared to 2.8 in the EA group (95% CI: 2.5–3.2). Neither ethnicity nor language preference influenced analgesia choice or postoperative pain scores.

Conclusions: In this ethnically diverse population, EA provided superior pain control after laparotomy for gynecologic malignancy. However, EA was associated with a longer length of stay, a delayed achievement of postoperative milestones, and a higher prevalence of postoperative complications. The optimal postoperative pain control method that achieves a balance of all pertinent postoperative outcomes remains elusive.

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200 – Poster Session
Beyond fertility: The safety of ovarian preservation in women with complex endometrial hyperplasia with atypia
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Objectives: To evaluate the safety of ovarian preservation in women undergoing surgical management of complex endometrial hyperplasia with atypia (CAH) and endometrial intraepithelial neoplasms (EIN).

Methods: The University HealthSystem Consortium database was queried from 10/2010 to 7/2014 to identify women with CAH and EIN managed with hysterectomy with or without adnexectomy. The risk of occult ovarian malignancy at the time of surgical management was calculated, then further stratified by age <65 or \( \geq 65 \) years.
**Results:** Over a 4-year period, 2730 women were identified with CAH and EIN who underwent any type of hysterectomy. Of these patients, 2315 had concurrent bilateral or unilateral oophorectomy (83.2%). Occult ovarian malignancy was found in 27 of these cases, representing an overall risk of 1.2%. Stratified by age, 15 of 1838 women <65 years of age and 12 of 477 who were ≥65 years old had ovarian cancer on final pathology, representing an 0.8% and 2.5% risk of ovarian cancer in these age groups, respectively. We determined the relative risk of occult ovarian malignancy at the time of surgical management of CAH to be 3.1 at age ≥65 vs. age <65 years (relative risk 3.08, 95% CI 1.5–6.5, Fisher’s exact test P < 0.006).

**Conclusions:** Conventional management of CAH/EIN in women who have completed childbearing does not differ from that of endometrial cancer, including total abdominal hysterectomy/bilateral salpingo-oophorectomy. This practice is compelled by the theoretical risk of continued hormonal stimulation of residual endometrial disease, the risk of a synchronous ovarian malignancy, and the risk of metastasis to the ovary. Studies endorsing the safety of hormone replacement therapy in endometrial cancer patients argue against the detrimental effect of estrogen in endometrial cancer patients and, therefore, in CAH/EIN as well. Our study demonstrates a low incidence of ovarian malignancy in women with CAH/EIN, especially in women <65 years of age, providing compelling evidence to support ovarian preservation. As data increase regarding the health benefits of ovarian preservation in postmenopausal women, a paradigm shift in the surgical management of CAH in these same women should follow.

**Objectives:** To evaluate the level of knowledge about intraoperative radiation therapy (IORT) among trainees and attending physicians and to characterize utilization of IORT in locally advanced primary or recurrent pelvic malignancies.

**Methods:** An anonymous, cross-sectional survey was sent to obstetrics and gynecology residents, radiation oncology residents, gynecologic oncology fellows in training, and attending physicians in both gynecologic and radiation oncology. The survey included demographic questions, practice characteristics, and accessibility or utilization of IORT. Survey participants were additionally asked to elucidate the modes and intensity of exposure to IORT training during residency and fellowship, and their knowledge was assessed through a short true–false quiz.

**Results:** Out of 1250 physicians surveyed, 403 responded (32%). Most respondents were gynecologic oncologists (68%), female (55%), attending physicians (58%), and worked in a city/urban university setting (75%). More than 70% of respondents reported no exposure to IORT during residency/fellowship training and only 17% reported using IORT in the past year (most commonly for cervical or uterine cancers). Twenty-eight percent of respondents had IORT available in their practice, 44% did not, and 28% were unaware of its availability. Leading reasons for not using IORT were: 1) lack of appropriate equipment, 2) absence of radiation oncology support, and 3) unfamiliarity with IORT. Only 60% of respondents correctly answered the true–false quiz questions. Only 6% to 7% of faculty reported training residents in IORT, and 7% of faculty reported training residents in IORT.

**Conclusions:** Lack of IORT in residency and fellowship training is a potentially modifiable reason for decreased utilization of this unique treatment modality that is effective in gynecologic malignancies. Organized didactic and hands-on instruction could improve familiarity and possibly utilization.

**Objectives:** The goals of this study were to identify predictors of 30-day readmission for patients undergoing surgery for gynecologic malignancies and to identify patients at a high risk of readmission.

**Methods:** Patients included in the National Surgical Quality Improvement Program (NSQIP) for the years 2011 and 2012 with...
a final diagnosis of gynecologic malignancy were identified. Exploratory analysis and logistic regression modeling were performed on the patients included in the 2012 file to develop the readmission prediction score (RPS). The RPS was then validated on the 2011 file.

Results: Of 4581 patients identified, 339 (7.4%) were readmitted within 30 days of surgery. Variables found to be significant for predicting readmission at the time of discharge on logistic regression modeling were occurrence of at least one complication prior to discharge (odds ratio [OR] 1.86, 95% CI 1.06–3.25), disseminated cancer (OR 2.68, 95% CI 1.35–5.35), and non-laparoscopic surgery (OR 2.06, 95% CI 1.12–3.8). Patients experiencing postdischarge complications were 20 times more likely to be readmitted (OR 19.8, 95% CI 15.24–25.8). Exploratory analysis of postdischarge complications revealed that 124 (36.5%) readmitted patients had developed infectious complications, including 32 (9.4%) with septic shock and 25 (7.3%) with thromboembolic complications. Using information available at the time of patient discharge, RPS can be calculated by assigning points as follows: 2 points each for disseminated cancer, open surgery, or postdischarge complication and 1 point for high-complexity surgery (>35 relative value units). A score of 0–1 had a readmission rate of <5%, 2–3 had a rate of 7.5%, and scores ≥4 had a rate of 15%. Validation on the 2011 file (n = 3041) categorized 40.2% of the patients as low risk (<5% risk of readmission), 39.2% of patients as intermediate risk (10%), and 20.6% of patients as high risk (>15%).

Conclusions: Our RPS system can identify patients at a high risk of readmission (>15%). The high-risk categories identify patients who should be targeted for prospective interventions to prevent readmissions. Interventions by home health care and social workers as well as early postoperative visits may decrease the overall health care resource utilization by preventing rehospitalization.

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204 — Poster Session
Caffeine intake and endometrial cancer risk in the PLCO cohort
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Objectives: Coffee has been associated with a decreased risk of endometrial cancer. However, it is unclear whether the association is related to caffeine intake.

Methods: We evaluated the association between intake of caffeine as well as coffee and tea and endometrial cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial, a multicenter trial investigating early cancer detection and etiologic determinants. Participants completed baseline and dietary history questionnaires. Out of a total of 33,428 eligible women, 343 incident cases of endometrial cancer were identified with 283,086 person-years. The Cox proportional hazard model was used to evaluate caffeine intake, coffee and tea consumption, and endometrial cancer risk.

Results: Coffee drinking was associated with a decreased risk of endometrial cancer. The adjusted relative risk of endometrial cancer was 0.82 (95% CI 0.59–1.13) among women drinking 1.1–1.9 cups/day and 0.73 (95% CI 0.57–0.94) among those drinking ≥2 cups/day. Decreased risk of endometrial cancer also was observed in women drinking caffeinated coffee but not among women drinking decaffeinated coffee. However, caffeine consumption estimated from both coffee and tea drinking was not associated with reduced risk of endometrial cancer. With ≤25.2 mg/day as the referent category (quartile 1) for caffeine intake, relative risks were 1.66 (95% CI 0.1.22–2.26), 0.99 (95% CI 0.70–1.40), and 1.10 (95% CI 0.78–1.54) for quartiles 2, 3, and 4, respectively.

Conclusions: Increased coffee drinking was associated with a decreased risk of endometrial cancer, but caffeine intake was not associated with reduced risk of the disease. Our observation indicates that other anticancer properties of coffee might be responsible for the observed risk reduction for endometrial cancer.

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205 — Poster Session
Predictive model of conversion to laparotomy in minimally invasive surgery for endometrial cancer
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Objectives: To identify risk factors associated with laparotomy conversion during total laparoscopic hysterectomy for endometrial cancer.

Methods: This retrospective study examined endometrial cancer cases that underwent hysterectomy-based surgical staging initiated via conventional laparoscopic approach. Patient factors, tumor factors, and surgeon factors were examined to establish the risk of laparotomy conversion using a logistic regression model.

Results: There were 251 cases identified, including 30 (12.0%) cases of laparotomy conversion. The most common indication for laparotomy conversion was a large uterus (27.0%), followed by extensive adhesions (24.3%) and surgical complications (18.9%). Outcomes of cases resulting in laparotomy conversion included longer surgical time (351 vs. 247 min, P < 0.001), larger blood loss (483 vs. 100 mL, P < 0.001), longer hospital stay (4 vs. 2 days, P < 0.001), and increased risk of hospital readmission (10% vs. 1.4%, P = 0.024). In multivariate analysis, morbid obesity (odds ratio [OR] 4.51, P = 0.011), suboptimal pelvic examination or enlarged uterus during preoperative evaluation (OR 3.55, P = 0.034), paraaortic lymphadenectomy (OR 10.5, P = 0.001), uterine size ≥250 g (OR 3.49, P = 0.026), and extrauterine disease (OR 4.68, P = 0.012) remained independent predictors for laparotomy conversion. The number of risk factors was significantly correlated with laparotomy conversion rate: none 1.1%, one risk factor 5.3% (OR 5.00, P = 0.15), two risk factors 21.7% (OR 24.9, P = 0.002), and three or more risk factors 50% (OR 90.0, P < 0.001) (Panel A). Ultrasonographic three-dimensional volumes of 478 cm3 in preoperative uterine size correlated with actual uterine weight of 250 g (Y = 1.39 + 0.52X, P < 0.001).

Conclusions: Laparotomy conversion significantly affects outcomes of endometrial cancer patients. In this setting, our predictive model for laparotomy conversion can help to guide the surgical management of endometrial cancer.
206 — Poster Session
Endometrial cancer survivor perspectives on weight loss and lifestyle modifications: A Uterine Cancer Action Network study
L. Tsenga, K.C. Longb, A.M. Jerniganb, R. Salanib, R.E. Bristowc, A. Nickles Fadera, John Hopkins Medical Institutions, Baltimore, MD, USA, bThe Ohio State University, Columbus, OH, USA, cUniversity of California, Irvine, Irvine, CA, USA

Objectives: To examine the experiences and preferences of uterine cancer (UC) survivors with regard to weight and lifestyle counseling performed by their cancer providers.

Methods: Members of the Uterine Cancer Action Network of the Foundation for Women’s Cancer were invited to complete a 45-item web-based survey. Standard descriptive statistical methods and chi square tests were used to analyze responses.

Results: For the 177/657 UC survivors who completed the survey (27%), the median age was 58 years, 90% were white, and the median length of survivorship was 4.4 years. Most were diagnosed with stage I disease (89%). Eighty-nine percent received their cancer care from a gynecologic oncologist (GO). Sixty-five percent classified themselves as overweight or obese. Increased respondent body mass index was associated with decreased exercise frequency (P = 0.016). Only 50% of respondents received any weight or lifestyle counseling. Counseling rates differed significantly between geographic regions, with respondents in the West and Southwest reporting the highest rates (70.8% and 69.2%, P = 0.011). Most who received counseling felt that discussions were motivating, were performed sensitively, and did not undermine the patient-physician relationship. However, 72% of respondents did not believe that specific recommendations or interventions were offered; no survivors reported referrals to weight loss programs or bariatric specialists and few (6%) reported referrals to nutritionists. Overweight patients experienced greater successes with weight loss/lifestyle changes compared to their obese or morbidly obese counterparts (30.8% vs. 15.8% vs. 12.5%, P = 0.011). Respondents (85%) preferred that their GO address weight using direct, face-to-face counseling, with specific recommendations for interventions and referral to weight specialists.

Conclusions: In this UC Action Network study, survivors reported high obesity and low activity rates and desire for substantive weight loss counseling from their GOs. Respondents suggested that current counseling practices are inadequate and incongruent with their needs, especially for morbidly obese survivors. Specific weight loss recommendations, with referrals to other specialists for lifestyle interventions, were desired.

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207 — Poster Session
A comparison of progression free survival and postoperative outcomes for early stage endometrioid adenocarcinoma following robotic-assisted staging and open laparotomy
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Objectives: The da Vinci robotic surgical system has had a significant impact on the availability of minimally invasive surgery for endometrial cancer. Robotic-assisted staging of endometrial cancer has been shown to have comparable outcomes to laparoscopic-assisted and open surgical staging. We sought to directly compare cancer recurrence and postoperative outcomes following robotic-assisted staging and open laparotomy in patients with early-stage endometrial cancer in a community setting.

Methods: A retrospective chart review was performed for patients who underwent surgical staging for stage I endometrioid adenocarcinoma of the uterus at the West Clinic in Memphis, TN, from 2007 to 2011. All staging was revised to FIGO 2009 staging. The cohort who received robotic-assisted staging was matched by age, body mass index (BMI), Gynecologic Oncology Group (GOG) 99 risk criteria, cancer stage, and tumor grade with the cohort who received staging by open laparotomy. Data regarding cancer recurrence and surgical complications were analyzed. Statistical analysis was performed with Statistical Package for the Social Sciences using chi square for discrete variables, t-test for continuous variables, and Kaplan–Meier curve for progression-free survival (PFS).

Results: A total of 165 patients who underwent open laparotomy and 166 patients who underwent robotic-assisted staging for stage I endometrioid adenocarcinoma were identified for analysis. There was no difference in age, BMI, GOG 99 risk criteria, cancer stage, tumor grade, or adjuvant therapy received between the two cohorts. Significantly more pelvic and periaortic lymph nodes were sampled using open laparotomy compared to robot-assisted staging (P = 0.003 and P = 0.002, respectively). There was no difference in cancer recurrence (P = 0.833), average months to recurrence (P = 0.999), or PFS (P = 0.890) between the cohorts. There were significantly more postoperative complications following open laparotomy compared to robotic-assisted staging (P < 0.001).

Conclusions: Patients staged using the da Vinci robotic system have the same risk of recurrence and PFS as those staged by open laparotomy with significantly less perioperative complications. Our data affirm the use of the da Vinci robotic system for surgical staging of early-stage endometrioid adenocarcinoma of the uterus in the community setting.

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outcomes for serous and clear cell uterine cancers are poor and not significantly different for patients treated with chemotherapy +/− radiation. This provides further evidence that rare tumors such as serous and clear cell uterine cancers should be studied separately and that there is a desperate need for novel therapies in this group.

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209 — Poster Session
Correlation between type I uterine cancer and diet and lifestyle in US-born versus immigrant Asian subgroups
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Objectives: To analyze the differences in body mass index (BMI) and lifestyle factors, including diet and physical activity, in various Asian subgroups.

Methods: Using the 2005 California Health Interview Survey (CHIS), we evaluated BMI, dietary intake, and physical activity among different Asian ethnic groups, including Chinese (CHN), Filipino (PHI), Indian (IND), Japanese (JPN), Korean (KOR), and Southeast Asian (SEA). Chi square, t-test, ANOVAs, and multivariate linear regression model analyses were used for statistical analyses.

Results: Of 2352 Asian women in California surveyed, 447 (19%) were born in the United States (US) and 1905 (81%) were immigrants. The ethnic breakdown was: 33% CHN, 17% PHI, 17% KOR, 14% SEA, 10% JPN, and 9% IND. US-born Asians had a higher BMI compared to their immigrant counterparts (24.2 vs. 22.9, P < 0.01). In our prior report using the National Cancer Institute (NCI) database, we showed a higher proportion of type I uterine cancer in US-born patients. Our CHIS data also found that US-born women consumed more servings of high-fat content foods per week (2.3 vs. 1.6, P < 0.01) and sugar-sweetened beverages (1.6 vs. 0.8, P < 0.01) but consumed less protein (0.8 vs. 1.6, P < 0.01) compared to immigrants. A larger proportion of US-born Asians exercised than immigrants (60% vs. 53%, P < 0.01). In subgroup analysis, PHI and IND groups (23.8 and 22.9) had higher BMIs vs. CHN and SEA (21.7 and 21.7) (P < 0.01). Moreover, the PHI population reported the highest rate of diabetes at 10% (P < 0.01). The NCI data also found that PHI had the highest proportion of type I uterine cancer compared to other Asian subgroups. Correspondingly, PHI women consumed more high-fat content foods (1.2 vs. 0.7, P < 0.01), had greater sugar intake (1.4 vs. 0.5, P < 0.01), and had lower consumption of leafy greens (5.1 vs. 7.6, P < 0.01) compared to CHN women.

Conclusions: There are significant differences in BMI, diet, and exercise patterns among various Asian subgroups and their immigration status. Longitudinal studies are warranted to determine the effects of lifestyle patterns on the risk of type I uterine cancer.

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210 — Poster Session
Lymph-vascular space invasion in uterine corpus cancer: What is its prognostic significance in the absence of lymph node metastases?
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Objectives: To analyze the differences in body mass index (BMI) and lifestyle factors, including diet and physical activity, in various Asian subgroups.

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Conclusions: There are significant differences in BMI, diet, and exercise patterns among various Asian subgroups and their immigration status. Longitudinal studies are warranted to determine the effects of lifestyle patterns on the risk of type I uterine cancer.

doi:10.1016/j.ygyno.2015.01.211
**Objectives:** Lymphovascular space invasion (LVSI) is an indicator of poor prognosis in uterine cancer due to its association with lymph node metastases. Little data are available regarding the prognostic significance of LVSI in the absence of nodal disease. We sought to determine if, after accounting for other prognostic factors, LVSI provides prognostic information regarding recurrence-free survival (RFS) or overall survival (OS) in women with uterine cancer and negative lymph nodes.

**Methods:** A retrospective review was performed using a database of women treated for uterine cancer at MUSC from 2005 to 2012. Patients with negative nodes after complete staging were identified. Cox regression modeling was used to evaluate models, including demographic and histopathologic covariates in addition to LVSI. The C-index was calculated for models of survival that included LVSI and those that did not. In addition to a standard Cox model, competing risk Cox regression was used to evaluate time to recurrence while treating death due to other causes as a separate event.

**Results:** A total of 205 women were completely staged and had negative nodes, 24 with LVSI and 181 without LVSI. Factors significantly associated with OS and RFS included age, race, disease stage, disease type (I vs. II), and LVSI status. Regression models for both OS and RFS had similar C-indices, regardless of whether LVSI was included. For OS, C-index = 0.886 with LVSI and 0.889 without LVSI. For RFS, C-index = 0.827 with LVSI and 0.805 without. Competing risks analysis showed no significant difference in time to recurrence for subjects with LVSI compared to those without LVSI ($P = 0.53$), adjusting for race, disease stage, disease type, lesion size, and adjuvant therapy.

**Conclusions:** There is no survival difference between women with uterine cancer and negative nodes who have LVSI and those who do not. Adjuvant therapy for patients with LVSI should not be administered unless otherwise indicated by disease stage, grade, or histology.

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212 – Poster Session

**Differences in survival between clear cell uterine and ovarian carcinoma patients**

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**Objectives:** To determine the differences in clinical presentation and survival of clear cell ovarian vs. uterine cancer patients.

**Methods:** Data were obtained from the National Cancer Institute between 1989 and 2010. t-Test, Kaplan–Meier, and Cox proportional hazards models were used for statistical analysis.

**Results:** Of 6124 patients, 3996 (65%) had ovarian (OCC) and 2128 (35%) had uterine (UC) clear cell carcinomas. The median age of OCC patients was 55 years (range, 24–94 years), while the median age for UC patients was 69 years (range, 26–99 years) ($P < 0.01$). The majority was white (81% for OCC and 77% for UC). Fifty-five percent of OCC patients were stage I, 11% were stage II, 22% were stage III, and 11% were stage IV. In contrast, 40%, 13%, 27%, and 19% of OCC patients had stage I, II, III, and IV cancers. The 5-year disease-specific survival of those with OCC and UC were 61% and 51%, respectively ($P < 0.01$). Adjusted for stage, the survival of those with stage I–II OCC was 81% vs. 70% in those with UC ($P < 0.01$). Among those with stage III–IV cancer, the survival rates for OCC and UC patients were 22% and 29% ($P = 0.12$). Based on multivariate analysis, age (HR = 1.03, 95% CI = 1.03–1.04, $P < 0.01$), higher stage (HR = 5.75, 95% CI = 4.96–6.68, $P < 0.01$), and ovarian origin (HR = 1.24, 95% CI = 1.07–1.44, $P < 0.01$) were independent predictors for poorer survival.

**Conclusions:** OCC patients have better survival rates compared to OCC patients. Age, higher stage, and ovarian origin were independent predictors for poorer survival.

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213 — Poster Session
Significance of omentectomy during surgical staging for uterine serous carcinoma
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Objectives: Uterine serous carcinoma (USC) comprises approximately 10% of endometrial carcinomas. It is confirmed as a particularly aggressive histologic variant because of its propensity for extratubal metastasis as well as its poorer prognosis compared to the endometrial subtype. FIGO staging advocated omentectomy as part of surgical staging, but recent studies indicate that the excision of a normal-looking omentum as part of surgical staging may not be necessary. The aim of our study was to evaluate the role of omentectomy during routine surgical staging for USC.

Methods: We conducted a retrospective review of the records of patients with USC treated in our institution over a period of 12 years (01/2001–12/2012), recording data regarding surgical procedures, disease stage, and disease histology.

Results: A total of 144 women (mean age, 67.2 years) were identified with USC during the study period. Omentectomy was performed in 99 patients (68.75%) and 83 patients (57.63%) had pelvic lymph node dissection. Overall complete surgical staging was performed in 66 patients (45.83%). Washing for cytology was positive in 25.68% of patients. Positive lymph nodes were found in 26%. The omentum was involved in 28/99 patients (28.28%) while 71 of the omentums were visually normal and benign on histologic review. Six of 28 omentums (21.43%) were visually negative and histologically positive for metastatic serous carcinoma. The remaining 22 specimens (78.57%) were grossly involved with histologic confirmation of disease. The sensitivity of a visually negative omentum was 0.79.

Conclusions: During surgical staging for USC, visual and pathological omentum evaluation may differ and would have been missed effect in women with stage IV disease if the staging procedure was incomplete. Our results confirmed microscopic omental involvement in 6/28 cases (21.43%) and in 6.1% (6/99 cases) of the total sample. Although microscopic omental disease is low, we strongly believe that excision of normal-looking omentum is necessary.

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214 — Poster Session
The impact of time between histologic diagnosis of endometrial cancer and surgical treatment on stage and survival
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Objectives: To determine if the time between diagnosis of endometrial cancer and surgery has an impact on survival or is associated with disease stage.

Methods: Women with preoperative histologic diagnoses of endometrial cancer between 2001 and 2011 treated initially with surgery were identified through the provincial cancer registry. Chi square and the Kruskal–Wallis tests looked at associations for categorical and nonparametric variables. Overall and endometrial cancer-specific survivals after surgery were calculated using the Kaplan–Meier method. The log rank test verified equality of survivor functions. Cox proportional hazards regression evaluated the effect of variables available from the registry for women who underwent surgery within 6 months of diagnosis.

Results: The cohort consisted of 2809 women with a median follow-up of 49 months. A total of 1687 (60.1%) had stage I endometrioid adenocarcinomas. Median time from diagnosis to surgery was 49 days (range, 2–490 days) and 1133 women (40.3%) had surgery within 6 weeks. At 5 years, overall survival was 87.1%, 84.1%, and 79.8% for women waiting 2 to 6, 6.1 to 12 and 12.1 to 26 weeks for surgery, respectively (P = 0.052). Endometrial-specific survival was 92.4%, 92.0% and 91.3%, respectively. Compared to women having surgery within 2 to 6 weeks of diagnosis, those waiting 12.1 to 26 weeks had a significantly higher risk of dying from any cause during follow-up (HR 1.41, 95% CI 1.03–1.93). However, endometrial-specific survival was similar. On further analysis, the increased risk with longer wait for surgery was only significant for stage I cancers. There was no significant relationship between time to surgery and stage. In multivariate analysis, the increased risk of death was never statistically significant after adjusting for stage in any model.

Conclusions: Although there are other benefits of timely surgery for endometrial cancer, we were unable to demonstrate a clear link between time to surgery and survival. Time from diagnosis to surgery was similar across all stages, but there appeared to be worse overall survival for women with stage I endometrial carcinomas when surgery was delayed. This may be due to confounding by comorbidities, which were not available in the dataset but are common in these women.

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215 — Poster Session
The effects of obesity on robotic-assisted pelvic and periaortic node sampling in endometrial cancer
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Objectives: The Da Vinci Robot is being increasingly employed for endometrial cancer staging in obese patients. While pelvic node sampling is comparable between open and robotic staging procedures, there are no data for periaortic node sampling in obese patients. We sought to determine the success of periaortic node sampling in obese patients undergoing endometrial cancer staging using the Da Vinci robot at a single institution.

Methods: Retrospective robotic and laparotomy cohorts for women with surgical management of primary stage IB to IVB endometrioid adenocarcinoma and all stages of papillary serous, clear cell, and mucinous endometrial cancer from January 2007 to July 2013 were formulated using a computerized database. Patient demographics and pathologic details were analyzed by t-test using SPSS software.

Results: A total of 103 patients underwent robotic surgical staging and 354 patients underwent staging using open laparotomy. There was a statistically significant difference in number of periaortic nodes sampled using the Da Vinci Robot in non-obese vs. obese patients (1.92 vs. 1.17, P = 0.033). A significantly higher number of periaortic lymph nodes was sampled in obese patients using open laparotomy vs. robotically (1.83 vs. 1.17, P = 0.025). There was no significant difference in pelvic sampling in obese patients using open vs. robotic staging (8.46 vs. 6.75, P = 0.102).

Conclusions: Significantly fewer periaortic lymph nodes were sampled using robotic-assisted staging for endometrial cancer in obese compared to normal-weight patients. Obesity also is associated with significantly fewer periaortic lymph nodes sampled robotically compared to open laparotomy. Further investigation is required to determine if the number of periaortic lymph nodes sampled robotically in obese patients is associated with a decrease in progression-free and overall survival.

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216 — Poster Session
Is hypothyroidism a risk factor for types of uterine cancer?
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Objectives: Endometrial cancers are considered to be hormone-driven. Thyroid status may influence the tumorigenesis of these cancers, but epidemiologic studies have failed to show a significant relationship. No known study has evaluated the incidence of specific types of gynecologic cancers in patients with thyroid disease. This study explored if there is a risk of a certain type of uterine cancer related to hypothyroidism.

Methods: We conducted a retrospective cohort study of 600 patients with uterine cancer. We evaluated age, parity, body mass index, diagnosis of thyroid disease, and histologic type of uterine cancer. Chi square and multivariate analysis were used to examine the relationship between hypothyroidism and types of uterine cancers.

Results: Nineteen percent of the patients (116) had hypothyroidism, and those without hypothyroidism were used as the control group. Types of cancer were divided into endometrioid, serous, clear cell, carcinosarcoma, and sarcomas, and we compared those with and without hypothyroidism. Seventy-six percent of both groups had endometrioid adenocarcinoma, 21% of the hypothyroid group and 8% without hypothyroidism had serous adenocarcinoma, 0% of hypothyroid patients and 8% without hypothyroidism had clear cell histology. 2% of the hypothyroid patients and 3% of the non-hypothyroid patients had carcinosarcoma, and 1% of the hypothyroid group and 3% of the nonhypothyroid group had sarcoma. Among those with serous adenocarcinoma, 38.5% had hypothyroidism (OR 3.04, 95% CI 1.9–5.3, P = 0.000), and fewer patients than expected in the carcinosarcoma (4%, P = 0.013) and clear cell groups (0%, P = 0.032) had hypothyroidism. There were no significant differences in age, parity, or body mass index.

Conclusions: Hypothyroidism may be an independent risk factor for histologic type of endometrial cancer. There is no increased risk for endometrioid adenocarcinoma, but unexpectedly a significantly increased risk for serous adenocarcinoma and significantly decreased risk for both clear cell adenocarcinoma and carcinosarcoma in patients with hypothyroidism.

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217 — Poster Session
Longitudinal analysis of cancer-associated biomarkers within weight loss intervention for endometrial cancer survivors with obesity
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Objectives: Obesity significantly increases the relative risk of the development of both endometrial hyperplasia and cancer. Cancer-associated biomarker levels may be altered after weight loss in this patient population, hypothetically affecting inflammation or host factors that may relate to oncogenesis. The objective of this study was to longitudinally evaluate biomarker changes in women with endometrial cancer/hyperplasia participating in a novel technology-based weight loss intervention.

Methods: Women age > 18 years with obesity (body mass index ≥ 30) and histologically confirmed endometrial hyperplasia or type I endometrial cancer were randomized 1:1 to a technology-based delivery of a 6-month weight loss and lifestyle intervention via either telemedicine or text messaging in which 90% of participants successfully lost weight. Serum samples from participants were obtained pre- and post-intervention. Read-based xMAP enzyme-linked immunosorbent assays were used to observe sera levels of cytokines interleukin (IL)-8, IL-6, IL-1 beta, IL-2, IL-7, vascular endothelial growth factor (VEGF), adipokine, and insulin-like growth factor binding protein (IGFBP). Paired t-tests were used to examine the difference between changes in biomarker expression.

Results: Mean serum levels of IL-2 demonstrated a significant difference pre- and postintervention, and there was a decrease in the level of IL-1 beta that trended toward significance. The levels of IGFBP, VEGF, IL-6, and IL-8 increased and the levels of adiponectin and IL-7 increased, although these changes did not demonstrate statistical significance in the pilot data. (See Table 1.)

Conclusions: In this pilot study, changes in expression of IL-2 were affected by participation in a novel technology-based weight loss intervention. Our results warrant further study in a larger trial to test the impact of weight loss on cancer-related biomarkers.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Baseline (n = 21)(pg/mL)</th>
<th>6 months (n = 18)(pg/mL)</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGFBP</td>
<td>140.63 (215.81)</td>
<td>159.81 (219.79)</td>
<td>0.689</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>9,326,925 (6,429,249)</td>
<td>1,060,907 (6,769,987)</td>
<td>0.238</td>
</tr>
<tr>
<td>VEGF</td>
<td>1778.0 (2764.0)</td>
<td>1635.93 (2654.95)</td>
<td>0.57</td>
</tr>
<tr>
<td>IL-1 beta</td>
<td>18.78 (75.61)</td>
<td>7.58 (14.38)</td>
<td>0.0554</td>
</tr>
<tr>
<td>IL-2</td>
<td>27.15 (112.65)</td>
<td>5.18 (7.97)</td>
<td>0.0495</td>
</tr>
<tr>
<td>IL-6</td>
<td>28.35 (81.35)</td>
<td>16.21 (30.37)</td>
<td>0.3464</td>
</tr>
<tr>
<td>IL-7</td>
<td>5.58 (103.60)</td>
<td>8.85 (18.24)</td>
<td>0.4611</td>
</tr>
<tr>
<td>IL-8</td>
<td>287.1 (728.18)</td>
<td>272.83 (813.34)</td>
<td>0.8866</td>
</tr>
</tbody>
</table>

a P = 0.05 considered statistically significant.

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218 — Poster Session
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Objectives: While some studies have shown that hospital size and surgeon volume affect patient operative outcomes, data are limited regarding robotic-assisted (RA) surgery outcomes, especially in population-based studies. We sought to identify factors that affect outcomes for women undergoing RA surgery for endometrial cancer (EC).

Methods: We performed a population-based retrospective cohort study using the Comprehensive Hospital Abstract Reporting System to identify EC patients managed with RA surgery in Washington State from 2008 to 2011. Regression analyses were used to assess length of stay (LOS), readmissions, and complications by hospital size, RA surgical volume, and surgeon group volume. All analyses were adjusted for year of surgery, lymphadenectomy (LND), and patients’ Charlson Comorbidity Index (CCI).

Results: We identified 1003 women with EC managed with RA surgery by 12 surgeon groups at 17 hospitals. One-third of patients were obese, 74% were older than age 55 years, and 8.6% had a CCI ≥ 2. More patients were treated at high- vs. low-volume hospitals (73.2% vs. 26.8%), large vs. small hospitals (72.3% vs. 27.7%), and by high- vs. low-volume surgeon groups (79.9% vs. 20.1%). LND was performed in 53% of patients. Mean LOS was 1 day (range, 1–26 days) and did not vary by hospital size or group volume. The 90-day readmission rate was 8.1%, the rate of major complications was 9.0%, and the rate of minor complications was 10.8%. These did not vary by hospital or surgeon factors. We identified four very low-volume groups performing <10 cases/year in at least 3 study years. Of these, three groups did not have a gynecologic oncolgist. These surgeon groups contributed a small total number of RA cases but had major complication rates of up to 20%.
Conclusions: In this population-based cohort, patients were predominantly managed by groups with a gynecologic oncologist and the complication and readmission rates were low. After adjusting for medical and surgical complexity, outcomes did not differ by any hospital or surgeon factor. While surgeon group volume did not affect the odds of an adverse outcome, we noted that three of the four lowest-volume groups that did not have a gynecologic oncologist had the highest rates of major complications. These data establish baseline complication rates for RA management of EC, which may be helpful in establishing quality measures.

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219 — Poster Session
Trends in treatment of uterine serous cancer in the Medicare population
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Objectives: To evaluate the rates of chemotherapy and radiotherapy use in the primary treatment of uterine serous carcinoma (USC) in the United States Medicare population and compare clinical outcomes for treated and untreated patients.

Methods: The linked Surveillance, Epidemiology, and End Results (SEER)—Medicare databases were queried to identify patients diagnosed with USC between 1992 and 2009. Demographic and clinical data were compared. The impact of chemotherapy on survival was analyzed using the Kaplan–Meier method. Factors predictive of outcome were compared using the Cox proportional hazards model.

Results: A total of 2188 patients met study eligibility criteria. Stage I, II, III, and IV disease accounted for 890 (41%), 174 (8%), 470 (21%), and 654 (30%) of the study population, respectively. Women who had unknown stage (218 [9%]) were not included in the analysis. Most patients (92.7%) underwent definitive surgery, and lymphadenectomy was performed in 64.4% of the patients. Chemotherapy was administered to 635 (29%) patients, radiotherapy to 536 (24.5%), and adjuvant chemoradiation to 308 (14%); 709 (32.4%) women did not receive adjuvant therapy during the study period. Utilization of chemotherapy stratiﬁed by time period and stage.

<table>
<thead>
<tr>
<th>Years</th>
<th>Stage I and II</th>
<th>Stage III</th>
<th>Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992–1997</td>
<td>24 (8.03%)</td>
<td>22 (26.51%)</td>
<td>91 (55.49%)</td>
</tr>
<tr>
<td>1998–2003</td>
<td>79 (21.81%)</td>
<td>63 (51.22%)</td>
<td>178 (64.49%)</td>
</tr>
<tr>
<td>2004–2009</td>
<td>157 (40.05%)</td>
<td>168 (63.64%)</td>
<td>161 (75.23%)</td>
</tr>
</tbody>
</table>

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220 — Poster Session
Signs and symptoms of venous thromboembolism and survival outcome in endometrial cancer
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Objectives: To evaluate whether subjective and objective measurements of physical examination for venous thromboembolism (VTE) correlate with survival outcome in endometrial cancer patients.

Methods: We conducted a retrospective study of endometrial cancer patients who developed VTE between diagnosis and follow-up from 1999 to 2013. Symptoms and vital signs at the time of VTE diagnosis were evaluated for overall survival time after VTE diagnosis.

Results: Among 827 endometrial cancer cases during the study period, 71 (8.6%) patients were identiﬁed with VTE (pulmonary embolism [PE] with or without deep vein thrombosis [DVT]) n = 33; and DVT alone n = 38). For the PE group, decreased overall survival after VTE was associated with fatigue (2-year rate, 16.7% vs. 52.0%, P = 0.005), systolic blood pressure (BP) < 120 mm Hg (18.2% vs. 52.9%, P = 0.018), diastolic BP < 70 mm Hg (20.0% vs. 54.7%, P = 0.028), and heart rate (HR) ≥ 90 beats per minute (bpm) (23.4% vs. 68.0%, P = 0.011) in a univariate analysis. Asymptomatic PE was associated with improved survival outcome (76.5% vs. 23.1%, P < 0.01). In multivariate analysis controlling for symptoms, signs, and tumor factors, diastolic BP < 70 mm Hg (adjusted hazard ratio [AHR] 10.8, P < 0.001) and HR > 90 bpm (AHR 7.09, P = 0.002) remained independent prognostic factors for decreased overall survival after VTE diagnosis. PE patients presenting with low diastolic BP and increased HR had a dismal survival outcome (diastolic BP < 70 mm Hg/HR ≥ 90 bpm vs. diastolic BP ≥ 70 mm Hg/HR < 90 bpm, 0% vs. 85.7%, P = 0.001 [Panel A]). For the DVT alone group, none of signs or symptoms correlated with survival outcome (all, P > 0.05).

Conclusions: Both signs and symptoms are important measurement considerations in the management of endometrial cancer patients with PE.
221 — Poster Session
Contributing factors for menopausal symptoms after surgical staging for endometrial cancer
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Objectives: Endometrial cancer patients are often affected by obesity, hypertension, diabetes, and hypercholesterolemia, requiring multiple medications. The aim of our study was to examine risk factors for developing menopausal symptoms after surgical staging for endometrial cancer, particularly in relationship to these pre-existing conditions.

Methods: This retrospective study examined endometrial cancer patients who were premenopausal at the time of hysterectomy-based surgical staging that included bilateral oophorectomy between 2000 and 2013. A multivariate logistic regression model was used to evaluate age, medical comorbidity, tumor factors, and medication history as risk factors for menopausal symptoms.

Results: There were 793 endometrial cancer patients identified, including 269 premenopausal women who underwent surgical menopause. Menopausal symptoms were seen in 72 (28.8%) women, with hot flushes (75%) being the most common symptom, followed by night sweats (15.3%). In multivariate analysis controlling for 29 covariates, age <40 years (40% vs. 10.8%, odds ratio [OR] 10.8, P < 0.001), age 40–49 years (27.1% vs. 10.8%, OR 4.01, P = 0.009), use of sulfonylurea (43.8% vs. 25.7%, OR 5.11, P = 0.045), or angiotensin-converting enzyme inhibitor or receptor blocker (30.4% vs. 25.5%, OR 3.62, P = 0.044) remained independent predictors for increased risk of menopausal symptoms, while hypoalbuminemia was associated with protective effects (19.3% vs. 31.4%, OR 0.35, P = 0.023). There were trends of protective effects with beta-blocker use (15.6% vs. 28.3%, OR 0.21, P = 0.079) and worsening effects with metformin use (31.5% vs. 25.0%, OR 3.00, P = 0.08) for menopausal symptoms. Body mass index was not associated with menopausal symptoms.

Conclusions: Assessing risk factors for the development of postoperative menopausal symptoms is a valuable step in the preoperative management of endometrial cancer patients.

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222 — Poster Session
Nonalcoholic fatty liver disease and risk of venous thromboembolism in endometrial cancer
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Objectives: Our recent studies have demonstrated that surgical menopause after oophorectomy results in a significantly increased risk of nonalcoholic fatty liver disease (NAFLD) in endometrial cancer. In addition, venous thromboembolism (VTE) is known to be one of the major prognostic factors for decreased survival in endometrial cancer. Given the role of coagulation factor production in the liver, we examined whether NAFLD correlates with VTE in endometrial cancer.

Methods: We conducted a retrospective study to examine endometrial cancer cases that underwent surgical staging, including oophorectomy, between 2000 and 2013 (n = 713). Cumulative risk of VTE was examined based on NAFLD status. A Cox proportional hazard regression model was used to determine independent risk predictors for VTE.

Results: VTE and NAFLD were seen in 57 (8.0%) and 181 (25.4%) patients, respectively. Two-year cumulative risks of VTE and NAFLD were 7.9% and 19.3%, respectively. In univariate analysis, VTE was significantly associated with decreased progression-free survival (2-year rate, 43.6% vs. 91.4%, P = 0.0001) and overall survival (65.8% vs. 96.8%, P = 0.0001) while NAFLD was associated with decreased risk of VTE (1.7% vs. 10.4%, P = 0.0001). In multivariate analysis controlling for clinicopathologic factors, NAFLD remained an independent predictor for decreased risk of VTE (HR 0.25, 95% CI 0.08–0.82, P = 0.023). Thrombocytosis (HR 2.31, 95% CI 1.21–4.38, P = 0.011), CA-125 ≥ 35 U/mL (HR 3.76, 95% CI 1.75–8.09, P = 0.001), and recurrent disease (HR 4.02, 95% CI 1.71–9.45, P = 0.001) remained independent predictors for increased risk of VTE.

Conclusions: Our results suggest that NAFLD may have an inhibitory role for developing VTE in endometrial cancer.

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223 — Poster Session
Outcomes of fertility-sparing treatment with progestin in patients with early-stage endometrial cancer or severe atypical hyperplasia: Preliminary results of a phase II study in China
K. Shen. Peking Union Medical College Hospital, Beijing, China

Objectives: To evaluate the outcomes of fertility-sparing treatment with progestin in women with severe atypical hyperplasia (SAH) or well-differentiated early-stage endometrial cancer (EC).

Methods: A multicenter cohort study was performed in China. Patients with an average age of 29.5 years were primarily treated with medroxyprogesterone acetate or megestrol acetate and were examined regularly after treatment. Factors related to the efficacy of the treatment, pregnancy, and recurrence were analyzed.

Results: Complete remission (CR) was attained in 90.5% (86.95) of cases; 9.5% of cases had failure of progestin treatment and received simple hysterectomy and 17 (24.3%) cases had recurrence. More than 6 months of treatment duration was proven to be a protective factor for recurrence (P = 0.030). Treatment time to CR of <3 months and >6-month duration of treatment were proven to prolong the progression-free survival. The pregnancy rate was 60.8%, and 20 patients delivered 22 healthy infants (delivery rate of 39.2%). The pregnancy rate in patients treated by in vitro fertilization and embryo transfer (IVF-ET) was 87.5%, which was higher than that in patients without IVF-ET (P < 0.05). The use of IVF-ET was significantly associated with successful pregnancy (P = 0.008).

Conclusions: Progestin treatment can be considered an effective treatment for young patients with EC and SAH. Duration of the treatment >6 months can prolong the progression-free survival and be considered as a protective factor for recurrence. IVF-ET should be performed in patients as soon as possible after CR to aid in successful pregnancy.

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224 — Poster Session
Impact of venous thromboembolism on mortality of elderly Medicare patients with epithelial endometrial cancer

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Objectives: To estimate and describe the incidence of thromboembolic events (TEE) before and after the diagnosis of epithelial endometrial cancer and to evaluate the impact of these events on survival.

Methods: The linked Surveillance, Epidemiology, and End Results (SEER)-Medicare databases were queried to identify patients with epithelial endometrial cancer diagnosed between 1992 and 2009. International Classification of Diseases-9 and Healthcare Common Procedure Coding System codes were used to identify TEE events 3 months before diagnosis and 6 months after diagnosis. Chi square and t tests were used to compare frequency distributions of categorical and continuous variables, respectively. The impact of TEE on survival was analyzed using the Kaplan–Meier method. Factors predictive of outcome were compared using the Cox proportional hazards model.

Results: A total of 26,174 patients were included, of whom 1246 (4.76%) developed a TEE. Patients with endometrioid adenocarcinoma had a significantly lower rate of postdiagnosis TTE (3.5%) compared with carcinosarcomas (7.5%), clear cell (7.6%), and uterine serous cancer (8%) (P < 0.001). On multivariate analysis, most recent time period of diagnosis, higher cancer grade, and high-risk histologies compared to endometrioid adenocarcinoma, higher disease stage, and chemotherapy delivery were all associated with increased risk of TEE. Over the entire study period, after adjusting for stage, age, time period of diagnosis, SEER registry region, urban vs. rural setting, marital status, treatment, surgery, lymph node dissection, socioeconomic status, and comorbidities, patients with a postdiagnosis TEE had worse disease-specific survival (HR 1.47; 95% CI, 1.31–1.64) and all-cause mortality (HR 1.45; 95% CI, 1.34–1.57). The Cox proportional hazards model identified an independent association of higher stage, older age, high-risk histologies, receipt of surgery, lymph node dissection, and adjuvant treatment with disease-specific survival.

Conclusions: Patients with uterine serous cancer, carcinosarcoma, and clear cell carcinoma have greater risk of TEE than patients with endometrioid adenocarcinoma. A new diagnosis of TEE significantly reduced survival rates for elderly patients with endometrial cancer.

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225 — Poster Session
Further stratification of subgroups with long-term survival after recurrence in endometrial cancer

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Objectives: To identify the prognostic factors for survival in patients with recurrent endometrial cancer and to use these factors to stratify subgroups with long-term survival after recurrence.

Methods: Between 1989 and 2013, all consecutive patients with recurrent endometrial cancer were retrospectively reviewed from a computerized tumor registry database. Survival estimates were calculated using the Kaplan–Meier method. Cox regression analyses were used to identify the clinicopathologic and demographic factors associated with overall survival from time of recurrence.

Results: One hundred eight patients were enrolled with a median recurrence time of 15 months (range, 3–163 months) after initial treatment. The median age at recurrence was 56 years (range, 27–80 years). Seven patients (6.5%) had the disease limited to the pelvis–vagina, 13 patients (12.0%) had pelvic region disease, and 88 patients (81.5%) had distant recurrence. The median post-recurrence overall survival was 22 months (range, 1–207 months). Fifty-seven patients (52.8%) were treated with chemotherapy and 18 (16.7%) received radiotherapy combined with chemotherapy or radiotherapy alone. Salvage cytoreductive surgery was performed in 29 (26.97%) patients and complete cytoreduction (no gross residual) was achieved in 19 patients (65.5%). Multivariate regression analysis revealed that time to relapse after initial treatment, CA-125 level at relapse, and CA-125 level at diagnosis were independent predictors of overall survival after recurrence. Survival after relapse could be stratified into four groups by the combination of three independent prognostic factors.

Conclusions: Time to relapse, CA-125 level at recurrence, and number of recurrence sites were significant predictive factors of prolonged survival after recurrence in endometrial cancer. In recurrent endometrial cancer patients with a broad spectrum of outcomes, survival after relapse could be stratified by the combination of three independent prognostic factors.

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226 — Poster Session

Sentinel lymph node mapping in women with high risk histology endometrial cancer

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Objectives: To determine the rate and performance of sentinel lymph node (SLN) mapping among women with high-risk endometrial cancers.

Methods: Patients diagnosed between 2012 and 2014 with uterine cancer of grade 3 endometrioid, clear cell, serous, or carcinosarcoma histology who underwent SLN mapping before full lymph node dissection were included. Patients underwent either methylene blue or indocyanine green injection for laparoscopic (n = 15) or robotic-assisted laparoscopic staging (n = 12). Outcomes examined included rates of SLN mapping using each surgical approach, SLN and non-SLN positive rates, false-negative SLN rate, and the negative predictive value of SLN. Ultrastaging of SLN was not routinely performed during the study period. Fisher’s exact test was used to compare mapping and node positivity rates.

Results: A total of 10/27 (37%) patients with high-risk uterine cancer had at least one positive lymph node identified. Twelve patients (44%) mapped bilaterally, 10 (37%) mapped unilaterally, and 5 (18%) did not map. Thirty-four of 54 sides (63%) mapped successfully. Successful SLN mapping rates by side were: 19/30 sides (63%) for the laparoscopic and 15/24 sides (66%) for the robotic approach (P = 0.53). Among 20 sides that failed to map, 4 (26%) had findings of grossly enlarged nodes, 7 (35%) had reportable adhesions, 6 (30%) had fibroids, and 4 (20%) were morbidly obese, making node visualization difficult. Nine of 75 (12%) sentinel nodes and 8/513 (2%) nonsentinel nodes were positive (P = 0.0009). Eight of nine (89%) positive SLNs were the only positive lymph nodes identified on that side. The false-negative SLN rate (negative SLN but other malignant lymph nodes identified on the same side) was 1/20 (5%); the negative predictive value of SLN was 95%.

Conclusions: In this series of women with high-risk uterine cancer, SLNs had a significantly higher rate of metastasis than nonsentinel lymph nodes. However, successful mapping rates may be slightly lower than historical controls among high-risk histology cancers. The 95% negative predictive value of SLN is consistent with larger subsets of lower risk endometrial cancers.

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227 — Poster Session

The role of cytoreductive surgery for recurrent endometrial cancer

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Objectives: Cytoreductive surgery (CS) does not have a definite role in the treatment of recurrent endometrial carcinoma. This study sought to determine the survival benefits of CS in patients with abdominal endometrial recurrences.

Methods: Between 1989 and 2013, all consecutive patients undergoing CS for recurrent endometrial cancer were retrospectively identified from medical records. Patients were classified according to the presence or absence of gross residual tumor after CS. The progression-free survival and disease-specific survival were defined as the time from secondary CS to the specific event and were evaluated by the Kaplan–Meier method and the log-rank test. A Cox proportional hazards regression model was used to compare survival with covariates.

Results: Twenty-nine patients were enrolled. A median recurrence time after initial treatment was 18 months (range, 3–108 months). The median age at CS was 53 years (range, 27–83 years). Three patients (10.3%) had disease limited to the central pelvis–vagina, six patients (20.7%) had pelvic region disease, and 20 patients (69.0%) had distant recurrence. Complete cytoreduction (no gross residual) was achieved in 19 patients (65.5%). There were no perioperative deaths, although seven (24.1%) patients experienced minor perioperative morbidity. Additional therapies included radiation therapy in 13 patients (44.8%) and chemotherapy in 26 patients (89.7%). From the time of secondary CS, the median progression-free survival was 11.0 months (range, 1–90 months) and the median disease-specific survival was 16.0 months (range, 2–109 months). Residual disease was the only significant predictor for both progression-free and disease-specific survival. Patients undergoing complete CS had a median disease-specific survival time of 34.0 months compared to 7.5 months for those patients with gross residual disease (P = 0.006, log-rank test).

Conclusions: Complete CS for recurrent endometrial cancer is associated with prolonged postrecurrence survival compared to patients left with any gross residual disease. In a selected patient population, CS could be beneficial for recurrent endometrial cancer.

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228 — Poster Session

Chemotherapy as single modality treatment for stage IA uterine papillary serous carcinoma

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Objectives: Early-stage uterine papillary serous carcinoma (UPSC) has significantly decreased progression-free (PFS) and overall survival (OS) compared to endometrioid adenocarcinoma. Recent therapeutic trends have focused on combination paclitaxel/carboplatin (T/C) regimens with and without radiation. We sought to compare survival outcomes of patients with stage IA UPSC who received adjuvant T/C vs. observation alone.

Methods: We performed a retrospective analysis of women with stage IA UPSC diagnosed from 2007 to 2013, comparing a cohort of patients who received adjuvant T/C to an observational cohort. Demographic and PFS data were analyzed and compared. Statistical Package for the Social Sciences software was used for analysis. A chi square test was used to compare discrete variables, t-test was used for continuous variables, and the Kaplan–Meier curve was used to compare PFS.

Results: A total of 27 patients with stage IA disease were identified for analysis. Nineteen received T/C, consisting of 4 to 6 cycles. Eight patients did not receive adjuvant therapy. There was no significant difference between groups in terms of number of nodes sampled, tumor size, depth of tumor invasion, containment to a poly, race, body mass index, or surgical modality. The 2-year OS rate was 100% for patients who received T/C and for those observed. There were no locoregional recurrences. There were two extraabdominal recurrences (7.4%) in the axilla and sigmoid colon, with mean time to recurrence of 22.9 months; both patients received T/C. There was no statistical difference in the 2-year PFS between patients who received T/C and those observed (P = 0.286).

Conclusions: This retrospective analysis suggests that adjuvant chemotherapy for stage IA UPSC alone may provide excellent PFS. Our data also support previous findings that recurrent disease is typically outside of the pelvis. Further studies are warranted on whether concurrent radiation provides additional benefit to adjuvant T/C.
Conclusions:
CI, 0.75 to 1983, 0.61 (95% CI, 0.54

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229 — Poster Session
Population-level survival trends for uterine cancer
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Objectives: Both primary therapy and adjuvant therapy for uterine cancer have evolved. Although survival estimates from randomized trials have shown improved survival, it remains unclear whether treatment changes have translated into improved survival in the broader population. Population-level survival analyses are complicated by improved longevity as a whole in women. We examined relative survival, a measure that compares survival in women with cancer to the general population, to determine the excess mortality associated with uterine cancer over the last 25 years.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER) database, women with uterine cancer diagnosed from 1983 to 2009 were identified. Survival was analyzed after adjustment for age, race, stage, year of diagnosis, and time since diagnosis. Relative survival was estimated by comparing observed survival after diagnosis of cancer to expected survival obtained from the general United States population matched on calendar year, age, and race.

Results: A total of 121,948 women were identified. For stages I–III uterine cancer, we found a temporal reduction in excess mortality. Among women with stage I uterine cancer, the excess HR for women diagnosed in 2009 was 0.53 (95% CI, 0.44–0.64) compared to those diagnosed in 1983, 0.63 (95% CI, 0.55–0.72) compared to those diagnosed in 1990, and 0.80 (95% CI, 0.75–0.86) compared to those diagnosed in 2000. Similarly, for women with stage II tumors, the excess HR for women in 2009 was 0.50 (95% CI, 0.44–0.59) compared to 1983, 0.61 (95% CI, 0.54–0.68) compared to 1990, and 0.79 (95% CI, 0.75–0.83) compared to 2000. Similar trends were noted for women with stage II tumors.

Conclusions: Relative survival has improved for stages I–III uterine cancer. Advances in surgical treatment and the delivery of adjuvant therapy may have resulted in improved population-level survival in the United States.

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230 — Poster Session
Incidence and risk factors of lymphatic-related complications after robotic staging of endometrial cancer
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Objectives: The incidence and risk factors of lymphatic-related complications in robotic surgical staging for endometrial cancer (EC) have not been extensively evaluated. We sought to examine the experience at our institution.

Methods: Patients who underwent robotic staging for EC between 10/2012 and 5/2014 were identified. Charts were retrospectively reviewed for demographics, preoperative albumin, American Society of Anesthesiologists (ASA) score, surgical and pathologic outcomes, and postoperative morbidities.

Results: A total of 105 patients were identified. Their mean age was 62 years (range, 36–84 years), the mean body mass index was 36 (range, 20–59), and 33% of patients were ASA class 3. In 62% of the patients, staging included at least bilateral pelvic and paraaortic lymphadenectomy. Eighteen cases (17%) were FIGO stage III or greater and cytoreductive efforts were carried out in seven. The mean total lymph node (LN) count was 32 (range, 2–67). LN metastases were identified in 15 patients (14%). The mean operative time was 244 min (range, 113–515 min). Twelve patients (11%) developed lymph leakage from port site or vagina. No risk factors were identified for this outcome. Twenty-four patients (23%) developed lymphatic ascites or lymphocysts, a finding significantly correlated with longer operative time (P = 0.034) on multivariate analysis. The lymphocysts were clinically significant in only nine patients (8.6%) and without identifiable risk factors. Eleven patients (10%) experienced grade 3 complications or were readmitted within 30 days of surgery, which were significantly correlated with ASA 3 and longer operative time on multivariate analysis. Six readmissions (5.6%) were due to infected lymphocysts or lymphatic ascites; five needed drainage and antibiotics. Three developed Clostridium difficile colitis, and two developed venous thromboembolism. Grade 1 lymphedema developed in 23 patients (22%) and was associated with lower albumin levels (P = 0.036) on multivariate analysis. The extent of lymphadenectomy, LN count, external irradiation, or operating surgeon was not predictive of lymphatic complications.

Conclusions: In this series of robotically staged EC, lymphatic-related complications occurred in approximately 20% of patients, 5% of whom required drainage. Future efforts for preventing postoperative or lymphatic-related complications may need to focus on patients at increased risk (ASA 3, low albumin).

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231 — Poster Session
Efficacy of adjuvant chemotherapy in patients with stage IV endometrial cancer
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Objectives: To determine the impact of adjuvant chemotherapy on disease progression rates as a function of residual disease in stage IV endometrial cancer (EC).

Methods: Treatment-specific variables were assessed with a singular focus on clinical outcomes following administration of adjuvant chemotherapy in surgically managed stage IV EC at a single institution. The progression rate per person-year of follow-up (PR/PY) was calculated within specific follow-up intervals and stratified by the amount of residual disease at completion of surgery.
Results: Following tumor-reductive surgery, adjuvant chemotherapy, predominantly platinum-based, was administered to 76 stage IV patients, 70% of whom had type II and 87% had grade 3 histology. Cytoreduction to 0 (R0), >0–1 cm (R1), and >1 cm (R2) residual diseases was achieved in 38%, 42%, and 20%, respectively. The exact date of progression was uncertain in nine patients for whom we assumed that progression occurred at a midpoint between surgery and death. The PR/PY during the first year of follow-up was similar for R1 and R2 patients at 1.30 and 1.49, respectively (P = 0.70), but significantly less favorable than for R0 (P < 0.001) (Table). However, the PR/PY for R0 patients during the second year of follow-up was 0.98 and did not differ statistically from the PR/PY for R1 during the first year (P = 0.39). Likewise, the PR/PY beyond year 1 for R1 and beyond year 2 for R0 were similar (P = 0.80). Twelve patients were still disease-free 2 years after surgery. Six remained disease-free at last follow-up (median follow-up, 7.9 years) and of the six who recurred after 2 years, four experienced extended longevity after additional therapy.

Conclusions: These observations suggest a predisposition to platinum resistance in the greater majority of stage IV EC patients, with delayed declaration during the second year of follow-up after treatment for R0 patients likely reflecting the impact of complete resection and required time for refractory tumor growth to become clinically evident. Those with favorable longevity (R1 after 1 year and R0 after 2 years of follow-up) suggest the presence of distinct tumor biology sensitive to platinum.

Table: Progression rate per person-years of follow-up stratified by amount of residual disease and follow-up interval.

<table>
<thead>
<tr>
<th>Follow-up interval (years)</th>
<th>Residual disease</th>
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<tbody>
<tr>
<td></td>
<td>0 (N = 29)</td>
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<tr>
<td></td>
<td>≤1 cm (N = 32)</td>
</tr>
<tr>
<td></td>
<td>&gt;1 cm (N = 15)</td>
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<tr>
<td>0–1</td>
<td>0.12 (9/72.77)</td>
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<tr>
<td></td>
<td>(95% CI, 0.03–0.35)</td>
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<tr>
<td></td>
<td>1.10 (26/19.96)</td>
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<td></td>
<td>(95% CI, 0.65–1.91)</td>
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<tr>
<td></td>
<td>1.85 (12/8.05)</td>
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<tr>
<td></td>
<td>(95% CI, 0.77–2.60)</td>
</tr>
<tr>
<td>1–2</td>
<td>0.59 (14/24.32)</td>
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<tr>
<td></td>
<td>(95% CI, 0.53–1.64)</td>
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<tr>
<td></td>
<td>0.17 (1/5.75)</td>
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<tr>
<td></td>
<td>(95% CI, 0.07–2.60)</td>
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<tr>
<td></td>
<td>2.71 (2/0.74)</td>
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<tr>
<td>2+</td>
<td>0.16 (4/25.57)</td>
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<tr>
<td></td>
<td>(95% CI, 0.04–0.40)</td>
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<tr>
<td></td>
<td>0.11 (2/17.50)</td>
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<tr>
<td></td>
<td>(95% CI, 0.01–0.41)</td>
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</table>

The numbers in each cell of the table denote the progression rate (number of patients with progression/total person-years of follow-up).

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233 — Poster Session

Sentinel lymph node mapping in non-endometrioid endometrial cancer

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Objectives: Sentinel lymph node (SLN) mapping is gaining importance in endometrial cancer because of its low morbidity and ability to stage patients more accurately. Recent studies included mostly patients with low-grade, early-stage endometrial cancer in which the baseline risk of having nodal metastasis is low. The present study’s objective was to evaluate and challenge the technique of SLN mapping in a cohort of high-risk patients for which the probability of nodal metastasis is higher.

Methods: The technique of SLN mapping by cervical injection with Tc99 and Patent Blue dye tracer was reviewed in patients who were surgically staged for nonendometrioid endometrial cancer followed by pelvic + paraaortic lymphadenectomy. SLNs were ultrastaged on final pathology. Detection rate, sensitivity, and negative predictive value were calculated.

Results: A total of 37 patients with serous (n = 19), carcinosarcoma (n = 16), or clear cell (n = 2) endometrial cancer were included in the analysis. The detection rate to identify at least one SLN was 86.5%. The bilateral detection rate was 67.5%. Mean number of identified SLNs was 2.0 (range, 0–5). The median number of total lymph nodes removed was 16 (range, 3–86). Nodal metastasis was identified in 24.3% (9/37) of patients of whom 44.4% (4/9) had isolated tumor cells and 55.6% (5/9) had macrometastasis. When at least one sentinel node was identified, sensitivity, specificity, and negative predictive value were calculated at 100%. Paraaortic node dissection was performed in 38% of patients.

Conclusions: In nonendometrioid endometrial cancer, the technique of SLN mapping showed comparable detection rates and negative predictive and sensitivity values compared to other studies of SLN mapping in endometroid endometrial cancer. The relatively high number of detected isolated tumor cells confirms the ability of the SLN mapping technique to detect small-volume metastatic disease.

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234 — Poster Session
Novel sandwich therapy protocol supports role for concurrent chemoradiation in endometrial cancer

Objectives: Treatment of locally advanced endometrial cancer is not well established. The “sandwich” approach offers combination treatment with chemotherapy and radiation. The aim of this study was to evaluate overall survival (OS) and progression-free survival (PFS) between two “sandwich” protocols.

Methods: Patients were retrospectively identified between 2006 and 2013 at a single institution. Clinical information was abstracted, including age, body mass index (BMI), surgical debulking method, “sandwich” protocol, disease status, and complications. OS and PFS were calculated using Kaplan–Meier method.

Results: A total of 58 patients with high-grade and/or advanced-stage disease were identified who received “sandwich” therapy. The median age was 61 years (range, 29–86 years). Median BMI was 31.9 (range, 19.5–56.1). All patients had no residual disease after surgical debulking, 19% by laparotomy and 81% by laparoscopy. Twenty-four patients received a “sandwich” protocol of 2 cycles of platinum/taxane chemotherapy followed by radiation and concurrent cisplatin, followed by 2 cycles of platinum/taxane chemotherapy. Thirty-four patients received a 3-cycle platinum/taxane “sandwich” around radiation therapy alone. Among patients treated with the 2-cycle protocol, 75% (18/24) remain with no evidence of disease (NED), 17% are alive with disease (AED), and 8% are dead of disease (DOD). Median time to recurrence was 12 months (range, 1–39 months). Among patients treated with the 3-cycle protocol, 82% (28/34) remain with NED, 6% are AED, and 12% are DOD. Median time to recurrence was 7 months (range, 4–44 months). PFS of the 2-cycle protocol was 12 months (range, 1–39 months) compared to 7 months (range, 4–44 months) in the 3-cycle protocol (P = 0.12). The OS of the 2-cycle protocol was 22 months (range, 7–65 months) compared to 33 months (range, 11–100 months) in the 3-cycle protocol (P = 0.76). Complications included pulmonary embolism in seven patients (4/7 in 2-cycle, 3/7 in 3 cycles) and severe grade 3/4 neutropenia in five patients (4/5 in 2-cycle, 1/5 in 3-cycle).

Conclusions: Optimizing care for locally advanced disease is challenging. In our study, no statistically significant difference was shown in PFS and OS between protocols. The concurrent use of cisplatin with radiation therapy needs to be further studied because it may provide the same efficacy in fewer chemotherapy cycles.

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235 — Poster Session
Changing trends in the management of early stage endometrial cancer over the past decade: Experience from a tertiary cancer center
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Objectives: The past decade has seen major developments in the treatment of apparent early-stage endometrial cancer. The results of major clinical trials have documented the benefits of both laparoscopic and robotic surgeries and adjuvant vaginal brachytherapy. The objective of this study was to document the time trends in the adoption of these techniques within a tertiary center and the impact on patient outcomes.

Methods: A retrospective chart review evaluated new consultations for early-stage endometrial cancer from January 2004 to June 2014 at a single tertiary institution. Patients with advanced disease at presentation or prior therapy were excluded. Data were collected regarding surgical approach, comprehensiveness of staging, surgical complications, adjuvant therapies, and tumor recurrence. Statistical analysis was performed using chi square tests for group comparison for single categorical variables and Fisher exact test to detect associations between two categorical variables.

Results: A total of 354 patients met the eligibility criteria. There were no significant trends in age, body mass index, or major comorbidities. Similar proportions of patients were offered primary surgical vs. medical therapy over the study period. Recurrence rates were higher among those who received primary medical therapy (P = 0.034). There was a significant increase in both laparoscopic procedures after 2008 and robotic procedures following its institutional adoption in 2009 (P < 0.0001). Rates of comprehensive staging were lower with laparoscopic procedures after 2008 compared with the preceding years of open procedures or robotic procedures after 2009 (P < 0.0001). Robotic surgery was associated with higher lymph node counts compared to both open and laparoscopic approaches (P = 0.0002) as well as a lower percentage of perioperative complications (P < 0.0001). More patients were offered adjuvant vaginal brachytherapy and fewer offered whole pelvic radiation after 2010 (P < 0.0001). A significant decrease in recurrence per year was noted, starting in 2007 (P = 0.005).

Conclusions: In the past decade, there have been trends towards minimally invasive surgical approaches, particularly robotic surgery, and adjuvant vaginal brachytherapy, with concomitant reductions in patient morbidity and improved observed recurrence rates.

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236 — Poster Session
Role of surgical staging and adjuvant chemotherapy in the treatment of uterine carcinosarcoma
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Objectives: To determine the clinical behavior and role of chemotherapy and surgical staging in the management of patients with carcinosarcoma of the uterus.

Methods: A retrospective study of patients with carcinosarcoma of the uterus treated at a single institution from 2002 to 2013 was included in the analysis. Kaplan–Meier curves were used to illustrate progression-free (PFS) and overall survival (OS) comparing administration of adjuvant chemotherapy, FIGO staging, and performance of lymphadenectomy. Cox's proportional hazard model was used to evaluate PFS and OS, controlling for age, race, lymphadenectomy, and laparotomy.
Results: Sixty-seven patients aged 71 ± 11.3 years who were diagnosed with uterine carcinosarcoma (35 stage I, 2 stage II, 22 stage III, and 5 stage IV) and had a median follow-up of 13.8 months were included in the study. Of 42 patients who received chemotherapy, seven were never disease-free. Of the 35 patients with no residual disease after surgery who received adjuvant chemotherapy, 16 developed recurrences and 10 subsequently died of their diseases. Of 25 patients who did not receive chemotherapy, three were never disease-free. Of 22 patients who had no residual disease after surgery and did not receive chemotherapy, 14 recurred and six died of their disease. The 5-year OS and PFS rates for the adjuvant chemotherapy group were 34.6% and 20.7%, respectively, compared to 7.7% and 4.8% in those without chemotherapy (P = 0.11, OS; P = 0.02, PFS). Patients with FIGO stage I had significantly better PFS (P = 0.013) and OS (P < 0.01). Advanced age (P = 0.04) and patients who received laparotomy (HR = 3.0, 95% CI: 1.25–7.21) and no lymphadenectomy (HR = 3.39, 95% CI: 1.25–9.09) were associated with increased hazard of recurrence. In addition, advanced age (P < 0.01) and patients with laparotomy (HR = 3.11, 95% CI: 1.22–7.92) were associated with decreased OS.

Conclusions: Adjuvant chemotherapy may reduce recurrences and improve PFS in patients with uterine carcinosarcoma.

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237 – Poster Session
Integration of adjuvant chemotherapy in first-line management of uterine carcinosarcoma
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Objectives: Uterine carcinosarcoma (UCS) is a rare, aggressive neoplasm of the female genital tract with poor survival that highlights the need for refined management strategies. We sought to evaluate an institutional cohort of UCS patients and the addition of chemotherapy (CT) in first-line management.

Methods: We reviewed records for patients with UCS from 1995 to 2013. Demographics, surgicopathologic features, treatment, and survival outcomes were abstracted and analyzed. Comparisons between subgroups and outcomes (recurrence, progression-free survival [PFS], overall survival [OS]) were evaluated and tested using Science Analysis System 9.0.

Results: We identified 93 patients with UCS whose median age was 67 years and stage distribution was 42% stage I, 5% stage II, 26% stage III, and 25% stage IV. The distribution of homologous (41.9%) and heterologous (48.4%) histology was similar. Recurrences were reported in 53.8% (50/93) of patients. Adjuvant therapy for the group included chemotherapy (CT) in 49.5%, chemotherapy + radiation (CRT) in 12.9%, and RT in 16.1%. CT consisted of carboplatin/paclitaxel (13), ifosfamide/paclitaxel (7), or ifosfamide/cisplatin (19). Risk of recurrence for patients receiving CT alone was 45.7% and median PFS and OS were 6.5 and 10.9 months, respectively. With a median follow-up time of 50.7 months, PFS and OS for the entire cohort were 8.2 and 14.6 months, respectively. Of the 39 patients with stage I disease, 46.2% received CT, 20.5% received RT, and 5.1% received CRT. Patients with stage I disease had a 41% risk of recurrence and a median PFS of 9.7 months and OS of 24.8 months. Fifty-one percent of patients were progression-free at 3 years. Stage I patients treated with CT had a significantly lower risk of recurrence (27.8% vs. 41.0%) and longer OS (79.3 vs. 24.7 months) compared to those treated with CRT or RT. Stage III patients treated with CT had similar recurrence risk (54.2% vs. 62.5%), PFS (6.5 vs. 7.1 months), and OS (8.9 vs. 10.9 months) as those treated with CRT or RT. Seventy percent (35/50) of patients who received recurrent salvage therapy and overall median time to death was 4.3 months. Median time to death for patients receiving one salvage regimen (n = 19) was 4.4 months, for those receiving two regimens (n = 9) was 11.2 months, and for those receiving three or more regimens (n = 7) was 17.9 months.

Conclusions: Our practice has moved CT into the first-line management of patients with UCS. In this large series of early-stage patients, CT appeared to produce an important benefit compared CRT or RT. Despite similar recurrence risks, heterologous histology appears to confer a substantial survival advantage. Sequential salvage regimens improved median time to death for a subset of patients with recurrent disease.

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238 – Poster Session
Uterine sarcoma: Ability of preoperative evaluation to identify malignancy and correct histology
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Objectives: To determine the pathologic concordance of preoperative biopsy with a final diagnosis of uterine sarcoma.

Methods: Using data from the Cleveland Clinic pathology database, we identified all cases of uterine sarcoma diagnosed between the years 2000 and 2013. Medical records were then reviewed and data, including preoperative endometrial evaluation, were abstracted from patient charts. The study aim was to determine pathologic concordance of preoperative endometrial evaluation with postoperative diagnosis of uterine sarcoma.

Results: A total of 127 cases of uterine sarcoma were identified on final pathology, of which 91 underwent preoperative sampling. Overall, preoperative sampling correctly revealed a diagnosis of cancer in 66 women (73%). Correct histology was identified on preoperative biopsy in 66% of cases overall. Preoperative biopsy concordance with final pathology was 75% for adenosarcoma, 100% for carcinosarcoma, 56% for leiomyosarcoma, and 60% for endometrial stromal sarcoma. Survival was improved in the cohort of patients with concordant pathology (1502 days vs. 1202 days), but this did not reach statistical significance (P = 0.317).

Conclusions: Preoperative endometrial biopsy is capable of identifying the presence of a malignancy in nearly two-thirds of cases of uterine sarcoma. While the accuracy of making the specific histologic diagnosis varies, based on the histology in
To investigate the efficiency of all-trans retinoic acid (ATRA) in single usage and combined with methotrexate (MTX) and actinomycin-D (Act-D) in choriocarcinoma on different cell culture models.

**Methods:** Human choriocarcinoma (hCG)-like JAR and JEG-3 cell lines were cultured. ATRA, MTX, and Act-D trial groups were determined according to the literature. The obtained synergistic apoptotic data indicated that the combination of ATRA, MTX, and Act-D could be used as an option against multidrug resistance encountered in the treatment of choriocarcinoma.

**Results:** Apoptosis ratios, P values, and β-hCG levels in different dosages on JAR and JEG-3 cell culture lines were shown in the table.

**Conclusions:** We report the application of an ATRA, MTX, and Act-D combination on JAR and JEG-3 cell line models for the first time in the literature. The obtained synergistic apoptotic data indicated that the combination of ATRA, MTX, and Act-D could be used as an option against multidrug resistance encountered in the treatment of choriocarcinoma.

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239 — Poster Session
The comparison of the effect of all-trans retinoic acid, methotrexate, actinomycin D and combined chemotherapy on the different choriocarcinoma cell culture models

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**Objectives:** To investigate the efficiency of all-transretinoic acid (ATRA) in single usage and combined with methotrexate (MTX) and actinomycin-D (Act-D) in choriocarcinoma on different cell culture models.

**Methods:** Human choriocarcinoma (hCG)-like JAR and JEG-3 cell lines were cultured. ATRA, MTX, and Act-D trial groups were determined as shown below.

For single-drug trial: MTX 2 μM, 4 μM, and 8 μM; ATRA 0.1 μM, 1 μM, and 10 μM; Act-D 0.05 μM, 0.1 μM, and 0.2 μM dosages were maintained.

For the combination of ATRA and MTX: ATRA 0.1 μM, 1 μM, and 10 μM dosages with MTX 2 μM dosage were maintained.

For the combination of ATRA, MTX, and Act-D: ATRA 0.1 μM, 1 μM, and 10 μM dosages with MTX 2 μM and Act-D 0.05 μM and 0.1 μM dosages were maintained.

The degree of apoptosis was obtained by flow cytometry (FCM). Supernatant was collected to investigate β-hCG levels.

**Results:** Apoptosis ratios, P values, and β-hCG levels in different dosages on JAR and JEG-3 cell culture lines are shown in the Table.

**Conclusions:** We report the application of an ATRA, MTX, and Act-D combination on JAR and JEG-3 cell line models for the first time in the literature. The obtained synergistic apoptotic data indicated that the combination of ATRA, MTX, and Act-D could be used as an option against multidrug resistance encountered in the treatment of choriocarcinoma.

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240 — Poster Session
Identifying potential therapeutic agents by molecular profiling of 136 cases of uterine clear cell carcinoma

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**Objectives:** Clear cell carcinoma of the endometrium (CCE) is a rare subtype of endometrial cancer (EC) associated with a worse prognosis when compared with other high-grade EC subtypes. We sought to evaluate molecular, genomic, and protein expression patterns in a large cohort of CCEs to direct patients to rational therapeutic strategies and clinical trials.

**Methods:** Of 3133 EC submitted to Caris Life Sciences from March 2011 to July 2014, 136 CCEs were identified based on reported pathology. Testing was ordered per physician request and included a combination of sequencing (Sanger or next-generation sequencing), protein expression (immunohistochemistry), and/or gene amplification (fluorescence in situ hybridization/chromogenic in situ hybridization).

**Results:** Among the samples evaluated by sequencing, the most common genetic mutations were TP53 (40%) and BRCA2 (33%). Hormone receptor expression was low: estrogen receptor-α (35%), progesterone receptors (22%) and androgen receptor (7%). ERBB2 was mutated at 8%, while its protein product Her2, a biomarker for HER2-directed therapies, was amplified in 12% and expressed in 5% of patients. Aberrations of the PI3K pathway, including 26% PTEN and...
25\% \text{PI3KCA} \text{mutation rate, with 69\% loss of PIK3CA, highlighted potential utility with inhibitors of this pathway.} \text{DNA repair pathway was altered in our CCE cohort as well: low ERCC1 (6\%) and MGMT (34\%) expression and high BRCA2 mutation rate, suggesting sensitivity to alkylating agents. Evaluation of the CMET pathway showed 40\% \text{IHC} \text{expression. TUBB3, a class III \text{β}-tubulin, was infrequently expressed (15\%), and TLE3 expression was high (29\%) compared to other EC subtypes, implicating sensitivity to microtubule-stabilizing agents. Increased TOP2A expression, associated with anaplastic efficacy, was seen in over 80\% of cases. Loss of RRM1, a DNA synthesis protein known to determine efficacy of gemcitabine, was seen in 78\% of cases.}

\textbf{Conclusions:} Our findings highlight the genetic heterogeneity of CCE and identified altered cellular pathways with potential diagnostic and predictive values for therapeutic intervention. \text{Drugs targeting the pathways for DNA repair, PI3K, and receptor tyrosine kinases, as well as gemcitabine and taxanes, may warrant consideration in selected patients with CCE.}

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\textbf{241 – Poster Session}  
\textbf{Comparing vaginal sarcoma and carcinoma in the Surveillance, Epidemiology and End Results program, 1988 to 2010: An analysis of 4062 patients}  
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\textbf{Objectives:} Vaginal sarcomas are rare and poorly understood tumors. We examined the survival outcomes of vaginal sarcomas in a large cohort compared to more common vaginal cancers.

\textbf{Methods:} The Surveillance, Epidemiology, and End Results (SEER) database was used to identify all women with primary invasive vaginal sarcomas, squamous cell carcinoma, and adenocarcinomas diagnosed between 1988 and 2010. Parametric and non-parametric methods were used to compare the demographic and clinical characteristics of women among the three tumor types as well as among sarcoma histologic subtypes. Survival was examined using multivariable Cox proportional hazards models and the Kaplan–Meier method.

\textbf{Results:} A total of 221 cases of invasive vaginal sarcoma were identified in the study period along with 3121 cases of squamous cell carcinoma and 720 cases of adenocarcinoma. Among women with vaginal sarcomas, leiomyosarcoma was the most common histologic type, accounting for 33\% (n = 72), followed by carcinomasarcoma with 22\% (n = 49). Compared to women with squamous cell carcinoma and adenocarcinoma, patients diagnosed with vaginal sarcomas tended to be younger, have larger tumors with less regional extension and lymph node positivity, and be treated primarily with surgery without radiation (P < 0.05 for all). After adjusting for other prognostic factors, patients with vaginal sarcomas had a 70\% greater risk of cancer-related mortality compared to those with squamous cell carcinoma (HR 1.70, 95\%CI 1.27–2.28). Sarcoma histology was not associated with survival, but age, tumor extension and metastasis, and lack of surgery were independently predictive of cancer-related mortality.

\textbf{Conclusions:} Primary vaginal sarcomas are aggressive neoplasms with different presenting characteristics and inferior survival outcomes compared to other more common vaginal cancer histologies.

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\textbf{242 – Poster Session}  
\textbf{Management of stage I uterine leiomyosarcoma: Is adjuvant chemotherapy beneficial?}  
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\textit{F. Miao;}  
\textit{J. De La Garza;}  
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\textit{bUniversity of Miami Miller School of Medicine, Miami, FL, USA;}  
\textit{cUniversity of Miami-Jackson Memorial Hospital, Miami, FL, USA}

\textbf{Objectives:} Leiomyosarcomas (LMS) are rare uterine tumors. Data regarding management of stage I disease after initial surgical resection are limited. The high rate of recurrence is the basis for considering adjuvant chemotherapy in stage I LMS, but the benefit of adjuvant chemotherapy in this setting is unclear. The aim of this study was to examine whether adjuvant chemotherapy after primary surgery improves survival in our patient population.

\textbf{Methods:} Patients diagnosed with LMS from 2005 to 2012 were identified using the Tumor Board Registry. Retrospective chart review was performed to obtain information on demographics, stage, grade, treatment regimens, and survival. Patients were staged based on the FIGO 2009 staging guidelines. Statistical analysis was performed using Science Analysis System.

\textbf{Results:} A total of 80 patients were treated for LMS from 2005 to 2012. The mean age of diagnosis was 53 years (range, 34–82 years). Twenty-nine patients (36\%) were stage I; four (13\%) of which were low grade while 62% were high grade. Of patients with stage I disease, 17 (58\%) were observed, 12 (41\%) received adjuvant chemotherapy with gemcitabine and docetaxel, and 3 received radiation. There was no difference in progression-free survival among those who received chemotherapy and those who were observed (P = 0.5). There was a nonsignificant inferior outcome in patients who underwent adjuvant chemotherapy; those who received adjuvant chemotherapy were nearly twice as likely to die as those who did not receive chemotherapy (HR 1.8, 95\%CI 0.46–7.07, P = 0.4).

\textbf{Conclusions:} At our institution, the majority of the patients diagnosed with stage I LMS did not receive adjuvant chemotherapy. Adjuvant chemotherapy had a negative effect on overall survival, suggesting that the risk of chemotherapy may outweigh any benefit.

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\textbf{243 – Poster Session}  
\textbf{Surgical outcomes in patients undergoing radical vulvectomy}  
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\textbf{Objectives:} To estimate patient and procedure risk factors associated with 30-day morbidity and mortality among patients undergoing radical vulvectomy.

\textbf{Methods:} Patients who underwent radical vulvectomy from 2005 to 2012 were abstracted from the American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP) database. Preoperative variables for patients with postoperative complications were compared to those without. Pearson’s chi square test, Student’s t-test, and binary logistic regression were used for analysis.

\textbf{Results:} We identified 343 patients who underwent radical vulvectomy, with 47.5\% undergoing concomitant lymphadenectomy. Median age was 65 years (range, 20–89 years), median body mass index was 28.9 (range, 15.2–72.0), and 9.6\% were of non-white race. The primary surgical team was gynecology in 90.7\% and general surgery in 9.3\% of cases. The rate of postoperative complications was 18.7\%, with 9.5\% experiencing major and 12.8\% minor complications. Mortality was 0.3\%. Major complications included myocardial infarction (0.3\%), deep surgical site infection (5.2\%), sepsis (1.5\%), pulmonary embolism (0.3\%),
and return to the operating room (5.5%). Minor complications included superficial wound infection (6.1%), urinary tract infection (2.9%), and blood transfusion (5.0%). Patients undergoing lymphadenectomy did not have a statistically significantly increased risk of complications (22.7% vs. 15.0%, P = NS); specifically, the risk of wound complication was not increased (13.5% vs. 8.3%, P = NS). Non-white race (P = 0.05), lower preoperative hematocrit (P = 0.002), lower preoperative albumin (P = 0.05), higher preoperative creatinine (P = 0.01), increased surgical complexity (P = 0.008), pulmonary comorbidity (P = 0.007), and diabetes (P = 0.02) were associated with complication. On multivariate analysis, only preoperative creatinine (P = 0.02) and surgical complexity (P = 0.05) remained associated with complication.

Conclusions: Radical vulvectomy is associated with some postoperative morbidity, mostly in the form of wound complications. Lymphadenectomy did not increase the risk of complication or wound complication. Laboratory values such as albumin, creatinine, and hematocrit may help preoperatively identify patients at risk for postoperative complication.

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244 — Poster Session
Sentinel lymph node mapping in patients with vulvar malignancies using indocyanine green and near-infrared imaging: Preliminary detection rate experience

Objectives: To assess our initial experience using indocyanine green (ICG) with near-infrared (NIR) imaging for sentinel lymph node (SLN) mapping in patients with vulvar malignancies.

Methods: Based on our positive experience with NIR imaging for SLN mapping in uterine and cervical malignancies, we evaluated this method for patients with vulvar malignancies. We captured all consecutive patients in whom NIR imaging was used from 1/1/13 to 8/13/14. Twenty-five milligrams of ICG powder was diluted in 20 mL of sterile water, and a standard peritumoral injection was performed on the vulva. NIR imaging was then performed. Technetium-99 (Tc99) was injected and lymphoscintigraphy performed the day before surgery in most cases; standard intraoperative gamma probe detection was used. At-risk groins were defined based on the location of the tumor, i.e., “midline” or “not”. Successful SLN mapping required the identification of lymph nodes in the specimen. Simple descriptive statistics were performed.

Results: NIR imaging was performed in 15 patients with 28 at-risk groins (13 midline tumors, 2 lateral tumors). Eleven (73%) primary tumors were squamous cell carcinomas; the remaining tumors were invasive melanomas. The median primary tumor size was 2 cm (range, 0.4–4 cm). ICG was used in all cases with Tc99 + blue dye (n = 2), Tc99 only (n = 10), blue dye only (n = 1), and alone (n = 2). Overall, Tc99 was used in 12 cases, encompassing 23 at-risk groins. Successful mapping was seen in 26 (93%) of 28 groins irrespective of detection method. Tc99 resulted in successful mapping in 19 (83%) of the 23 groins. In comparison, ICG resulted in successful mapping in 25 (89%) of the total 28 groins. No SLN was blue alone. ICG detected SLNs in four groins that were not mapped with Tc99. Only in one case did the ICG not map but the Tc99 did. ICG alone without any other detector was used in two patients with three at-risk groins. SLNs were identified in all three groins. Inguinofemoral lymphadenectomy was only performed in the one patient who did not map at all. SLN metastases (macro- or micro-metastases) were identified in six (43%) of the other 14 patients.

Conclusions: The interstitial/cutaneous injection of ICG and NIR imaging for SLN mapping of vulvar malignancies seems feasible and quite promising. It may eliminate the inconvenience and cost of Tc99-based SLN mapping, pending more experience and validation.

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245 — Poster Session
Gyn/onc partnership with sarcoma center yields superior clinical trial enrollments for uterine leiomyosarcoma patients
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Objectives: This retrospective chart review was designed to determine the difference in chemotherapy (CT) treatment and clinical trial enrollment practices by gynecologic oncologists (GYN) and medical oncologists (MED) involved in the treatment of recurrent metastatic (RM) uterine leiomyosarcoma (uLMS) at an institution with a sarcoma center.

Methods: Medical records of RM uLMS patients cared for by either GYN/ONC service and/or the medical oncology sarcoma service between 1/1/2000 and 4/1/2014 were audited for patient characteristics, tumor characteristics, treatment, and clinical trial enrollment. A total of 58 patients with RM uLMS were identified.

Results: Of the 58 patients with recurrent metastatic uLMS identified, 26 (48%) were treated by GYN alone and 32 were treated by a combination of GYN and MED (MED/GYN) (52%) after the formation of a dedicated sarcoma center. Age of diagnosis and stage were not statistically different between the two groups. Tumor size, average number of mitotic figures/10 high-power field, grade, presence of lymphovascular space involvement, cervical involvement, and FIGO stage at diagnosis were also not statistically different. There was a significant difference between the number of clinical trial enrollments in the GYN group and the MED/GYN group (2 vs. 22, P = 0.001). There was also a significant difference between the number of CT regimens (palliative + clinical trial) prescribed by GYN and MED/GYN (2.67 vs. 4.29, P = 0.03), but the number of palliative CT regimens was not statistically different between the two groups (2.67 vs. 3.26, P = 0.249), supporting the fact that the difference between the total CT regimens is driven by the number of clinical trial enrollments and that practice patterns are similar with regard to number of palliative CT regimens.

Conclusions: uLMS is a rare and aggressive disease. The standard of care for RM uLMS remains enrollment in a clinical trial. Although the number of palliative CT regimens prescribed by the two groups was the same, referral of GYN uLMS patients with RM disease to dedicated trials based at a sarcoma center resulted in an increase in total number of CT regimens and clinical trial enrollments. This partnership between gynecology oncology and a dedicated sarcoma medical oncologist with access to clinical trials should be encouraged for all tertiary care oncology centers.

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246 — Poster Session
Concordance of uterine sarcoma diagnosis based on method of preoperative evaluation
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Objectives: To determine if the method of preoperative sampling affected the concordance of pre- and post-operative diagnosis of uterine sarcoma.
Methods: Using data from the Cleveland Clinic pathology database, we identified all cases of uterine sarcoma diagnosed between the years 2000 and 2013. Medical records were then reviewed and data, including preoperative endometrial evaluation, were abstracted from patient charts. The study aim was to determine if the method of preoperative sampling affected concordance with postoperative diagnosis of uterine sarcoma. Carcinosarcomas and adenosarcomas were excluded.

Results: A total of 80 cases met inclusion criteria: 58 leiomyosarcomas (LMS) and 22 endometrial stromal sarcomas (ESS). Preoperative sampling was performed in 52 cases and included: 24 endometrial biopsies (EMB), 19 dilation and curettages (D&C), and 9 other (cervical biopsy, interventional radiologic biopsy of metastatic lesion). Preoperative sampling identified cancer in 32 cases of the 52 sampled (62%), and the correct histology in 30 cases (58%). In the 32 cases of LMS with preoperative sampling, cancer was identified in 20 (63%) and the correct histology in 18 (56%). In the 20 cases of ESS with preoperative sampling, cancer was identified in 12 (60%) and the correct histology in 12 (60%). Diagnostic accuracy varied with the mode of sampling. For LMS, concordance was 30% for EMB, 63% for D&C, and 83% for others (P = 0.106 EMB vs. D&C; P = 0.04 EMB vs. other). For ESS, concordance was 43% for EMB, 100% for D&C, and 100% for other (P = 0.07 EMB vs. D&C; P = 0.07 EMB vs. other).

Conclusions: Preoperative evaluation of uterine sarcoma has variable accuracy in identifying final pathologic diagnosis. There was a trend toward significance of D&C over EMB for accuracy in identifying LMS and ESS. These findings add to previous results suggesting that preoperative sampling can identify sarcomas preoperatively.

<table>
<thead>
<tr>
<th>Leiomyosarcoma</th>
<th>Endometrial stromal sarcoma</th>
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</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>58</td>
</tr>
<tr>
<td>Number with preoperative sampling</td>
<td>32</td>
</tr>
<tr>
<td>EMB</td>
<td>10</td>
</tr>
<tr>
<td>D&amp;C</td>
<td>16</td>
</tr>
<tr>
<td>Others</td>
<td>6</td>
</tr>
<tr>
<td>Cancer identified</td>
<td>20</td>
</tr>
<tr>
<td>Correct histology</td>
<td>18</td>
</tr>
<tr>
<td>EMB</td>
<td>3</td>
</tr>
<tr>
<td>D&amp;C</td>
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<td>Others</td>
<td>5</td>
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247 — Poster Session
Factors associated with recurrence of vulvar squamous cell carcinoma
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Objectives: The objective of this study was to evaluate patients with squamous cell carcinoma (SCCA) of the vulva treated at a single institution to determine factors associated with increased risk of local recurrence.

Methods: Patients treated for SCCA of the vulva with an excisional procedure from 1991 to 2010 at a single institution were included. All pathology was re-reviewed by a single gynecologic pathologist for tumor size, histology, and margin status. Paper and electronic medical records were reviewed for demographic information, treatments received, date of recurrence, and last follow-up. Risk of recurrence was analyzed using Wilcoxon rank sum test and Fisher’s analysis. Disease-free survival was calculated with the log rank test and Cox regression.

Results: Sixty-nine patients with invasive SCCA of the vulva treated surgically were included in this study. Stage distribution was as follows: 5 (7.2%) stage IA, 49 (71.1%) stage IB, 3 (4.4%) stage II, 11 (15.9%) stage III, and 1 (1.4%) stage IV. Survival data were available for 58 patients and recurrence data for 61 patients. Five-year survival was 81% and median recurrence-free survival was 88 months. Thirty-nine percent of patients recurred locally. Rates of local recurrence were not affected significantly by stage (P = 0.98). Tumor distance from the surgical margins was not associated with either risk for recurrence (lateral margin P = 0.44, deep margin P = 0.22) or shortened disease-free survival (lateral margin P = 0.22, deep margin P = 0.10). Receiving operating characteristic curves did not provide a disease-free margin cut-off predictive of recurrence (lateral margin AUC 0.55, deep margin AUC 0.60). Likewise, recurrence risk was not associated with tumor size (P = 0.11), tumor differentiation (P = 0.44), or presence of lymphovascular invasion (P = 0.33). No patient factors were found to be predictive of risk of local recurrence or recurrence-free survival.

Conclusions: Prior studies had demonstrated a correlation between margin status and risk of local recurrence of SCCA of the vulva. In our study in which a single pathologist reviewed all pathologic slides, no pathologic factors were found to be predictive of local recurrence.

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248 — Poster Session
Utility of intraoperative frozen section of the inguinofemoral sentinel lymph node in vulvar cancer: A retrospective cohort
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Objectives: To evaluate the utility of frozen section for the intraoperative assessment of sentinel lymph nodes.

Methods: A total of 130 patients with vulvar cancer were treated at The University of Tennessee-West Clinic between 2006 and 2012; 110 were eligible for evaluation. All patients were restaged to FIGO 2009. The clinical records were reviewed for clinical lesion size, primary site of tumor, recurrence of disease, type of therapy, and follow-up status. Surgical margins, depth of invasion, tumor thickness, cell type, grade, and presence of lymphovascular invasion were obtained. The distance between the tumor and the surgical margin and overall margin status were also obtained.

Results: Thirty-two of 65 eligible patients underwent sentinel lymph node detection. No significant differences were found between the cohorts. The rate of positive sentinel lymph node detection was 90.6% (95% CI 75.0% - 98.0%). Frozen pathology results and final pathology had extremely high (100%) correspondence with both positive and negative node results. Frozen section was used to direct further dissection in 29 patients. No difference in progression-free or overall survival was seen between those who did and did not undergo sentinel detection.

Conclusions: Sentinel lymph node dissection is an acceptable method in a community private practice, with similar outcomes and detection rates to national trials. Furthermore, frozen section can be effectively used.

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249 — Poster Session
Evaluating risk factors for wound complications after radical vulvar surgery in a national cohort
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Objectives: The objective of this study was to identify risk factors associated with wound infection and dehiscence after radical vulvar surgery.
Methods: Using the prospectively collected National Surgical Quality Improvement Program (NSQIP) database, we reviewed all cases of radical vulvectomy from 2006 to 2012. Demographics, comorbidities, functional status, preoperative laboratory values, lymph node dissection (LND), operative time, and postoperative wound complications (infection and dehiscence) were evaluated. Wound classification was defined as clean, clean-contaminated, contaminated, and dirty/infected. Surgical complexity was characterized by concurrent non-gynecologic surgery. Descriptive analysis using univariate and bivariate tests and multivariant logistic regression models were used.

Results: We identified 387 patients who underwent radical vulvar surgery. Wound complications developed in 8% (31/387) of cases (2% developed wound dehiscence and 6% developed wound infection). In those who had LND ($n = 131$), the wound infection rate was 9% and dehiscence rate was 4%. In contrast, those who did not have LND had a wound infection rate of 8% and dehiscence rate of 1% ($P = 0.7$ and $P = 0.09$, respectively). Flap procedures were performed in five patients, and only one patient developed wound infection. Thirteen patients had reoperations (4%). Eighteen patients (8%) were discharged to skilled facilities. Those who were >66 years were 4 times more likely to be discharged to skilled facilities ($95\% CI 1.2–12.8$, $P = 0.025$). In univariate analysis, risk factors for wound complications were longer operative time, lower serum albumin, and higher wound classification. Age, body mass index, and American Society of Anesthesiologists class were not associated with wound complications. In multivariate analysis, longer operative time (odds ratio 1.43, $95\% CI 1.1–1.9$, $P = 0.014$) was associated with wound complications controlling for surgical complexity.

Conclusions: Standard metrics such as age and body mass index were not associated with increased wound complications following radical vulvectomy and should not prohibit proceeding with surgery. Instead, factors such as nutritional status (albumin) and extent of resection should be considered and optimized. Prolonged operative time should be minimized, particularly where it is not attributed to more complex resections and closures.

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250 — Poster Session

Therapeutic dilemma: Prognostic factors and outcome for patients with neuroendocrine tumors of the cervix

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Objective: We reviewed treatment and outcomes for neuroendocrine tumors (NET) of the cervix at a National Cancer Institute-designated Comprehensive Cancer Center.

Methods: After institutional review board approval, data on women with NET of the cervix treated at our institution between January 1, 1999 and June 30, 2014 were abstracted for analysis. Demographic, clinical, radiological, pathological, and progression-free and overall survival (PFS, OS) data were collected. T-test was used for univariate and multivariate analyses.

Results: Of 1469 women with cervical cancer, 21 (1.4%) had NET histology. The median age of those with NET was 47 years and average tumor size was 5.2 cm. Tumors >4 cm and small cell subtypes were seen in 48% and 52%, respectively. Stage IA–IB1 was noted in nine (43%), IB2–IVA in sic (29%), and IVA in sic cases. Six patients underwent primary radical hysterectomy with lymph node (LN) dissection (25%) and four (15%) received neoadjuvant treatment with external pelvic radiation (RT) or chemotherapy (CT) (2) followed by hysterectomy. Adjuvant therapy was administered in five cases (24%), with two receiving CT alone and three receiving combined CT and RT (CCR). Three patients received definitive CCR (14%), four definitive RT (19%), and one palliative CT alone. Three never followed-up after diagnosis. CT consisted of etoposide/cisplatin ($n = 5$), etoposide/carboplatin ($n = 5$), and carboplatin/paclitaxel ($n = 1$). Patients who received RT had significantly shorter OS ($P = 0.02$). Median PFS of 26.9 months and median OS of 35.7 months were noted, with seven recurrences in 18 patients available for follow-up (39%). Although patients with stage IA–IB1 disease had improved outcomes compared to stage IB2–IVA and IVA PFS: 35.7 vs. 8. vs. 7.8 months; OS: 39.8 vs. 13.7 vs. 7.8 months) and lower recurrence rate (RR) (20% vs. 60% vs. 66%), this did not reach statistical significance. Other variables, including tumor size, type of treatment, age, LN status, and tobacco use, were not associated with survival or RR.

Conclusions: NET of the cervix is a rare malignancy that presents at a relatively young age with bulky tumors and advanced-stage disease. No prognostic factors were identified, although early-stage disease seems to be associated with improved survival. Optimal management is yet to be determined, and multimodality treatment is often advocated.

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251 — Poster Session

Comprehensive genetic testing: The next generation in an ovarian cancer risk assessment clinic


Objective: In the era of personalized medicine, identifying specific genetic mutations other than BRCA1 and BRCA2 that confer increased risk of heritable breast and ovarian cancer susceptibility is increasingly important. In an effort to meet these demands, we have employed several multigene next-generation genetic screening panels. The purpose of this study was to describe our experience with panel testing in an ovarian cancer risk assessment clinic.

Methods: We reviewed an institutional review-board approved, prospectively gathered database of patients evaluated in an ovarian cancer risk assessment clinic since 2013. Data evaluated included general demographics, family and personal history of cancer, frequency of genetic testing, type of test performed, frequency and types of deleterious mutations, and performance of prophylactic surgery.

Results: Since 2013, 76 women were evaluated in our clinic; 60 (79%) were Caucasian and 12 (16%) were African American. Thirty-four patients (45%) had a personal history of breast or ovarian cancer with or without a significant family history, while the remaining 42 (55%) patients had a family history of breast or ovarian cancer. Thirty-eight had BRCA1 testing, site-specific or comprehensive, and 25 underwent multigene panel testing. Panels varied from small, clinically actionable to larger. Seven of the patients who underwent panel testing had negative BRCA1 testing first. Twenty-two patients had BRCA1/2 mutations or variants, seven had Lynch syndrome mutations, and one had a MUTHY+ mutation. Nine patients have panels pending. Seven patients with noted mutations have undergone risk-reducing surgery, none with malignancy.

Conclusions: These data demonstrate that after appropriate pretest counseling on the benefits and challenges of multigene panel testing, patients are interested in expanded genetic testing. The use of multigene panels may allow for the identification of rarer genetic causes of personal/family histories of cancer as well as genetic causes in individuals and families with atypical presentations of well-known cancer syndromes and may be more cost-effective in cases where multiple cancer syndromes are suspected. Multigene panels
may be appropriate in patients with suspicious personal and family histories of breast and/or ovarian cancer, especially after negative genetic testing for more common causes.

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252 — Poster Session
Role of laparoscopy in determining optimal cytoreduction in patients with ovarian, fallopian tube and primary peritoneal cancer
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Objectives: The objective of our study was to evaluate the role of laparoscopy (LS) in triaging patients with ovarian, fallopian tube, and primary peritoneal cancer undergoing primary cytoreductive surgery (PCS) and determine its role in predicting optimal cytoreduction (OC).

Methods: We identified all patients who underwent PCS for ovarian, fallopian tube, and primary peritoneal cancer at our institution between 01/2008 and 12/2013. Determination of resectability by LS was based on the site, pattern, and tumor burdens. Patients were divided in two cohorts. In group A, LS was used at the time of PCS and group B had open PCS without LS. Patients with stages I–II disease were considered as early-stage and III–IV as advanced-stage disease. OC was defined as residual disease < 1 cm. Survivals were estimated using the Kaplan–Meier method.

Results: LS assessment was used in 55 (36%) of 153 patients who underwent PCS. An OC was achieved in 48 of 49 cases (98%) evaluated as resectable at the time of LS. The surgery was minimally invasive in 23 patients (47%) and LS was converted to an open procedure in the remaining 26 patients (53%). Six patients (11%) were found to be unresectable at the time of LS. Four of those (7%) received neoadjuvant chemotherapy followed by interval debulking. Our estimate for conservative sensitivity of LS in determining OC was at least 87% (95% CI: 79%-96%). There were no statistically significant differences in mean operating time (OT) and estimated blood loss (EBL) between group A and group B. The mean OT and EBL were 207 min (range, 49–434 min) and 370 mL (range, 10–2000 mL) for group A and 192 min (range, 57–412 min) and 580 mL (range, 50–5000 mL) for group B, respectively. There was no port site metastasis in our series. The median overall survival (OS) for patients in group A with advanced disease that was optimally cytoreduced was not reached and the upper 25th percentile for OS was 36 months (95% CI: 12-noncalculable). For patients in group B with advanced disease that was optimally cytoreduced, the upper 25th percentile for OS was 32 months (95% CI: 18–53). The difference in OS was not statistically significant (P = 0.76).

Conclusions: LS has high sensitivity in predicting OC and is a feasible tool in triaging patients with ovarian, fallopian tube, and primary peritoneal cancer. LS is not associated with adverse surgical outcomes and seems not to have a negative effect on survival.

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253 — Poster Session
The impact of age on the risk of 30-day postoperative morbidity and mortality in patients undergoing surgery for ovarian cancer
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Objectives: To examine the effect of age on postoperative 30-day morbidity and mortality after surgery for ovarian cancer.

Methods: The American College of Surgeons National Surgical Quality Improvement Program files were used to identify ovarian cancer patients who underwent surgery from 2005 to 2011. Women were divided into four age groups: <60, 60–69, 70–79, and ≥80 years. Multivariable logistic regression models were performed.

Results: Of 2063 patients included, 47% were <60 years, 28% were 60–69 years, 18% were 70–79 years, and 7% were ≥80 years. Overall 30-day mortality and morbidity rates were 2% and 30%, respectively. Patients ≥80 years were more likely to die within 30 days compared to patients aged <60, 60–69, and 70–79 years (9.2% vs. 0.6% vs. 2.8% vs. 2.5%, P < 0.001). Patients <60 years were less likely to have postoperative complications compared to patients aged 60–69, 70–79, and ≥80 years (25% vs. 34% vs. 35% vs. 39%, P < 0.001), including surgical (23% vs. 29% vs. 32% vs. 30%, P = 0.001), nonsurgical (6% vs. 12% vs. 10% vs. 16%, P < 0.001) and cardiac (2% vs. 5% vs. 5% vs. 6%, P = 0.017) complications. Patients aged ≥80 years were more likely to develop pulmonary (9% vs. 2% vs. 5% vs. 3%, P < 0.001) and septic (9% vs. 3% vs. 5% vs. 4%, P = 0.01) complications compared to patients aged <60, 60–69, and 70–80 years, respectively. No difference in the risk of renal (0.2% vs. 1% vs. 1% vs. 1%, P = 0.20) complications and surgical re-exploration (4% vs. 4% vs. 3% vs. 5%, P = 0.80) was found among the four age groups. In multivariable analysis after adjusting for other confounders, patients aged 60–69 years (odds ratio [OR] 1.3, 95% CI 1.0–1.7, P = 0.03), 70–79 years (OR 1.4, 95% CI 1.0–1.8, P = 0.03), and ≥80 years (OR 1.7, 95% CI 1.1–2.5, P = 0.01) were more likely to have 30-day mortality than patients aged <60 years. Similarly, patients aged 60–69 years (OR 3.7, 95% CI 1.5–10.6, P < 0.001), 70–79 years (OR 3.1, 95% CI 1.1–9.6, P = 0.03) and ≥80 years (OR 9.3, 95% CI 3.4–28.1, P < 0.001) were more likely to have 30-day morbidity than patients aged <60 years.

Conclusions: Elderly patients with ovarian cancer have a higher risk of perioperative mortality and morbidity, especially pulmonary, cardiac, and septic complications. Age was a significant predictor of perioperative outcome, even after adjusting for other confounders. Therefore, elderly patients should be counseled thoroughly about the risk of primary debulking surgery vs. neoadjuvant chemotherapy.

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254 — Poster Session
Access to high quality food and survival from ovarian cancer: An analysis of Cook County, Illinois
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Objectives: Non-Hispanic blacks (NHB) have poorer ovarian cancer survival than non-Hispanic whites (NHW). Previous research has shown that increased consumption of fresh fruits and vegetables improves ovarian cancer survival, and consumption of antioxidants in fresh fruits and vegetables have been linked to improvements in chronic disease as well. Access to fresh produce varies by geographic area, with fewer fresh fruits and vegetables consumed in predominantly NHB areas. Our purpose was to investigate whether density of high-quality grocery stores (HQS) was associated with ovarian cancer 5-year survival in patients diagnosed in highly segregated Cook County, IL, between 1995 and 2007.

Methods: Data for ovarian cancer cases were obtained from the Illinois State Cancer Registry. Residential address at diagnosis was geocoded using ArcGIS to obtain patient census tract and matched to 2000 United States Census data to obtain tract-level demographic variables and used to create quartiles of neighborhood-level concentrated disadvantage and affluence. Grocery store data, obtained from Dun and Bradstreet,
were used to dichotomize stores as HQS, and the kernel density of HQS per census tract was estimated in ArcGIS. Chi square statistics were used to test the difference in HQS density for covariates. Multivariate proportional hazards models were used to estimate the association between 5-year survival and HQS density, adjusting for clinical and demographic factors.

**Results:** Fewer NHB patients lived in census tracts with high HQS density (NHB: 94 of 836, 11%; NHW: 721 of 3,628, 20%; \( P < 0.0001 \)). Census tracts with high HQS density also had the highest concentrated affluence and lowest concentrated disadvantage \( (P < 0.0001) \) for both. HQS density was significantly associated with improved 5-year survival in crude models \( (HR = 0.80, 95\% CI 0.70–0.91) \), which persisted after adjusting for age, race, clinical factors, and neighborhood-level concentrated disadvantage and affluence \( (HR = 0.83, 95\% CI 0.73–0.95) \).

**Conclusions:** Results indicate that HQS density is significantly associated with improved 5-year survival among women diagnosed with ovarian cancer in Cook County, IL. Access to fresh fruits and vegetables may contribute to ovarian cancer survival disparities and may have implications for chronic disease as well.

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**255 — Poster Session**

**The effect of time on racial differences in ovarian cancer stage at diagnosis among cases identified through the National Cancer Database**

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**Objectives:** Past research is inconclusive regarding racial differences in stage at diagnosis between non-Hispanic black (NHB) and non-Hispanic white (NHW) women with epithelial ovarian cancer. The purpose of this analysis was to determine whether racial differences in stage at diagnosis were present in women diagnosed with ovarian cancer in the United States and Puerto Rico between 1998 and 2011 and to assess whether differences changed over time.

**Methods:** NHW and NHB cases reported in the National Cancer Database (NCDB) were analyzed to evaluate differences in stage at diagnosis. Stage was dichotomized as early (stages I and II) vs. late (stages III and IV), and year of diagnosis was analyzed in three periods (1998–2002, 2003–2007, 2008–2011). Chi square was used to test differences between demographic and clinical factors (age, income, education, insurance status, facility location, tumor grade, period of diagnosis) and stage at diagnosis. Multivariable logistic regression was used to estimate the adjusted odds ratio (OR) and 95% CI for the association between race and late stage at diagnosis. Interaction between race and year of diagnosis was tested in the final model.

**Results:** A total of 142,088 (92.2%) NHW and 12,086 (7.8%) NHB women were analyzed. NHB women had a significantly higher odds of late-stage diagnosis than NHW women \( (OR = 1.34, 95\% CI 1.27–1.41) \). Interaction between race and period of diagnosis was statistically significant \( (P = 0.04) \), with disparities decreasing over time \( (OR and 95\% CI, 1998–2002: 1.49, 1.36–1.63; 2003–2007: 1.33, 1.22–1.45; 2008–2011: 1.21, 1.11–1.32) \).

**Conclusions:** Results indicate that within NCDB, NHB women are more likely to be diagnosed with late-stage ovarian cancer, yet these differences are decreasing with time. These findings of improved black-white differences in stage at diagnosis could be due, in part, to improved access to care. Results may be underestimated because NCDB reflects approximately 70% of United States cases annually, generally including higher-tier, Commission on Cancer (CoC)-approved hospitals, whose members may have changed over time.

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**256 — Poster Session**

**Oral contraceptive use and reproductive characteristics affect survival in patients with epithelial ovarian cancer**

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**Objectives:** Prognostic risk factors influencing survival in patients with epithelial ovarian cancer (EOC) include tumor stage, grade, histologic subtype, debulking status, and platinum sensitivity. Little is known about the impact of the hormonal milieu and reproductive factors before cancer diagnosis on clinical outcome. We sought to evaluate whether oral contraceptive (OC) use, gravidity, and parity have any prognostic significance on overall survival (OS) in patients with EOC.

**Methods:** We included 387 patients with EOC, fallopian, and primary peritoneal cancers treated from 1982 to 1998 who completed a comprehensive epidemiologic questionnaire. Retrospective chart review was performed to abstract clinicopathologic data. OS was determined; Kaplan–Meier analysis was performed to compare survival across categorical exposures with differences tested using the log-rank test, while continuous variables were analyzed with Cox regression. Cox regression model was used to compute adjusted hazard ratios (aHRs) and 95% CIs.

**Results:** After adjusting for age at diagnosis, stage, and histologic subtype, decreased risk of death was observed in women who reported prior use of OC \( (aHR 0.79, 95\% CI 0.58–1.09) \), previous pregnancy \( (aHR 0.77, 95\% CI 0.57–1.04) \), or a live birth \( (aHR 0.81, 95\% CI 0.60–1.08) \). OC use was associated with a crude reduced risk of death \( (HR 0.55, 95\% CI 0.42–0.72) \), with reported median OS of 81 months in OC users compared with 46 months in nonusers. Patients who reported a single live birth experienced the largest potential survival advantage \( (aHR 0.61, 95\% CI 0.39–0.94) \). OC use and prior pregnancy were associated with improved survival across all histologic subtypes, stages, and grades.

**Conclusions:** Our findings suggest that OC use, gravidity, and parity may have long-lasting effects on epithelial ovarian tumor characteristics conferring favorable prognosis. Putative mechanisms may stem from complex interactions between ovarian cells, host immune cells, and hormonal microenvironment during carcinogenesis that ultimately affect tumor biology. Future efforts should be directed at determining the role of host reproductive factors in antitumor immunity.

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**257 — Poster Session**

**Diagnostic value of combined 18F-FDG positron emission tomography/computed tomography in recurrent epithelial ovarian cancer with non-disseminated lesions: Correlation with pathologic diagnosis of the secondary cytoreduction**

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**Objectives:** To evaluate the diagnostic accuracy of combined 18F-fluoro-2-deoxyglucose-positron emission tomography/computed tomography (18F-FDG-PET/CT) imaging in suspected recurrence of
epithelial ovarian cancer with nondisseminated lesions by correlating with pathologic diagnosis after the secondary cytoreduction.

Methods: In this retrospective study, we enrolled 134 patients who underwent secondary cytoreduction after imaging studies such as conventional CT or combined 18F-FDG-PET/CT. We estimated the sensitivity, positive predictive value (PPV), and accuracy of combined 18F-FDG-PET/CT imaging and compared them with those of CT correlating with the pathologic diagnosis of the secondary cytoreduction.

Results: Overall, 124 (92.5%) patients were positive for malignancy after secondary cytoreduction. In 68 patients who underwent both 18F-FDG-PET/CT and CT, 60 (88.2%) were confirmed to be positive for recurrent tumor. Among these, 59 patients were detected by combined 18F-FDG-PET/CT, with 98.3% sensitivity, 88.1% PPV, and 86.8% accuracy, while 60 patients were detected by CT, with 100% sensitivity, 88.2% PPV, and 88.2% accuracy. In 68 patients who underwent both imaging studies, 60 (88.2%) were confirmed to be positive for recurrent tumor. Among these, 59 patients were detected by combined 18F-FDG-PET/CT, with 98.3% sensitivity, 88.1% PPV, and 86.8% accuracy, while 60 patients were detected by CT, with 100% sensitivity, 88.2% PPV, and 88.2% accuracy. In 68 patients who underwent both imaging studies, 60 (88.2%) were confirmed to be positive for recurrent tumor. Among these, 59 patients were detected by combined 18F-FDG-PET/CT, with 98.3% sensitivity, 88.1% PPV, and 86.8% accuracy, while 60 patients were detected by CT, with 100% sensitivity, 88.2% PPV, and 88.2% accuracy. In 68 patients who underwent both imaging studies, 60 (88.2%) were confirmed to be positive for recurrent tumor.

Conclusions: Our study demonstrated a discrepancy from previous studies in the diagnostic value of combined 18F-FDG-PET/CT in recurrent epithelial ovarian cancers with nondisseminated lesions. Combined 18F-FDG-PET/CT showed higher lesion-based sensitivity and accuracy. A prospective study with a larger cohort is needed.

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258 — Poster Session
Anti-NMDA receptor encephalitis: Consider the ovaries
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Objectives: Anti-N-methyl-d-aspartate receptor (NMDAR) encephalitis has been described in the literature for the past decade, but its association with ovarian pathology has only recently been elucidated. This study reviews the presentation and clinical courses of four consecutive cases of anti-NMDAR encephalitis in young women with ovarian teratomas.

Methods: Four patients with anti-NMDAR encephalitis secondary to ovarian teratomas diagnosed between May 2013 and February 2014 were identified at a single institution. All patients had anti-NMDAR antibodies within their cerebrospinal fluid (CSF), and all patients underwent adnexal surgery confirming the presence of an ovarian teratoma. Demographic, clinical, and histologic information was abstracted from medical records.

Results: Characteristics of the four consecutive patients who met the criteria were reviewed. Age at time of diagnosis ranged from 17 to 42 years. The time from presentation to diagnosis ranged from 3 to 5.5 weeks. All patients presented with anxiety and insomnia. Other acute symptoms included agitation, choreiform movements, psychosis, delirium, and seizure-like activity. All patients had normal head imaging and underwent psychiatric evaluations before the final diagnosis was made. All were noted to have a lymphocytic pleocytosis upon lumbar puncture, and all were eventually diagnosed by confirmatory anti-NMDAR antibodies within the CSF. Pelvic ultrasonography demonstrated ovarian masses ranging in size from 1 to 10 cm. One patient demonstrated modest improvement in symptoms after receiving plasmapheresis before surgery. Three patients were found to have mature teratomas, and one was diagnosed with a high-grade immature teratoma and underwent reoperation to complete tumor staging. While all patients demonstrated clinical improvement after their teratomas were removed, only three patients have made full recoveries to date.

Conclusions: Anti-NMDAR encephalitis should be considered early in a young patient with sudden-onset encephalitis. Pelvic imaging should be performed early to determine the presence of an ovarian mass. Patients with this diagnosis have variable clinical courses, despite the timing of diagnosis and surgery. Excision of the teratoma improved the condition of all four patients in this study.

259 — Poster Session
The influence of staging system in pediatric ovarian cancer clinical outcomes
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Objectives: Due to the rarity of malignant ovarian tumors (MOT) in children, a number of approaches to treatment have been suggested for these patients. We sought to compare the clinical and surgical outcomes based on staging system used (Children’s Oncology Group [COG] vs. International Federation of Obstetrics & Gynecology [FIGO], Tables 1 and 2).

Methods: Retrospective chart review was performed including all female primary MOTs from 1991 to 2011 at a single tertiary children’s hospital. Demographic data, surgical staging, pathology, postoperative treatment, and survival outcomes were collected. The two groups were compared using t-test, chi square, and Fisher exact tests. Kaplan–Meier curves and Cox proportional HR were used to compare recurrence of disease.

Results: A total of 38 patients were identified based on surgical service: pediatric gynecology/gynecologic oncology (GYN, n = 16) or pediatric surgery (PS, n = 22). Germ cell and stromal ovarian tumors comprised the majority of MOTs in both groups. Mean age was 13.9 ± 2.8 years for GYN and 10.2 ± 5.6 years for PS (P = 0.01). Mean body mass index (BMI) was 25.7 for GYN and 21.2 for PS (P = 0.06). Eighty percent of GYN and 90% of PS patients underwent laparotomy based on positive tumor markers (TM); the remainder had laparoscopy with negative TM. Of those with staging, 55% were FIGO-based and 45% were COG. GYN submitted more tissue biopsies of the bladder (P = 0.03) and colon

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There were no significant differences in recurrence among patients in either group univariately (HR = 1.5, 95% CI 0.30–7.49, P = 0.62) or after adjustment for age and BMI (aHR = 1.29, 95% CI 0.21–7.93, P = 0.78). Overall mortality was 5.6%.

**Conclusions:** Despite the use of several surgical staging criteria by PS and GYN surgery services, pediatric patients with MOT did not have significantly different clinical outcomes. Pediatric ovarian cancer patients referred to gynecologic oncologists after surgical intervention by pediatric surgeons may not require further staging. Larger multi-institutional studies are needed to study MOT in this population.

**Table 1**

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**260 — Poster Session**

**Transvaginal ultrasound-guided biopsy of adnexal masses as a useful diagnostic alternative replacing cytology or laparoscopy in advanced ovarian cancer patients**

S.J. Chang, T.W. Kong, J.H. Son, S.W. Kang, J. Paek, E.J. Lee, H.S. Ryu, Ajou University Hospital, Suwon, South Korea

**Objectives:** The aim of this study was to evaluate transvaginal sonography (TVS)-guided core needle biopsy of adnexal masses for neoadjuvant chemotherapy (NACT) in patients with advanced ovarian malignancy.

**Methods:** We retrospectively reviewed the medical records of 60 patients who underwent TVS-guided core needle biopsies in our gynecologic cancer center between March 2009 and August 2014. TVS-guided core biopsies were performed for patients with advanced ovarian malignancy who were considered for neoadjuvant chemotherapy (NACT) and patients with adnexal masses who required differential diagnosis of non-gynecologic tumors.

**Results:** NACT was planned for 50 patients (83.3%) due to the presence of coexisting illness, age, disease burden, location of metastatic sites, performance status, and tumor stage. Ten patients (16.7%) underwent TVS-guided core needle biopsy for differential diagnosis of primary and secondary ovarian tumors. Histopathologic examinations revealed primary ovarian tumors in 46 patients (76.7%). Non-gynecologic tumors, including metastatic lymphoma, gastrointestinal stromal tumor, colorectal and gallbladder cancer, and malignant mesothelioma, were the second most common disease (n = 6, 10.0%). In five patients (8.3%), histopathologic evaluations revealed ovarian abscess. Findings in the samples were nondiagnostic in three patients (5.0%). There were no biopsy-related complications.

**Conclusions:** TVS-guided core needle biopsy might be a feasible procedure for diagnosing adnexal masses, particularly in patients with advanced ovarian malignancy who are more likely to benefit from NACT.

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**261 — Poster Session**

**Perioperative β blockade improves overall survival in patients with ovarian cancer**

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**Objectives:** To quantify the impact of perioperative use of β blockers on patient survival after debulking of epithelial ovarian cancer.

**Methods:** We conducted a multicenter retrospective study of all consecutive women after primary debulking of ovarian cancer (2002–2007). One institution had routinely been using perioperative β blockers (BBP) for at-risk patients and the other institution did not. Patients at risk were those with history of coronary artery disease or two of the following: age > 65 years, obesity, diabetes, or hypertension. Demographic, operative, and follow-up data were collected. Cox proportional hazards models were used to assess the effect of BBP on overall survival (OS) and progression-free survival (PFS).

**Results:** We identified 185 patients: 70 received BBP and 115 did not. The groups were similar in demographics. Within the two respective groups, Caucasian race constituted 93% and 93%, advanced-stage disease (III, IV) 72% and 74%, advanced grade 97% and 90%, and optimal debulking 77% and 83%. Hypertension was seen more in the BBP compared to the no BBP group (22% and 6%, P = 0.002). PFS in the BBP group compared to the no BBP group was 18.2 vs. 15.8 months (P = 0.66), while the OS was 44.2 vs. 39.3 months (P = 0.1). In multivariate analysis, in addition to patient age and disease stage, BBP administration was associated with a statistically significant improvement in OS 0.68 (HR 0.46–0.99, P = 0.046) but not in PFS 0.75 (HR 0.54–1.11, P = 0.16).

**Conclusions:** Perioperative administration of β blockers in patients after ovarian cancer surgery improves patient overall survival. A prospective clinical trial in this population is warranted to further evaluate these results.

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Methods: A single-institution retrospective review was performed that included patients who had received neoadjuvant carboplatin/paclitaxel (C+P) followed by interval cytoreduction from 2005 to 2012 for clinical stage IIIC/IV ovarian cancer. Patients were categorized by immediate postoperative adjuvant therapy chosen at the provider’s discretion: additional C+P, carboplatin/liposomal doxorubicin (C+D), carboplatin/topotecan (C+T), or other (O). Progression-free (PFS) and overall survival (OS) were estimated using the Kaplan–Meier method. Cox regression analyses were employed.

Results: Eighty-nine patients were identified who received C+P (46%, n = 41), C+D (19%, n = 17), C+T (19%, n = 17), or O (16%, n = 14). Patient, disease, treatment, and survival characteristics are presented in Fig. 1. At the study conclusion, 38 (42.7%) patients were alive, 51 (57.3%) were dead, 18 (20.5%) remained without progression, and 18 had refractory disease. Median OS/PFS across the entire cohort was 43.5 (95% CI 37.8–50.7)/22.2 (95% CI 19.0–28.5) months. Age, histology, initial CA-125 value, and tobacco use were not independent predictors of PFS/OS. Using a multivariate approach, there was no difference in OS between patients who received C+P, C+D, or C+T, although patients who received O had an HR for death of 2.7 (95% CI 1.04–7.00) compared to patients who received C+P. Both higher body mass index (BMI) (P = 0.0009) and CA-125 value at completion of neoadjuvant regimen (P = 0.0003) predicted poor PFS. Those with residual disease at debulking had worse PFS (HR 2.58, 95% CI 1.30–5.13).

Conclusions: C+P, C+D, or C+T result in equivalent outcomes following neoadjuvant C+P and interval debulking. Any of these regimens may, therefore, be chosen according to provider preference/patient tolerance. Confirmation with larger sample sizes is warranted. Elevated BMI and CA-125 at completion of neoadjuvant C+P as well as the presence of residual disease after interval debulking predict poor survival.

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263 — Poster Session
Trainee participation in surgery for ovarian cancer: Impact on patient outcomes
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Objectives: To estimate the impact of trainee involvement on morbidity following primary surgery for the treatment of ovarian cancer.

Methods: Patients who underwent primary surgery for ovarian cancer from 2005 to 2012 were extracted from the American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP) database. Trainee involvement was defined as resident or fellow participation in the surgery. Patients with and without trainee involvement were compared with 30-day complication rate. Major complications included myocardia infarction, thromboembolism, sepsis, deep surgical site infection, and need for ventilator support >48 h. Minor complications included urinary tract infection, superficial wound infection, and blood transfusion. Pearson's chi square test, Student's t-test, and binary logistic regression were used for analysis.

Results: We identified 732 patients and trainees participated in 70.6% of cases. The highest-level trainee was a resident in 62.9% and a fellow in 37.1% of cases. The rate of any postoperative complication was 34.7%, with 27.3% experiencing minor complications and 14.3% major complications. Some patients experienced both minor and major complications. Mortality was 2.0%. On univariate analysis, trainee involvement was not associated with an increased risk of major complication (P = 0.79) but was associated with minor complication (P < 0.001). In contrast, the risk of postoperative death was twice as high in cases with no trainee (3.3% vs. 1.5%), but this did not reach statistical significance (P = 0.13). On multivariable analysis controlling for age, American Society of Anesthesiologists score, body mass index, diabetes, smoking, medical comorbidities, and surgical complexity, trainee involvement remained associated with minor complications (P = 0.005). However, when operative time was added to the model, trainee involvement was no longer associated with minor complication.

Conclusions: Trainee involvement in surgery for ovarian cancer was associated with an increase in minor but not major postoperative complications. Interestingly, cases with no trainee trended toward twice the risk of postoperative death. The increase in minor complications was mediated by longer operative times, which may be a target for continuous quality improvement.

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264 — Poster Session
The impact of blood transfusion on tumor recurrence and survival in patients with epithelial ovarian cancer
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Objectives: Limited research has evaluated the effect on time to recurrence and survival in patients with epithelial ovarian cancer who receive packed red blood cell transfusions (PRBC). Available literature suggests a decrease in progression-free survival (PFS) in patients receiving perioperative PRBC. Our study sought to validate this association and to further evaluate whether the timing of transfusion (intraoperative, postoperative, or perichemotherapy) increases the risk of recurrence or death in this patient population.

Methods: A retrospective chart review was performed of 150 women with epithelial ovarian cancer, divided equally into a transfusion and nontransfusion group. PRBC time points that were analyzed included: overall transfusion group, intraoperative, postoperative (<6 weeks), and perichemotherapy (≥6 weeks). Clinical and pathologic data as well as time to recurrence and overall survival were extracted from the medical record. Times to event outcomes were evaluated via construction of Kaplan-Meier curves, and univariate and multivariate regression analyses were performed.

Results: Cardiovascular comorbidities, diabetes, preoperative anemia, and prior abdominal surgeries were associated with a higher risk of need for PRBC in univariate analysis. In multivariate analysis, an increased risk of recurrence was associated with PRBC given at any point in time (HR 1.6, P = 0.02) and in the postoperative period (HR 1.6, P = 0.04). A trend was noted in the perichemotherapy period as well (HR 1.7, P = 0.07). There was no difference in PFS between the transfusion and nontransfusion groups when PRBC was given intraoperatively. Other factors significantly related with shorter PFS in all transfusion groups included older age, elevated CA-125 value, advanced disease stage, and diabetes (P < 0.05). There was no difference in overall survival in the PRBC group at any transfusion time point.

Conclusions: Patients with ovarian cancer who receive postoperative PRBC have decreased time to recurrence when compared to similar patients who do not receive PRBC. Additional studies are needed to determine the etiology of this association.

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265 — Poster Session
Pathologic assessment of response to neoadjuvant chemotherapy in ovarian cancer: Correlation with survival
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Objectives: To determine if the degree of pathologic response correlates with survival in cases of ovarian cancer treated with neoadjuvant chemotherapy.

Methods: A cohort of patients with ovarian cancer treated with neoadjuvant chemotherapy followed by interval cytoreductive surgery at the Cleveland Clinic was collected. Data were abstracted from the medical records. Pathology reports were reviewed to assess the degree of pathologic response of tumor. Categories of response were graded as follows: gross disease without mention of treatment effect, gross disease with treatment effect, microscopic disease with treatment effect, and no viable tumor. These categories were then correlated with survival data.

Results: A total of 119 cases of ovarian cancer treated with neoadjuvant chemotherapy followed by interval cytoreduction were available for analysis. Degree of pathologic response was graded as: gross disease without mention of treatment effect (n = 29), gross disease with treatment effect (n = 32), microscopic disease with treatment effect (n = 54), and no viable tumor (n = 4). Median overall and progression-free survivals (in months) were as follows:
35.4 and 8.9 for gross disease without mention of treatment effect, 36 and 7.5 for gross disease with treatment effect, and 40 and 9.5 for microscopic disease with treatment effect. Median overall and progression-free survival had not yet been reached for the cohort of patients with no viable tumor ($P = 0.90$ and $P = 0.24$).

**Conclusions:** The degree of pathologic response to neoadjuvant chemotherapy showed a trend toward improved survival with greater grades of pathologic response, but this did not reach statistical significance. A larger dataset is needed for further investigation. If a correlation were to be noted, this could possibly help inform decisions regarding further adjuvant therapy and provide an additional source of prognostic information.

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**266 – Poster Session**

**Accuracy of frozen section in the diagnosis of mucinous ovarian tumors**

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**Objectives:** To assess the diagnostic accuracy of the intraoperative frozen sections (FS) of ovarian mucinous tumors compared to final paraffin sections (PS) diagnosis and to detect potential factors for misdiagnosis at the time of FS.

**Methods:** A retrospective analysis was conducted of intraoperative FS for mucinous ovarian tumors. A total of 105 samples were surgically removed in our institution between 2005 and 2013. Each specimen was evaluated for histopathologic diagnosis using both FS and PS. All information regarding FS and PS were selected and correlated.

**Results:** Out of 105 cases, 45 were diagnosed as benign, 37 as low malignant potential (LMP), and 23 as malignant at the time of FS diagnosis. The overall accuracy of FS diagnosis accounted for 82.6%, while diagnostic discrepancy was observed in 18/105 cases, including underdiagnosis in 14 and overdiagnosis in 4 cases. Of 45 cases diagnosed as benign in FS, five were LMP and one was malignant. The sensitivity of FS for benign tumors was calculated as 95.1% and the positive predictive value as 86.7%. In contrast, the sensitivity of FS appeared to be low in LMP (79.4%) and malignant tumors (70%). FS had low accuracy among LMP and malignant mucinous ovarian tumors. The median tumor size was calculated at 17.92 cm (SD = 10.1 cm). Misdiagnosis was associated with a mean tumor size of 23.26 cm (95% CI 19–27.5 cm). The median tumor size was 14.5 cm (95% CI 13–16 cm) for overdiagnosed and 24.4 cm (95% CI 22.2–26.6 cm) for underdiagnosed cases. The number of sections examined at FS and PS had a statistically significant association with the diagnostic accuracy of FS.

**Conclusions:** FS has low accuracy among LMP and malignant mucinous ovarian tumors. The median tumor size constitutes an important factor, and the discrepancy between FS and PS may be related to a tumor size > 19 cm. Three or more sections should be performed in cases of mucinous ovarian tumors with size > 22 cm, especially in the solid and most complex foci of the tumor. Diagnostic discrepancy is more frequent in cases with four or more FS and tumor size > 13 cm.

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**267 – Poster Session**

**IL-6, VTE and ovarian clear cell carcinoma: A dangerous triad**

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**Objectives:** Venous thromboembolism (VTE) is a prevalent problem in ovarian clear cell carcinoma (OCCC), but its clinical implications are not known. The aim of our study was to examine the risk of VTE and survival outcomes of OCCC and potential links with interleukin (IL)-6 levels.

**Methods:** A case–control study comparing OCCC (n = 370) and serous ovarian cancer (SOC, n = 938) was conducted to evaluate cumulative risk of VTE and survival outcomes in a stage-specific manner. Among subsets of cases (OCCC n = 85, SOC n = 115), pretreatment plasma IL-6 levels were examined.

**Results:** Advanced-stage OCCC had the highest risk of VTE (2-year cumulative rate: advanced-stage OCCC 42.4%, advanced-stage SOC 16%, early-stage OCCC 12%, and early-stage SOC 6.4%, $P < 0.0001$, Panel A). In multivariate analysis, advanced-stage OCCC (HR 4.33, $P = 0.001$) and thrombocytosis (HR 1.48, $P = 0.024$) remained independent risk factors for VTE. In survival analysis, advanced-stage OCCC (HR 3.74, $P = 0.001$), thrombocytosis (HR 1.40, $P = 0.001$), and VTE (HR 1.31, $P = 0.016$) remained independent prognostic factors for decreased progression-free survival. Advanced-stage OCCC had the highest prevalence of increased IL-6 level (frequency of ≥ 10 pg/mL: advanced-stage OCCC 83.3%, advanced-stage SOC 47.7%, early-stage OCCC 15.6%, and early-stage SOC 27.3%, $P = 0.001$, Panel B). Magnitude of significance of elevated IL-6 for progression-free survival was larger in OCCC (2-year survival rate: 50% vs. 87.5%, HR 4.89, $P = 0.016$) than SOC (24.9% vs. 40.8%, HR 1.40, $P = 0.07$).

**Conclusions:** Advanced-stage OCCC is associated with a high incidence of VTE and decreased survival outcomes. These findings have major implications for clinical management of OCCC.

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**268 – Poster Session**

**Primary debulking surgery and neo-adjuvant chemotherapy in the Medicare population: An analysis of cost of care**

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**Objectives:** To compare the cost of care for women with advanced-stage epithelial ovarian cancer (EOC) undergoing primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT).

**Methods:** The Surveillance, Epidemiology, and End Results — Medicare database was used to evaluate the 7-month cost of care following PDS and NACT in the management of advanced-stage EOC.

**Results:** Of 4518 women deemed eligible for this analysis, 82.4% underwent PDS and 17.6% received NACT. No significant difference in the cost of care between PDS and NACT existed in women with stage IIIC EOC ($59,805 vs. $62,565). There was a 12% increase in adjusted cost of care for stage IV patients ($63,067 vs. $55,237) who received PDS ($59,805 vs. $62,565). There was a 12% increase in adjusted cost of care for stage IV patients ($63,067 vs. $55,237) who received PDS and NACT who received PDS ($P = 0.0001). NACT was associated with a decreased 5-year overall survival.

**Conclusions:** NACT and PDS are comparable in cost for women with stage IIIC EOC, and PDS is minimally more expensive for women with stage IV EOC.

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**269 – Poster Session**

**Clinical characteristics and outcomes of patients with stage I epithelial ovarian cancer compared to fallopian tube cancer**

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**Objectives:** To compare clinical characteristics and survival between patients with stage I epithelial ovarian cancer (EOC) and fallopian tube cancer (FTC).

**Methods:** We identified women with stage I EOC and FTC who underwent treatment between 2000 and 2010. Correlation between categorical variables was assessed with chi square test. The Kaplan–Meier survival analysis was used to generate overall survival data (OS). Factors predictive of outcome were compared using the log-rank test and Cox proportional hazards model.

**Results:** The study group consisted of 385 women with EOC and 43 with FTC. Patients with FTC had a higher rate of stage IA disease (65% vs. 48%, $P = 0.02$) and grade 3 tumors (60.4% vs. 30.9%, $P = 0.001$). Patients with FTC had a significantly higher rate of breast cancer (25.6% vs. 5.7%, $P < 0.001$) and BRCA1 mutations (45.8% vs. 9.1%, $P < 0.001$). When these demographics were analyzed only in patients with serous histology, women with FTC had a higher rate of stage IA disease compared to EOC (57.7% vs. 38.7%, $P < 0.001$). However, there was no difference in the rate of grade 3 tumors (65.4% vs. 62.9%, $P = 0.1$). In this population, there was no difference in the rate of concurrent endometrial cancer between FTC and EOC patients (11.5% vs. 6.5%, $P = 0.4$). Women with FTC, however, had a significantly higher rate of breast cancer (38.5% vs. 9.7%, $P = 0.001$). In the whole population, there was no difference in the rates of platinum-based and paclitaxel chemotherapy between the groups. Women with FTC were more likely to have received six or more cycles of chemotherapy (58.1% vs. 44.1%, $P = 0.02$). The 5-year disease-free survival (DFS) rates were 100% in women with FTC and 93% in patients with EOC ($P = 0.04$). The 5-year OS rates were 100% and 95% for FTC and EOC, respectively ($P = 0.7$).

**Conclusions:** We found a higher rate of stage IA, grade 3, and serous carcinoma in FTC. Women with FTC had a higher rate of breast cancer. There was no difference in OS between the groups.

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**270 – Poster Session**

**Investigating the metabolic relationship between ovarian cancer cells and adipocytes: The role of fatty acid beta-oxidation**

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**Objectives:** To investigate the metabolic relationship between ovarian cancer (OvCa) cells and adipocytes, including the role of fatty acid beta-oxidation (FABO).

**Methods:** Ovarian cancer cells lines (OVKATE, OVSaho, NIHOCV3) and a patient-derived primary cell line (CD13-13P) were utilized for experiments. The Seahorse Flux Analyzer with metabolic inhibitors including etomoxir (a carnitine palmitoyltransferase 1 inhibitor), 2-deoxy glucose (2DG), FCCP, and rotenone were used to evaluate the role of FABO in ovarian OvCa cells. Co-culture experiments used differentiated 3T3L1 adipocytes in Boyden chambers with OvCa cells. Co-culture assays were conducted to evaluate changes in gene expression using reverse transcription-polymerase chain reaction and fatty acid accumulation using confocal microscopy.

**Results:** All OvCa cell lines demonstrated a significant decrease in the oxygen consumption rate (OCR) with administration of etomoxir (OVSaho 78%, OVKATE 71%, NIHOCV3 75%, CD13-13P 66%, $P < 0.001$). The administration of 2DG had essentially no effect on the basal OCR of OvCa cells. However, the OCR was significantly decreased with subsequent administration of etomoxir. The co-culture of NIHOCV3 cells and differentiated adipocytes resulted in increased visualization of BODIPY fluorophore staining of cytoplasmic free fatty acids compared to controls. The addition of the fatty acid synthase (FAS) inhibitor orlistat to control cell culture media was lethal, but co-culture with adipocytes rescued OvCa cells from the effect of FAS inhibition. Gene expression array of co-cultured OvCa cells demonstrated a twofold increase in several genes associated with fatty acid transport and utilization, including fatty acid-binding protein 2 (FABP2) and lipoprotein lipase (LPL), as well as a twofold decrease in several genes associated with fatty acid synthesis, including FAS and hormone-sensitive lipase (HSL).

**Conclusions:** These results indicate that OvCa cells derive a significant portion of their energy from FABO, despite the presence of abundant glucose. Additionally, co-cultured OvCa cells use exogenous free fatty acids donated by adipocytes. These results further support the hypothesis that metastasis of ovarian cancer to fatty-rich areas such as the omentum and mesentery may provide a metabolic advantage, which may help explain the clinical behavior of ovarian cancer.

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Methods: Total RNA was isolated from laser-captured microdissected formalin-fixed, paraffin-embedded tumor tissue from women diagnosed with stage III/IV serous EOC on which survival data were available. MiRNA and mRNA expression profiles were generated on 8 long overall survivors (LOS, >4 years survival) and 14 short overall survivors (SOS, <2 years survival). Available miRNA and mRNA data on 177 subjects (75 LOS, 102 SOS) from the Cancer Genome Atlas (TCGA) were downloaded from the data portal. Integrated network analysis was performed on each dataset independently using netClass software to create a signature profile that distinguished LOS from SOS subjects. Known biologic information from public databases (protein–protein interactions, biologic pathways, and biologic gene proximity) was incorporated to refine the analysis. Each independent dataset was cross-validated with multiple repeats.

Results: After 10-fold cross-validation with 10 repeats, integrated network analysis of our dataset identified a combination of 55 miRNAs and mRNAs that were chosen 75% of the time. Using the same analytic approach, 50 of these same RNAs were chosen 100% of the time in the larger independent TCGA dataset. Eight miRNAs (APP, CDK2, CUL3, ELAVL1, FN1, NRF1, SUMO2, and UBC) and two mRNAs (miR-506 and miR-548c) were chosen 100% of the time in each dataset. Enrichment of these genes was found in several cancer-related KEGG pathways.

Conclusions: Using an integrated network analysis approach incorporating known biologic relationships, we found a combination of 55 miRNAs and mRNAs that differentiated LOS from SOS subjects in our dataset. These results suggest that specific interactions between miRNAs and mRNAs differentiate women with divergent survival outcomes. Specific gene–gene, gene–miRNA interaction networks distinguish EOC survivors, allowing development of defined targets for therapies in the future.

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272 – Poster Session
The significance of paracardiac lymph-node enlargement in patients with newly diagnosed ovarian cancer

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Objectives: Epithelial ovarian cancer commonly spreads intra-abdominally, and metastases to other sites are relatively rare. During interpretation of the computed tomography (CT) scans used to plan treatment and assess response, little attention is focused on the enlargement of paracardiac lymph nodes (PCLN) and their significance is not clear. We sought to examine whether the presence of enlarged PCLN during initial diagnosis of ovarian cancer influences disease-free interval (DFI) and overall survival (OS).

Methods: This retrospective study included patients with stage III ovarian cancer who underwent CT scan during evaluation of newly diagnosed ovarian cancer. The CT scans were reviewed by a single radiologist for peritoneal involvement, distal metastases, and the presence of PCLN. Patient charts were reviewed for all clinicopathologic information. Disease status at diagnosis, results of surgery, chemotherapy and response, DFI, and OS were recorded.

Results: A total of 33 patients with stage III ovarian cancer with PCLN on initial CT scan were included and compared with 41 consecutive controls with stage III disease. Both groups were well-balanced for clinicopathologic features. There was no significant difference between groups in abdominal optimal cytoreduction rate. In spite of this, lower rates of complete response to initial treatment were detected in the study group (48.5% vs. 78.0%, \textit{P} = 0.008). In eight of 33 patients in the study group, persistent PCLN were detected on follow-up CT scan and a shorter DFI was observed in these patients (7.4 vs. 18.8 months, \textit{P} = 0.021). The DFI for patients with PCLN at diagnosis was lower compared to controls (14.2 vs. 32.2 months, \textit{P} = 0.004) and OS was shorter (33.4 vs. 58.7 months, \textit{P} < 0.001). Logistic and linear regression, after adjusting for confounders, showed that PCLN was significantly associated with a lower rate of complete response (odds ratio [OR] 0.319, 95% CI 0.112–0.912) and a shorter DFI, but OS was significantly affected.

Conclusions: Our study suggests that the presence of PCLN at presentation is associated with poor prognosis in stage III ovarian cancer. Further attention should be given to the detection and follow-up of such findings when considering treatment in these patients.

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273 – Poster Session
Findings at laparoscopy, not debulking status, are associated with survival in advanced stage ovarian cancer after neoadjuvant chemotherapy

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Objectives: In women with epithelial ovarian cancer (EOC), high predictive index value (PIV) based on intraoperative disease burden has been associated with decreased likelihood of optimal debulking. Our goal was to evaluate the role of PIV on overall survival (OS) in women with EOC receiving neoadjuvant chemotherapy followed by interval debulking surgery (IDS).

Methods: We conducted an institutional review board-approved retrospective analysis of all women receiving neoadjuvant chemotherapy with IDS for advanced EOC between 1/2000 and 9/2013. Demographic and clinical data were abstracted from medical records. PIVs were assigned based on the findings at time of IDS. OS was calculated from time of first cycle of neoadjuvant chemotherapy. Cox regression modeling was used for univariate and multivariate analyses. Median survival times were estimated using Kaplan–Meier methods.

Results: A total of 102 patients met study inclusion criteria: 20 (19.6%) with stage III, 31 (30.4%) with stage IV, and 51 (50%) with advanced disease based on imaging. The majority (74%) had serous cancers. Sixty-seven (65.7%), 25 (24.5%), and 10 (9.8%) were assigned low, intermediate, or high PIV scores, respectively. More than half of the patients were debulked to no gross residual disease (56%), while 23% had gross disease <1 cm. Residual disease status (<1 cm: 2.7 years vs. >1 cm: 2.2 years, \textit{P} = 0.049) and PIV (low: 3.7 years vs. intermediate/high: 2.2 years, \textit{P} = 0.049) were associated with longer survival in univariate analysis. Among those optimally debulked, the OS was 3.7 years in women with low PIV and 2.0 years for those with intermediate/high PIV (\textit{P} = 0.03). However, in multivariate analysis, only PIV was associated with survival. Women with intermediate/high PIV had a 2.5-fold (95% CI: 1.4–5.0) and 2.4-fold (95% CI: 1.1–5.3) increased risk of death compared to those with low scores (\textit{P} = 0.01) in the entire cohort and those with optimally debulked disease, respectively.

Conclusions: Patients with a lower disease burden at time of IDS had statistically significant longer OS compared to those with more extensive disease (high PIV), even among those who were optimally debulked. This suggests that PIV may have a prognostic role in the overall outcomes of patients with EOC treated with neoadjuvant chemotherapy.

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274 - Poster Session
Predicting overall survival in patients with ovarian cancer: A new clinical model

Objectives: Overall survival (OS) in ovarian cancer has been largely researched and many prognostic factors have been explored, including the serum carbohydrate antigen 125 (CA-125). In the last few decades, a novel biomarker, the human epididymis protein 4 (HE4), has been introduced. The present study aimed to explore and evaluate HE4 measurements, along with CA-125, in OS prediction after adjusting for common prognostic factors such as stage, residual tumor disease, grading, age, and histotype.

Methods: A retrospective study was performed in ovarian cancer patients who underwent primary cytoreductive surgery and first-line adjuvant chemotherapy. Serial measurements of patients’ CA-125 and HE4 were collected at different frequencies of treatment. A statistical model coupling the Cox proportional hazards and the mixed effects models was applied to determine the association between each patient’s OS and longitudinal CA-125 and HE4 profiles. A multivariate analysis was performed to assess a correlation between the common prognostic factors and CA-125, HE4, and OS.

Results: A total of 110 patients were recruited and 850 values of CA-125 and HE4 were collected. Preoperative age, HE4 and CA-125 levels, cancer stage and grading, residual tumor, and histotype were included into a multivariate logistic regression model. This model correctly predicted a high or low risk of death at a given time point in 88% of patients.

Conclusions: Longitudinal CA-125 and HE4 values, measured at the diagnosis of ovarian cancer and during chemotherapy, could be used to reliably predict OS after adjusting for common prognostic factors. This model could be potentially useful in clinical decision making and management of ovarian cancer patients.

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275 - Poster Session
Secular trends in relative survival for ovarian cancer
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Objectives: The last three decades have seen numerous advances in the treatment of ovarian cancer. Although median survival times have improved in randomized trials, whether these therapeutic advances have affected survival in real-world populations remains unclear. Secular estimates of survival are complicated by advances in medical treatment in general and improved longevity in women. We examined relative survival, a metric that incorporates changes in survival within a population, to estimate changes in survival for ovarian cancer over the last 35 years.

Methods: Women diagnosed with ovarian cancer from 1975 to 2011 and recorded in the Surveillance, Epidemiology, and End Results database were examined. Survival was analyzed after adjustment for age, race, stage, year of diagnosis, and time since diagnosis. Relative survival was estimated by comparing observed survival after diagnosis of cancer to expected survival obtained from the general United States population matched on age, race, and calendar year.

Results: A total of 49,932 women were identified. For all stages of ovarian cancer, we found reductions in excess mortality over time. Among women with stage I ovarian cancer, the excess hazard ratio for women diagnosed in 2006 was 0.51 (95% CI, 0.41–0.63) compared to those diagnosed in 1975. The reduction in excess mortality for patients treated in 2006 remained significant when compared to patients diagnosed in 1980 and 1985, although there was not a statistically significant reduction in excess mortality compared to women diagnosed after 1990. For women with stage III-IV tumors, the excess hazard of mortality was lower in 2006 compared to all other years of study, ranging from 0.49 (95% CI, 0.44–0.55) compared to 1975 and 0.69 (95% CI, 0.65–0.73) relative to 1985 to 0.93 (95% CI, 0.87–0.99) relative to 2000.

Conclusions: Relative survival has improved for all stages of ovarian cancer. Advances in surgical treatment and chemotherapy delivery have translated into improved outcomes at the population level for women with the disease.

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276 - Poster Session
Peritoneal vascular cell adhesion molecule 1 (VCAM-1) is a marker of response to therapy and overall survival in epithelial ovarian cancer (EOC)
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Objectives: Peritoneal VCAM-1 expression in the metastatic EOC microenvironment is induced by tumor and mediates tumor cell invasion. VCAM-1 imaging suggests that expression during treatment is an indicator of platinum resistance. Here we assess whether peritoneal VCAM-1 expression is prognostic of overall survival. We also prospectively evaluate whether serum VCAM-1 (sVCAM-1) is a surrogate for peritoneal expression.

Methods: A retrospective review of EOC patients was performed to correlate overall survival with peritoneal VCAM-1 expression. A prospective cohort of EOC patients was identified and followed through primary treatment. Serum for sVCAM-1 evaluation was collected before surgery or neoadjuvant chemotherapy (NACT) and at each treatment cycle. Peritoneal specimens were obtained at the time of debulking for analysis. sVCAM-1 levels were determined by enzyme-linked immunosorbent assay. Median survival was determined by Kaplan–Meier analysis with log rank test for significance.

Results: Retrospective review identified 54 EOC patients. Median age was 62 years, 76% were stage III, and 24% were stage IV. Peritoneal VCAM-1 expression was seen in 60%. Thirty percent received NACT. Overall survival was significantly less in patients with peritoneal VCAM-1 expression (43 months vs. 99 months, P = 0.008) with a minimum of 5 years of follow-up. Eighty percent of platinum-resistant patients expressed VCAM-1 at the time of surgery. In our prospective cohort, 18 EOC patients have completed primary treatment and had serum sVCAM-1 analyzed. This revealed no correlation between sVCAM-1 and peritoneal VCAM-1 expression. Median progression-free and overall survival in this cohort has not been reached.

Conclusions: These results suggest that peritoneal VCAM-1 expression is a negative predictor of overall survival in EOC. This is especially compelling in light of prior data suggesting that persistent VCAM-1 expression during treatment is an indicator of platinum resistance. Our pilot study suggests that sVCAM-1 is not a surrogate for this expression. Therefore, further exploration of peritoneal VCAM-1 imaging is warranted as a novel means of monitoring the tumor microenvironment and identifying in real time a molecular
marker that may predict response to treatment and overall survival, both clinically relevant endpoints in treatment planning.

**277 - Poster Session**

**Does performance of omentectomy in epithelial ovarian cancer affect survival? An analysis of the SEER database**

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**Objectives:** Although omentectomy is part of the staging and treatment of epithelial ovarian cancer (EOC), its performance in a grossly normal omentum, acknowledging its role in debulking gross tumor deposits, has never been definitively shown to improve survival.

**Methods:** Using Surveillance, Epidemiology, and End Results data from 1998 to 2010, we identified patients with EOC and assessed their age, race, year of diagnosis, tumor grade, histologic subtype, FIGO stage, lymph node dissection, nodal findings, and performance of omentectomy. We compared disease-specific survival (DSS) based on presence or absence of omentectomy using log-rank univariate analysis, Cox multivariate analysis, and Kaplan-Meier survival curves.

**Results:** A total of 20,975 patients with invasive EOC underwent surgical treatment. Initial univariate analysis indicated a lower mean survival with performance of omentectomy (101 vs. 107 months, P < 0.001). However, after multivariate analysis, there was no significant association between DSS and performance of omentectomy (HR 0.978, P = 0.506).

**Conclusions:** In this analysis, performance of omentectomy in EOC patients without bulky disease (up to and including stage IIIA) did not appear to confer improvement in survival.

**278 - Poster Session**

**Does digoxin improve ovarian cancer survival by inducing immunogenic cell death? A SEER–Medicare database analysis**

Women's Cancer Program/Cedars-Sinai Medical Center, Los Angeles, CA, USA, Cedars-Sinai Medical Center, Los Angeles, CA, USA

**Objectives:** Cardiac glycosides, when combined with platinum chemotherapy, induce immunogenic cell death. Digoxin + chemotherapy resulted in improved survival for patients with breast and colorectal cancers compared to chemotherapy alone. The objective of this study was to determine whether digoxin improves survival in epithelial ovarian cancer patients treated with platinum.

**Methods:** Surveillance, Epidemiology, and End Results (SEER) data (2007–2009) from 3707 ovarian cancer patients was linked to Medicare claims' data to capture platinum administration, prescription digoxin use, and cardiac comorbidities. Exclusion of nonepithelial histologies, second and third cancer diagnoses, and patients who did not undergo cancer-directed surgery left 1756 patients, of whom 762 received platinum chemotherapy. Patients were considered digoxin users if a prescription was filled within 6 months after cancer diagnosis. Patients were considered to have heart disease if coded with International Classification of Diseases-9 diagnoses of myocardial infarction or atrial fibrillation while enrolled in Medicare. Charlson scores were computed to control for medical comorbidities. Cox proportional hazards' regression models were used to determine the impact of digoxin use on overall survival (OS) among those receiving platinum.

**Results:** Among 762 epithelial ovarian cancer patients treated with surgery and platinum chemotherapy, 53 (7%) received ever-digoxin and 38 (5%) received digoxin during platinum administration. Associations of digoxin use with OS were analyzed for all stages and grades (n = 762), all stages and G2+ (n = 747), stage III/IV, G2+ (n = 573), and serous stage III/IV, G2+ (n = 264) subsets. Adjusting for age, heart disease, and Charlson comorbidity score, digoxin use was not associated with OS (adjusted HR = 1.29, 95% CI 0.81, 2.06). The results did not vary by stage, grade, or histology.

**Conclusions:** In this SEER–Medicare database analysis, digoxin use during chemotherapy did not improve OS outcomes in patients with epithelial ovarian cancer treated with surgery and platinum chemotherapy.
279 - Poster Session
Cytoreductive surgery (CRS) and HIPEC in recurrent platinum-resistant ovarian cancer
C.K. Brown, S. Williams, L. McNutt, S. Beilick, R. Flynn, D. Litvack, H. Huss, A.R. Nair, G. Del Priore, Cancer Treatment Centers of America, Boca Raton, FL, USA, aTexas Tech University Health Sciences Center, Lubbock, TX, USA, bMorehouse School of Medicine, Atlanta, GA, USA, cCancer Treatment Centers of America, Newnan, GA, USA

Objectives: Hyperthermic intraperitoneal chemotherapy (HIPEC) use is increasing in the management of recurrent epithelial ovarian cancer. We report a series of heavily pretreated and platinum-resistant ovarian cancer patients undergoing HIPEC.

Methods: We explored a prospective registry of all ovarian cancer patients for HIPEC from across a multihospital tertiary care system.

Results: Between 2009 and 2013, approximately 1550 nonanalytic recurrent ovarian cancer patients were evaluated for HIPEC across the entire system. Eligibility included the following: adequate performance status (Eastern Cooperative Oncology Group 0–1), no tumor board consensus alternative option, and image review confirming potential R0 or R1 resection. Fewer than 5% of all ovarian cancer patients (n = 53) were considered candidates for HIPEC and explored, representing 23.9% of all HIPEC surgeries (n = 221) during the same period. Mean target tissue temperature was 41.5 °C with a 90-minute perfusion of mitomycin C (platinum-resistant patients, n = 41) or carboplatin/oxaliplatin (platinum-sensitive patients, n = 12). Median age was 53 years (range, 26–70 years) and body mass index was 30.5 (range, 21–42), with initial stage > IIIC in 79%. Original histology was 3% mucinous, 7% clear cell, 59% serous, and 31% all others. Ninety-six percent of the patients were Caucasian. Median number of prior cycles was 5 (range, 1–8). Median time from last prior chemotherapy to HIPEC was 42 weeks. One patient was platinum-refractory and two were not taken to the operating room due to rapid deterioration. Mean preoperative Peritoneal Cancer Index score was 19.1, median operating room time was 240 min, median estimated blood loss was 1400 mL, and 42% had R0 or R1 resections. Postoperative complications included fistula (4%), anastomotic leaks (4%), and all others (including infections, thrombus, small bowel obstruction, or grade 4 neutropenia) (63% of patients at least one). There were no perioperative deaths. Mean overall survival (OS) was 34.1 months (range, 26.7–41.5 months). Stratified by number of prior salvage regimens, OS with > 2 prior regimens was 30.9 months (range, 24.3–37.6) compared with 34.8 months (range, 18.2–51.4 months) for < 2 prior chemotherapy regimens (P = 0.71). When analyzed by histology (mucinous + clear cell) vs. all others, OS did not differ. OS in platinum-resistant patients was 33.9 months (range, 26–41.8 months) vs. platinum-sensitive 19.7 months (range, 12.2–23.6 months) (P = 0.75).

Conclusions: Even in heavily pretreated ovarian cancer patients with multiple relapses, HIPEC is feasible with high R0 or R1 resection rates in a high-volume center. OS is not affected by prior cycles or histology. Ovarian cancer comprises almost one third of all HIPEC cases done.

doi:10.1016/j.ygyno.2015.01.283

281 - Poster Session
The significance of preoperative carbohydrate antigen (CA125) and human epididymis protein 4 (HE4) serum level to predict pelvic or paraaortic lymph node metastasis in epithelial ovarian cancer patients
A. Soochit, Sun Yat-Sen University, Cancer Center, Guangzhou, China

Objectives: To determine hospital charges and their trends in association with open, laparoscopic, and robotic surgical procedures for ovarian cancer patients in the United States.

Methods: Data were obtained from the National Inpatient Sample (NIS) from the years 2006 through 2011. ANOVAs and chi square tests were conducted for statistical analysis.

Results: The study included 83,552 ovarian cancer patients (median age, 63 years). Of these women, 43,301 (52%) were older than 63 years, while the remaining 40,251 (48%) were younger than 63 years. Ethnic breakdown was as follows: 52,527 (63%) white, 6073 (7%) black, 5987 (7%) Hispanic, 2050 (2%) Asian, 359 Native American (1%), and 16,556 (20%) other races. Of the 12,544 patients who underwent surgery, 11,947 (95%) received open surgery (OS), 365 (3%) received laparoscopic surgery (LS), and 232 (2%) received robotic surgery (RS). The overall median total charges for OS, LS, and RS were $41,198, $34,463, and $43,076, respectively (P < 0.001). Overall median lengths of hospitalization were 5, 2, and 2 days for OS, LS, and RS, respectively (P < 0.001). Over the time periods of 2006 to 2007, 2008 to 2009, and 2010 to 2011, the median total charges for OS increased from $36,366 to $42,655 to $49,776 (P < 0.001). The median total charge for LS did not change significantly during these time intervals. From 2008 through 2009 and from 2010 through 2011, the median total charges for RS increased from $38,499 to $47,230, respectively (P < 0.001). Lengths of hospitalization did not significantly differ for each type of surgery throughout the time periods described. The rate of complications did not change over time.

Conclusions: The hospitalization charges associated with ovarian cancer treatment have significantly increased over time. However, duration of hospitalization and rates of surgical complications have not changed. Further research is warranted to determine the underlying factors responsible for these increases in charges.

doi:10.1016/j.ygyno.2015.01.283

280 - Poster Session
The increase in hospital charges associated with ovarian cancer treatment: An economic analysis of 83,552 patients
A.B. Gardner, D.S. Kapp, N. Young-Lin, E.J. Simons, X. Yu, L.K. Chan, Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA, aStanford University, Stanford, CA, USA, bUCSF Helen Diller Comprehensive Cancer Center, San Francisco, CA, USA, cUniversity of Memphis, Memphis, TN, USA, dCalifornia Pacific & Palo Alto Medical Foundation/Sutter Research Institute, San Francisco, CA, USA

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doi:10.1016/j.ygyno.2015.01.282
whereas sensitivity and negative predictive value (NPV) of HE4 were higher than CA-125 (specificity 57.7% vs. 53.8%, NPV 78.8% vs. 78.2%). Combining the two serum cancer markers resulted in significantly higher sensitivity (76.9%) and higher NPV (85.9%). After logistic regression analysis with other factors (age, histologic type and grade), the two cut-off values were statistically significant for lymph node metastasis in EOC (CA-125: 986.45 U/mL, 95% CI 1.72–21.14, P = 0.005; HE4: 400.65 pmol/L, 95% CI 1.04–12.52, P = 0.044).

Conclusions: Combining preoperative CA-125 and HE4 serum levels may provide higher accuracy in predicting lymph node metastasis in EOC.

doi:10.1016/j.ygyno.2015.01.284

282 - Poster Session
Feasibility of tertiary and quaternary cytoreduction in recurrent epithelial ovarian cancer
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Objectives: The optimal strategy for secondary and tertiary treatments of platinum-sensitive epithelial ovarian cancer relapse is not clearly defined and still remains controversial. The aim of this observational study was to evaluate the feasibility and efficacy of cytoreduction on survival outcome and to assess the primary operative procedures performed.

Methods: We retrospectively reviewed 49 consecutive patients who underwent cytoreduction for secondary and tertiary treatments of ovarian cancer. We selected the patients for surgery with presumed isolated peritoneal or nodal recurrence. We found isolated disease in 36 patients (73.5%) and 13 patients (26.5%) had diffuse disease. The same selection was made for quaternary surgery: 10 patients (71.4%) had isolated disease, and four (28.6%) showed greater localization of disease.

Results: The 49 patients with recurrent epithelial ovarian cancer underwent tertiary surgery; 13 (26.5%) also required quaternary cytoreduction. Complete (residual tumor [RT] = 0) cytoreduction was achieved in 38 patients (77.5%). Optimal (RT < 1 cm) and suboptimal cytoreduction (RT > 1 cm) was achieved in 3 (5.1%) and 4 patients (8.2%), respectively. Four patients (8.2%) were deemed as unresectable. Major upper abdominal surgery was performed in 20 patients (40.8%), peritoneectomy in 14 patients (28.6%), at least one bowel resection in 12 patients (24.5%), and pelvic and aortic lymphadenectomy in 19 patients (38.7%). We did not observe any severe intra- or postoperative complications. At quaternary cytoresection, complete cytoreduction was achieved in 12 patients (92.3%). Median progression-free interval was 24 months (range, 10–96 months) and 22 months (range, 9–96 months) for completely debulked patients at tertiary and quaternary cytoreduction, respectively. Median overall survival was 96 months (range, 36–108 months) and 132 months (range, 39–204 months) for completely debulked patients at tertiary and quaternary cytoreduction, respectively.

Conclusions: Our data suggest that cytoreduction for secondary and tertiary ovarian cancer could be performed with a lengthy survival rate and without severe intra- or postoperative complications. The comparison with chemotherapy is indispensable to identify the best treatment modality for these patients.

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283 - Poster Session
Heterogeneity of energy dynamics in ovarian cancer cell lines
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Objectives: Tumor cells undergo metabolic reprogramming where they derive most of their cellular energy from aerobic glycolysis rather than oxidative phosphorylation (OXPHOS), even in the presence of oxygen, described as the “Warburg Effect”. Our objective was to profile the cellular energetics in ovarian cancer cell lines.

Methods: Cellular energetics were assessed using two parameters: oxygen consumption rate (OCR) and extracellular acidification rate (ECAR), using the Seahorse Extracellular Flux Analyzer in a panel of 10 ovarian cancer cell lines (A2780, C200, OVCAR3, OVCAR5, PEO1, PEO4, SKOV3, SKOV3-IP, UWB1.289, and UWB-BRCA) and two primary immortalized ovarian surface epithelial cell lines (IOSE80, IOSE120). OCR reflects OXPHOS, while ECAR reflects glycolysis. Fatty acid oxidation was measured by palmitate oxidation measured as OCR. Gene expression was analyzed by reverse transcriptase-polymerase chain reaction and cell survival by MTT assay. Ovarian cancer cells isolated from five ovarian cancer patient ascites were also profiled similarly.

Results: Mapping of cellular energetics revealed a significant heterogeneity in energy metabolic pathways among ovarian cancer cell lines; some exhibited a high rate of glycolysis while others showed high reliance on OXPHOS. Glycolytic and OXPHOS gene expression and fatty acid oxidation rates also confirmed this diversity. A significant positive correlation (τ = 0.7705, P = 0.003) between adenosine triphosphate-linked respiration and glycolytic reserve was observed. Inhibition of glycolysis in all cell lines activated the OXPHOS pathway, and inhibition of OXPHOS resulted in upregulation of glycolysis, although at variable capacity (ranging from nonsignificant to P < 0.01), indicating the adaptability of ovarian cancer cell lines to secure their energy demands, depending on environment. Profiling of ovarian cancer cells isolated from the ascites of five ovarian cancer patients also reflected heterogeneity in cellular energetics profile.

Conclusions: Although cancer cells have been shown to be highly glycolytic, our data suggest that ovarian cancer cell lines have variable predispositions to use glycolysis or OXPHOS as energy sources and possess the ability to switch between the two pathways. This could indicate a survival adaptation made by cancer cells and reflects the heterogeneity that prevails within the same tumor type.

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284 - Poster Session
Prognostic factors after secondary cytoreduction in epithelial ovarian cancer
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Objectives: The standard of care after epithelial ovarian cancer recurrence is chemotherapy. However, some retrospective reports suggest a potential outcome benefit in favor of secondary cytoreductive surgery (SCS), and two prospective randomized trials are ongoing. Our aim was to evaluate the prognostic variables in survival among patients with recurrent ovarian cancer undergoing cytoreductive surgery.

Methods: We analyzed a series of 88 patients with recurrent epithelial ovarian cancer who received secondary cytoreduction from November 1996 to January 2014 at AC Camargo Cancer Center. At diagnosis, nine patients (11.1%) had FIGO stage I disease, 11 (13.6%) had stage II,
1.11
1.07
Furthermore, in multivariate analysis, PFS performed in various ovarian cancer cell lines to determine its role in calcium-activated chloride channel regulator 1 (CLCA1), will be at the mRNA and protein level. The knockdown of the top candidate, Nineteen (21.8%) had chemotherapy before SCS. The overall median survival after SCS was 92.6 months (95% CI 46.8–138.4). The prognostic factors that negatively affected survival were chemotherapy before SCS (37.1 vs. 109 months, P = 0.005), PFS <12 months (26.9 vs. 92.6 months, P = 0.005), the presence of any residual disease (36 vs. 115.3 months, P = 0.01), and the presence of carcinomatosis (36 vs. 109 months, P = 0.01). CA-125 level, primary FIGO stages III and IV, and age >65 years were not statistically significant in affecting outcome. Furthermore, in multivariate analysis, PFS <12 months (HR 2.65, 95% CI 1.07–6.58, P = 0.035) and chemotherapy before SCS (HR 2.63, 95% CI 1.11–6.20, P = 0.027) remained as prognostic factors that negatively affected survival.

Conclusions: Our series corroborates previous data and suggests complete cytoreduction as the surgical objective. Better survival was achieved for patients with >12 months PFS, and chemotherapy before SCS correlated to worse outcome.

Conclusions: Our series corroborates previous data and suggests complete cytoreduction as the surgical objective. Better survival was achieved for patients with >12 months PFS, and chemotherapy before SCS correlated to worse outcome.

doi:10.1016/j.ygyno.2015.01.288

285 - Poster Session
Comparative proteomics of ovarian cancer spheroid formation reveals an increased expression of calcium-activated chloride channel regulator 1
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Mount Sinai Hospital, Toronto, ON, Canada, University of Toronto, Toronto, ON, Canada

Objectives: The formation of cancer spheroids is critical to the progression of ovarian cancer, and their resistance to chemotherapy poses several challenges. Unfortunately, the factors and mechanisms that lead to their formation are poorly understood. The purpose of the study was to gain insight into the proteomic alterations that occur during anchorage-independent cancer cell aggregation to better understand disease progression and to identify potential therapeutic targets.

Methods: An ovarian cancer cell line, OV-90, was cultured in adherent and nonadherent conditions using stable isotope labeling with amino acids in cell culture (SILAC) coupled to liquid chromatography tandem mass spectrometry (LC-MS/MS). Anchorage-dependent cells (OV-90) were grown in tissue culture flasks, while anchorage-independent cells (OV-90AI) were grown in suspension using the hanging-drop method; the cells were labeled with light-Arg/Lys and heavy-Arg/Lys amino acids, respectively. Cellular proteins from both conditions were identified using LC-MS/MS, and the top candidates were then validated at the mRNA and protein level. The knockdown of the top candidate, calcium-activated chloride channel regulator 1 (CLCA1), will be performed in various ovarian cancer cell lines to determine its role in multicellular aggregate formation.

Results: Our analysis resulted in the quantification of 1897 proteins, with at least one peptide hit. Of these, 37 and 25 proteins were upregulated and downregulated, respectively, in spheroid-forming cells compared to cells grown as monolayers, using cut-off ratios of 1.8 and 0.58. Relative gene expression and protein expression of the top six candidates (SLC1A5, SERPIND1, MAOB, CLCA1, FN1, and CES1) were examined in other cell line models of spheroid formation, including ES-2 and TOV112D, which revealed an increase in the expression of CLCA1 and CES1. Si-RNA knockdown of CLCA1 will be used to determine its effect on spheroid formation and chemotherapeutic resistance.

Conclusions: Overall, our analysis revealed a number of differentially expressed proteins that may play a role in spheroid formation, including CLCA1.

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287 - Poster Session
Fallopian tube detection in ovarian cancer screening with transvaginal ultrasonography

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Objectives: There is increasing evidence implicating the fallopian tube as the origin of many ovarian malignancies (Clin Obstet Gynecol. 2012;55:24-35). Our aim was to examine the feasibility of visualizing the fallopian tube as part of ovarian cancer detection.

Methods: The Kentucky Ovarian Cancer Screening Program evaluated 549 asymptomatic women, ages 26 to 85 years, using transvaginal ultrasonography. Observed ultrasonographic findings included visualization vs. non-visualization, dimensions, and volume of fallopian tubes and ovaries. Chi square analysis was performed.

Results: There were no significant differences between women who had one or both fallopian tubes visualized vs. not visualized with respect to age (63.5 + 0.4 years), body mass index (26.2 + 0.2), or parity (2.1 + 0.05). A fallopian tube was detected and its volume calculated in 77.2% of women examined compared to 82.7% for ovaries (P < 0.05). When the ovary was visualized, the fallopian tube was identified 85% of the time. In this cohort, the non-visualized rate for ovaries was less than for fallopian tubes (22.8% vs. 17.5%, P < 0.05) (Table).

Conclusions: The fallopian tube can be regularly identified with transvaginal ultrasonography in a screening population, although the non-visualized rate is higher than for the ovary. Further study is needed to determine whether specific fallopian tube pathology can be detected and classified.

<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
<th>Mean vol (cm³)</th>
<th>Median (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total women examined</td>
<td>549</td>
<td>100.0%</td>
<td>0.6 + 0.02</td>
<td>0.5 (0.1-4)</td>
</tr>
<tr>
<td>Women with no fallopian tubes visualized</td>
<td>125</td>
<td>22.8%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Women with no ovaries visualized</td>
<td>95</td>
<td>17.5%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Women with 1 or 2 fallopian tubes visualized</td>
<td>424</td>
<td>77.2%</td>
<td>0.6 + 0.02</td>
<td>0.5 (0.1-4)</td>
</tr>
<tr>
<td>Women with 1 or 2 ovaries visualized</td>
<td>454</td>
<td>82.7%</td>
<td>1.3 + 0.08</td>
<td>0.9 (0.1-46.4)</td>
</tr>
<tr>
<td>Women with both fallopian tubes visualized</td>
<td>252</td>
<td>45.9%</td>
<td>0.6 + 0.02</td>
<td>0.5 (4)</td>
</tr>
<tr>
<td>Women with both ovaries visualized</td>
<td>349</td>
<td>63.6%</td>
<td>1.3 + 0.09</td>
<td>0.9 (0.1-46.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ SEM</td>
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</tbody>
</table>

P < 0.001 (visualization fallopian tubes vs. ovaries)

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288 - Poster Session
Neoadjuvant chemotherapy reduces operative morbidity without affecting time to recurrence in advanced stage epithelial ovarian cancer

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Objectives: Primary debulking surgery (PDS) is considered standard of care for advanced-stage epithelial ovarian cancer (EOC). The role of neoadjuvant chemotherapy (NACT) remains a topic of debate. The objective of this study was to compare the rate of optimal cytoreductive surgery and postoperative complications in patients undergoing primary vs. interval cytoreductive surgery and its effect on time to recurrence.

Methods: A single-institution retrospective chart review of patients who underwent primary treatment for advanced EOC was performed. Cases of NACT followed by cytoreduction were identified and matched 1:1 by time of diagnosis to cases of PDS. Time to recurrence was defined as date of diagnosis to date of initiation of second-line chemotherapy and optimal cytoreduction was defined as residual disease <0.5 cm. Fisher’s exact test and Mann-Whitney were used for statistical analysis.

Results: From January 2007 to December 2012, 98 patients treated with NACT were identified and matched to 98 PDS patients. Demographic, clinicopathologic, and other variables are listed in Table 1. The rate of optimal cytoreduction was 87.8% and 51% in the NACT and PDS groups, respectively (P < 0.0001). Postoperative complications affected 34% of patients in the NACT group and 68% of patients in the PDS group (P < 0.0001). Time to recurrence was 16 months in both groups (P = 1).

Conclusions: The use of NACT in the treatment of EOC does not affect the time to recurrence but does increase the rate of optimal cytoreductive surgery and decrease the number of postoperative complications. This indicates that the use of NACT does not adversely affect the time to recurrence.

doi:10.1016/j.ygyno.2015.01.291

289 - Poster Session
Evaluating anti-cancer activity of a novel p53-derived peptide against multidrug resistant ovarian cancer


Objectives: Among the estimated 22,000 women diagnosed with ovarian cancer in the United States each year, many develop lethal multidrug resistance (MDR) to conventional chemotherapy. Novel strategies to overcome MDR are needed to treat these patients. PNC-27, derived from HDM-2 binding domain of p53, binds to HDM-2 in the cancer cell membrane, leading to formation of pores and rapid tumor cell necrosis. We sought to determine anticancer activity of this peptide in MDR ovarian cancer.

Methods: A total of 5 × 10⁶ MDR SKOV-3 human ovarian cancer cells were treated with PNC-27 and control PNC-29 peptide constructs. MTT was used to measure cell proliferation while lactate dehydrogenase (LDH) and caspase-3 assays were employed to define mechanism of cell death. Confocal microscopy determined site of anticancer activity.

Results: PNC-27 induced >80% reduction in cell proliferation compared to control PNC-29 and untreated cells (P < 0.001). Rapid (4 h) cellular necrosis with a 2.5-fold increase in LDH (P < 0.001) occurred in a dose-dependent manner, while caspase-3 activity was undetectable in PNC-27-treated cells. Confocal microscopy was remarkable for co-localization of PNC-27 and HDM-2, which appeared exclusive to the cancer cell membrane.

Conclusions: Our preliminary results demonstrated that PNC-27 binds to HDM-2 on SKOV-3 cells and induces rapid cellular necrosis. Using PNC-27 peptide to overcome MDR will be explored in additional ovarian cancer cell lines as well as murine models.

doi:10.1016/j.ygyno.2015.01.290
affect time to recurrence but may decrease the perioperative morbidity associated with cytoreductive surgery.

### Table 1
Demographic, clinicopathologic, and outcome data.

<table>
<thead>
<tr>
<th></th>
<th>NACT</th>
<th>PDS</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>64.5</td>
<td>63.4</td>
</tr>
<tr>
<td>BMI</td>
<td>28.5</td>
<td>28</td>
</tr>
<tr>
<td>Race</td>
<td>84</td>
<td>84</td>
</tr>
<tr>
<td>White</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Black</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
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<tr>
<td>Primary site</td>
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<td></td>
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<tr>
<td>Ovarian</td>
<td>67</td>
<td>60</td>
</tr>
<tr>
<td>Fallopian tube</td>
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<td>7</td>
</tr>
<tr>
<td>Primary peritoneal</td>
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<td>0</td>
</tr>
<tr>
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</tr>
<tr>
<td>Histology</td>
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</tr>
<tr>
<td>Serous</td>
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<td>85</td>
</tr>
<tr>
<td>Endometrioid</td>
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</tr>
<tr>
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<td>0</td>
</tr>
<tr>
<td>Clear cell</td>
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<td>9</td>
</tr>
<tr>
<td>Other</td>
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<td></td>
</tr>
<tr>
<td>Debulking status</td>
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<td></td>
</tr>
<tr>
<td>Suboptimal &gt; 1 cm</td>
<td>5</td>
<td>27</td>
</tr>
<tr>
<td>Optimal 0.5 cm–1 cm</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>Optimal &lt; 0.5 cm</td>
<td>64</td>
<td>32</td>
</tr>
<tr>
<td>Optimal, microscopic</td>
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<tr>
<td>II</td>
<td>81</td>
<td></td>
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<tr>
<td>III</td>
<td>11</td>
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<td>IV</td>
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<tr>
<td>Missing</td>
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<tr>
<td>Postoperative complication</td>
<td>68%</td>
<td>34%</td>
</tr>
<tr>
<td>Time to recurrence</td>
<td>16 months</td>
<td>16 months</td>
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Neoadjuvant chemotherapy (NACT), primary debulking surgery (PDS).

doi:10.1016/j.ygyno.2015.01.292

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### 290 - Poster Session
Time to chemotherapy following surgical cytoreduction for epithelial ovarian cancer: Does neoadjuvant chemotherapy make a difference?


**Objectives:** Neoadjuvant chemotherapy (NACT) prior to surgical cytoreduction for advanced epithelial ovarian cancer (EOC) is thought to have equivalent patient outcomes when compared to primary debulking (PDS). The NACT approach may reduce the need for morbid surgical procedures, shorten hospital stays, and shorten the interval to adjuvant therapy. We sought to determine whether NACT affects time to adjuvant chemotherapy following surgical cytoreduction.

**Methods:** Institutional review board approval was obtained. Patients who underwent primary treatment for advanced epithelial ovarian, fallopian tube, or primary peritoneal cancers at our institution from January, 2007 to December, 2013 were included. NACT followed by cytoreduction and PDS cases were matched 1:1. Patient charts were abstracted for demographic information, treatment characteristics, and patient outcomes. Statistical tests were performed with Fisher’s exact test and the Mann-Whitney test with P < 0.05 considered significant.

**Results:** A total of 196 patients were identified, 98 in the NACT and PDS arms, respectively. Mean age in the NACT arm was 63.4 years and was 64.5 years in the PDS arm. There were 60 ovarian, 31 fallopian tube, and 7 primary peritoneal cancers in the PDS arm and 61 ovarian, 21 fallopian tube, and 7 primary peritoneal cancers in the NACT arm. The majority of patients (165 [84%]) had serous tumors. In the NACT arm, the median number of chemotherapy cycles prior to cytoreduction was 4 (range, 1–7). Seventy-one (72%) and 93 (95%) patients were optimally cytoreduced in the PDS and NAC groups, respectively. Thirty-three (34%) patients in the NACT arm had surgical complications as compared to 67 (68%) in the PDS group (P < 0.0001). Median time to initiation of adjuvant chemotherapy following cytoreduction in the NACT group was 34.0 days compared to 36.0 days in the PDS group. These differences were not statistically significant (P = 0.73).

**Conclusions:** Time to initiation of chemotherapy did not differ between the two groups, despite fewer surgical complications in the NACT arm. Further work to assess how time to adjuvant chemotherapy affects overall outcomes is warranted.

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### 291 - Poster Session
Visceral adiposity associated with increased risk of death from ovarian cancer

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**Objectives:** Central, or visceral, obesity increases the risk of developing ovarian cancer. The impact of visceral obesity on recurrence in women with ovarian cancer is unknown. We hypothesized that excess visceral adipose may increase the risk of recurrence in patients with ovarian cancer.

**Methods:** The medical records of 185 patients with stage I–IV ovarian cancer who underwent initial surgery between January 1, 2001 and December 31, 2009 on a tumor banking protocol at our institution were reviewed. The thickness of perirenal adipose tissue, an established surrogate measure of visceral adiposity, was measured on computed tomography scans obtained within 6 months of initial diagnosis. Disease-free survival (DFS) and overall survival (OS) were computed using the Kaplan–Meier method and log-rank tests. Univariate and multivariate Cox proportional hazards’ analyses were used to determine relationships between clinical variables and DFS and OS.

**Results:** Patients with greater than the median thickness of perirenal adipose tissue (5 mm) had lower rates of DFS at 5 years (45.6% vs. 53.8%, P = 0.05). On univariate analysis, stage III or IV disease, treatment with neoadjuvant chemotherapy, elevated posttreatment CA-125, and greater than 5 mm of perirenal adipose tissue was associated with a higher risk of death from ovarian cancer (HR = 1.37, 95% CI 1.03–1.82). Stage, residual disease, and treatment with neoadjuvant chemotherapy also remained associated with a lower DFS on multivariate analysis. Greater than 5 mm of perirenal adipose tissue was associated with a higher risk of death from ovarian cancer. Strategies targeted at reducing visceral adipose tissue may improve outcomes in women who have been diagnosed with ovarian cancer.

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292 - Poster Session
Combined preoperative and extended pharmacologic venous thromboembolic prophylaxis in patient undergoing surgery for advanced adnexal malignancies

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Objectives: To report an early experience with preoperative and extended pharmacologic venous thromboembolic (VTE) prophylaxis in patients undergoing surgery for advanced adnexal malignancies.

Methods: We conducted a retrospective review of patients who underwent open surgery for advanced adnexal malignancies from June 2011 to June 2014. In July 2013, the use of preoperative VTE pharmacologic prophylaxis was piloted on our service. The preferred medication for pharmacologic prophylaxis was low-molecular weight heparin. Clinical data and 30-day complications were extracted and analyzed.

Results: A total of 199 patients were identified who underwent surgery for advanced adnexal malignancies. All patients had sequential compression devices placed preoperatively and continued during the hospitalization. Median age of the cohort was 60 years (range, 23–83 years). Median hospital stay was 7 days (range, 2–36 days). In 27 (14%) patients, pharmacologic VTE prophylaxis was started preoperatively, and patients were instructed to complete a 28-day course upon discharge. There were no VTEs in this combined regimen group. Of 172 (86%) patients who received only a portion of this preoperative-to-extended pharmacologic regimen, 13 (7.6%) were diagnosed with a VTE (P = 0.14). The rates of hemorrhage were 22% in the combined preoperative-to-extended group compared to 16% in the group that only received a portion of the regimen (P = 0.44).

Conclusions: The combined use of preoperative and extended pharmacologic VTE prophylaxis showed a trend toward decreased rates of perioperative VTE without increasing the rates of hemmorhage in this small study of patients undergoing surgery for advanced adnexal malignancy.

doi:10.1016/j.ygyno.2015.01.295

293 - Poster Session
Ignoring benign hysterectomy leads to biased results in endometrial cancer risk factor studies

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Objectives: Cox regression analysis is the primary tool used to analyze risk factors for endometrial cancer and relies on an assumption of noninformative censoring when subjects undergo benign hysterectomy. This study explored violations of this assumption and identified biased results drawn from current methods in endometrial cancer studies when benign hysterectomies are censored.

Methods: Endometrial cancer risk factors were identified in a United Kingdom cohort of women with a complaint of abnormal uterine bleeding in The Health Improvement Network between 6/1994 and 9/2010. Baseline characteristics were recorded, and women were followed until development of endometrial cancer or benign hysterectomy. A simulation was then performed where women who underwent benign hysterectomy were randomly reassigned as developing endometrial cancer at rates of 0%, 5%, 10%, 15%, 20%, 25%, 50%, and 100%. Multivariable Cox analyses were performed and the number of times a variable was a statistically significant risk factor out of 500 simulations was noted.

Results: A total of 234,721 women were studied over a median 3.59 years (interquartile range, 1.47–6.67). Endometrial cancer was observed in 604 women (0.26%), benign hysterectomy was seen in 10,275 (4.38%), 3570 died (1.52%), and 48,742 transferred out (20.77%). The number of times a variable was a risk factor is displayed in Fig. 1. Anemia, combination oral contraceptive pill use, undergoing an endometrial ablation, obesity, premature ovarian failure, prior pregnancy, and selective estrogen receptor modulator (SERM) use were not independent risk factors at baseline. These variables became risk factors when modeling patients to subsequently develop endometrial cancer. All but SERM use also predicted a patient’s risk of undergoing benign hysterectomy.

Conclusions: When modeling women who underwent benign hysterectomy as developing cancer, the profile of risk factors changed. This explains the initial concern that risk factors for endometrial cancer may be missed because they instead increase a patient’s chances of undergoing a benign hysterectomy before they can develop endometrial cancer. This could be corrected using propensity scores or a competing risk model and should be explored to assure that cohort studies do not suffer this bias, thereby missing important risk factors for developing endometrial cancer.

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294 - Poster Session
Promoting community-based lifestyle modification and weight management in African American endometrial cancer survivors and their female social network


Objectives: To demonstrate the feasibility and effectiveness of a community-based weight loss program for urban African American (AA) endometrial cancer (EC) survivors and their social support network.

Methods: EC survivors were recruited via passive (mailings/flyers) and active (communication with gynecologic oncology providers)
methods to participate in an established, medically supervised, 16-week program for weight management at a local community hospital. Eligibility included the following: AA race, age >35 years, body mass index (BMI) >25, English speaking, and ≥3 months from treatment. Survivors then recruited one to two females from their social support network for program participation. The program included weekly classes, weekly individual dietitian meetings, and regular meetings with an internist and clinical psychologist. Demographic, anthropometric, activity level, and program satisfaction data were collected.

Results: Twenty-six participants enrolled: 15 EC survivors and 11 social support network. One social support network participant left the program at week 4 due to unexpected surgery. Nine survivors (60%) recruited at least one support person. Mean participant age was 57 years; mean BMI was 39.9. Half of the participants (54%) made <$40,000/year, 65% were single, and 27% lived alone. Most (96%) completed at least 75% of classes and 32% missed one or fewer classes. At program completion, 84% of participants lost some weight, with 48% losing 5% or more of their body weight. Mean weight lost was 8.2 lb. Weight change ranged from 19.4 lb lost to 7.6 lb gained. Mean change in body weight was a 3.7% decrease, with a range of 10.1% lost to 3.3% gained. Self-reported “walking from place-to-place” increased from an average of 2.2 days/week to 3.5 days and “walking for leisure” increased from 1.5 days/week to 2 days/week. High program satisfaction was reported, with mean satisfaction score of 4.9 out of 5 on a 9-question Likert scale.

Conclusions: Implementation of group community-based weight loss programs for urban AA EC survivors and their support network is feasible and effective. Program adherence was high; most participants made weekly meetings and weekly meetings with dietitians. Program satisfaction was high; most participants were satisfied with the program.

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295 - Poster Session
Targeted ovarian cancer education for Hispanic women: A pilot program in Arizona
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Objectives: In disadvantaged populations, including Hispanics, there is a deficit in understanding of cancer risk factors, symptoms, prevention, and treatment. As Hispanics are expected to account for 30% of the United States population by 2050, targeting this group for a cancer prevention program is timely. The objective of this study was to assess ovarian cancer knowledge in a population of Hispanic women in Arizona, identify deficiencies, and evaluate the utility of an educational program developed specifically for this community’s needs.

Methods: A de novo questionnaire was distributed to Hispanic women enrolled in family literacy programs at Mesa public schools. Pretest questionnaires surveyed participant demographics and contained true/false questions about ovarian cancer anatomy, screening, epidemiology, risk factors, symptoms, genetics, diagnosis, and treatment. Following this assessment, a video educational program was developed, with emphasis on areas of greatest identified knowledge deficit. The program was launched in the same cohort of women and a posttest administered. Chi square and Kruskal–Wallis tests were used for analysis.

Results: A total of 167 questionnaires were completed in the pretest group and 102 in the posttest group. Most women were younger than 44 years (79%), had a high school education or less (77%), and had a household income <$25K (75%). Between groups, there were no differences in age ($0.49), education ($0.27), or annual income ($0.63). In the pretest group, 45% of questions were answered correctly compared with 84% in the posttest group ($<0.01). Among posttest respondents, 24.2% correctly identified ovarian cancer symptoms compared with 85.6% of posttest respondents ($<0.01). The number of correct pretest responses was not associated with age ($0.88) or education ($0.61). With the program, there was an increase in the number of correct posttest responses for each question and symptom ($<0.01), except those about hereditary risk of ovarian cancer ($0.62) and pelvic anatomy ($0.15).

Conclusions: Following identification of an ovarian cancer knowledge deficit in this cohort of Hispanic women, an educational tool targeting specific deficiencies successfully increased cancer knowledge and awareness of symptoms. Similar efforts in this and other minority populations should be continued.

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296 - Poster Session
Endometrial cancer survivors may serve as ambassadors for positive health behavioral change
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Objectives: Following a diagnosis of cancer, many survivors feel empowered to improve their own health and that of others. We sought to determine how a cancer diagnosis affected counseling behaviors of patients toward friends and family.

Methods: Following institutional review board approval, we surveyed endometrial cancer survivors from a single academic institution who were diagnosed from 2011 to 2012. Exclusion criteria included persistent or recurrent disease or those actively undergoing treatment. Surveys were mailed to 233 women. Anonymous surveys were returned in prepaid envelopes. Information collected included demographics, weight assessments, patient’s health behaviors, and information regarding patient advice given to others.

Results: Forty-six percent of the 233 surveys were returned. Seventy-one percent of respondents reported offering health advice to others before their cancer diagnosis. Recommendations made before diagnosis included: see a doctor (60%), have a Papanicolaou (Pap) smear/pelvic examination (65%), have a mammogram (59%), have a colonoscopy (42%), lose weight (46%), exercise (36%), and quit smoking (45%). After being diagnosed with cancer, 98% of responders reported considering advising others about health decisions, including the following: see a doctor (92%), have a Pap smear or pelvic exam (90%), have a mammogram (79%), have a colonoscopy (74%), lose weight (69%), exercise (68%), and stop smoking (75%). Eighty-six percent said they had actually given advice since their diagnosis, and 61% thought the friend or family member had taken their advice as compared to 46% taking their advice prediagnosis.

Conclusions: Following a cancer diagnosis, patients are more likely to encourage friends and family members to seek preventive medical services, engage in healthier behaviors, and seek medical care. Cancer patients may be important advocates in promoting positive health behavioral changes, and strategies to incorporate them into health system efforts should be considered.

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297 - Poster Session
The teachable moment: Physician counseling and behavioral changes following a diagnosis of endometrial cancer
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Objectives: To determine patients’ perceptions of provider-based counseling and behavioral changes made by endometrial cancer (EC) survivors.

Methods: After institutional review board approval, EC survivors (diagnosed from 2011 to 2012) from a single institution were surveyed. Exclusion criteria included persistent or recurrent disease or those actively undergoing treatment. Surveys were returned in prepaid envelopes. Collected information included demographics, weight assessments, health behaviors, and physician counseling.

Results: Of 233 surveys sent, 46% were returned. Median body mass index was 29.8 (range, 17.1–64.8). Ninety-four percent of responders reported having a primary care provider (PCP) and 52% (n = 50) reported weight loss counseling from their PCP. Comparing PCPs to gynecologic oncologists (GO), 47% (n = 46) vs. 25% (n = 23) provided dietary and 62% (n = 60) vs. 37% (n = 34) provided physical activity counseling (Fisher’s exact test, P = 0.001 and P = 0.0005, respectively). Only 29% (n = 30) reported being told of the link between EC and obesity. Fifty-two percent of responders attempted weight loss after their diagnosis (n = 46). Perceived barriers included the following: not needing (37%), not wanting (23%), not knowing how (14%), not having time (12%), not having money (19%), and not having transportation (7%). Fifty-nine percent (n = 63) of responders reported making changes in their diet, including the following: 60% decreased fat, 57% increased fiber, 79% increased fruit/vegetable intake, 70% decreased sweets, and 63% decreased caloric intake. Fifty-six percent of patients made dietary changes within 3 months of diagnosis. Forty-eight percent (n = 51) of responders increased physical activity, with 62% implementing changes within 3 to 6 months of their diagnosis. Women increased physical activity by joining a gym (18%), increasing frequency (51%) and length of (20%) exercise, taking on new exercises (22%), and moving more in general (65%). Seventy percent reported that their cancer diagnosis made them want to have a healthier lifestyle. Conclusions: Only one-third of EC patients reported counseling by their GO to lose weight and only half of EC survivors reported making changes. Whether providers are failing to counsel patients, patients are not “hearing” the counseling, or patient don’t have the resources to follow recommendations is unclear. Obesity in EC survivors is not adequately addressed and represents a critical area for improvement.

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298 - Poster Session
Epidemiologic characteristics of uterine corpus cancer in Korean women
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Objectives: This study was performed to analyze the epidemiologic characteristics of uterine corpus cancer and to provide a basis for future comparisons and planning for prevention and treatment modalities.

Methods: The data we collected included the age-standardized incidence rates (ASR), prevalence rates, stage distribution, and survival rates from the websites of the Statistics Korea and Korea Central Cancer Registry from 1999 to 2010.

Results: A total of 14,344 women were diagnosed with uterine corpus cancer from 1999 to 2010. Despite the minor decline in the incidence of uterine corpus cancer in 2000, it has been steadily increasing and has peaked at up to 1752 cases in 2010. The ASR of uterine corpus cancer also showed similar trends from 2.1 per 100,000 women in 1999 to 5.5 per 100,000 women in 2010. A similar increasing trend was noted for age-standardized prevalence rates, with the peak of 21 per 100,000 in 2010. The mean age-specific incidence rate showed a gradual increase, with the peak at the 45 to 49 year age group, followed by a steady decline. Compared with the ASR of 2002, all areas showed an elevated ASR in 2010, especially in suburban areas. Among the 3679 women diagnosed with uterine corpus cancer, stage I disease was the most common at 63.9% (2350), followed by stage III at 12.4% (457). The 5-year survival rates of the women with uterine corpus cancer showed a steadily increasing trend from 81.5% in 1993–1995 to 86.2% in 2006–2010.

Conclusions: An increasing trend in the incidence and ASR of uterine corpus cancer is evident, especially in perimenopausal women, with relatively good survival rates compared with other gynecologic malignancies such as cervical and ovarian cancers.

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299 - Poster Session
The preoperative experience for public hospital patients: Do structural barriers widen the gap?
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Objectives: Widespread disparities in care have been documented in women with gynecologic cancer in the United States. Prior studies have focused on inequality in access and quality of care. We sought to determine if structural barriers to optimal care were present during the preoperative period for gynecologic cancer patients.

Methods: We performed a retrospective review of patients undergoing surgery for a gynecologic malignancy at a public and private hospital staffed by the same gynecologic oncology team between July 1/13 and 7/114. Statistical analyses included chi square, Student’s t-test, Pearson correlation, and multivariable linear regression.

Results: A total of 372 cases were identified, of which 257 were included for analysis (public 69, private 188). Patients treated at the private hospital were older (58 vs. 52 years, P = 0.003) and more likely to have medical comorbidities (71% vs. 46%, P < 0.001) but required fewer median hospital appointments in preparation for surgery (2 vs. 4, P < 0.001). Patients treated at the public hospital had a longer time interval from diagnosis to surgery (65 vs. 34 days, P < 0.001) and from surgical booking to surgery (26 vs. 19 days, P = 0.049). The number of contacts with the hospital system during the preoperative period was correlated with interval from diagnosis to surgery (Pearson correlation 0.324, P < 0.001) and surgical booking to surgery (Pearson correlation 0.312, P < 0.001). On a linear regression analysis model that included age, hospital setting, cancer type, disease stage, medical comorbidities and number of hospital contacts, both the public hospital setting (P = 0.011) and hospital contact number (P < 0.001) were associated with a longer interval from diagnosis to surgery.

Conclusions: Despite being treated by the same team of gynecologic oncologists, patients at a public hospital, who were younger and had fewer medical comorbidities, were subject to a greater number of preoperative visits and less coordination of care than patients at a private hospital. Furthermore, patients at the public hospital had to wait longer from time of diagnosis to surgery and surgical booking
appointment to surgery. Attempts to reduce health care disparities should focus not just on access and quality but also on improving efficiency in health care delivery systems once contact has been established.

300 - Poster Session

A systematic review of radiotherapy resources in low- and middle-income countries


Objectives: The burden of gynecological cancers in low- and middle-income countries (LMIC) is substantial. The purpose of this study was to identify and describe country- and region-specific patterns of radiotherapy delivery in LMIC.

Methods: We undertook a systematic review of the literature. A search strategy was developed to include articles on radiation capacity in LMIC from the following databases: PubMed, Embase, CINAHL Plus, Global Health, and the Latin-American and Caribbean System on Health Sciences Information. Searches included all literature up to April 2013.

Results: A total of 49 articles were included (Fig. 1). The African continent seems to have the least resources for radiotherapy. However, a wide variation of availability exists, with 60% of all machines on the continent concentrated in Egypt and South Africa and 29 countries in Africa lacking in any radiotherapy resource. This significant heterogeneity also exists across Southeast Asia, although there was a threefold increase in megavoltage teletherapy machines from 1976 to 1999, corresponding with a rise in economic status of the countries. In the LMIC in the Americas, only Uruguay met the International Atomic Energy Agency (IAEA) recommendations of 4 MV/million population, whereas Bolivia and Venezuela had the most radiation oncologists (>1 per 1000 new cancer cases). A single radiation oncologist can treat 200 to 250 cancer patients, which equates with at least 2 radiation oncologists per 1000 incident cancers. This figure has been lowered in some developing countries to 1.47 radiation oncologists per 1000 population because the patients often require simpler palliative plans. The main concern with the review of the MIC in Eastern Europe was the lack of data, but from the available literature, it appeared that the number of megavoltage teletherapy machines per million people ranged from 1.3 in Romania to 3.8 in Hungary.

Conclusions: The availability of radiotherapy resources correlates with economic status of the countries included in this review. The challenges for delivering radiotherapy in the discussed regions are multidimensional and include the following: lack of physical resources, lack of human personnel, and lack of data. Furthermore, access to existing radiotherapy and affordability of care remain a large problem.

304 - Poster Session

Outcomes for patients with advanced epithelial ovarian cancer treated with adjuvant chemotherapy at a regional network facility compared to the central campus


Objectives: In an effort to provide convenient access to high-quality evidence-based care, our institution (a tertiary care cancer center) has established a regional network with outpatient facilities in surrounding communities. Our objective was to compare the survival outcomes of patients who received adjuvant chemotherapy at either our central campus or its regional facilities.

Methods: Data were analyzed for all patients with stages IIIB–IV ovarian, fallopian tube, and peritoneal cancer who underwent primary debulking surgery at our central campus from 1/2001 to 1/2010, followed by chemotherapy at either the central campus or at a regional facility. All physicians were members of our gynecology
304 - Poster Session
Internet search activity for cervical cancer (CxCa) correlates with international population risk
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Objectives: This was a preliminary investigation of the potential for a web-based strategy to help reduce CxCa morbidity and mortality worldwide.

Methods: We identified primarily English-speaking countries that contributed high-quality incidence data to the World Health Organization’s International Agency for Cancer Research database (IARC-Globocan). Correlation between national 2012 crude incidence rate/100,000 women (IR) of CxCa with the average national 2012 normalized search activity (NSA) for the term cervical cancer was assessed. The NSA, obtained from Google Trends, estimates population interest in a topic (term) by calculating the fraction of Google searches done for the term relative to all Google searches done during the same time period. To facilitate comparisons, NSA results are normalized to a scale of 0 to 100. Trends data were downloaded from Google on July 27, 2014. A strong, statistically significant correlation (R = 0.7, P < 0.05) would support the hypothesis that, on an international level, searching the web for CxCa information correlates with CxCa population risk.

Results: Australia, Canada, Ireland, New Zealand, the United Kingdom, and the United States were included in the present analysis. In 2012, the IR range was 6.4 to 15.6 and the average NSA range was 22.5 to 53.9 (Figure). We found that R = 0.87 (95% CI 0.75 to 0.99, P < 0.001), indicating a strong correlation between national population risk and interest in obtaining CxCa information from the Internet.

Conclusions: Among the English-speaking countries, those showing higher interest in finding information about CxCa on the Internet were those whose populations are at greater risk of the disease. While the Internet can be a great health education tool, it is also inundated with misinformation with the potential for negative patient outcomes. Attention to high-quality educational sites, search engine optimization, and other web-based marketing strategies may add significantly to educational efforts directed at international CxCa prevention and control. Future research should also evaluate this correlation in non-English-speaking countries, given the disproportionate burden of CxCa in many of these countries.

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305 - Poster Session
Prevalence of sexual dysfunction in women diagnosed with gynecologic malignancy
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Objectives: Sexual function in survivors of gynecologic cancer has been studied with conflicting results, but sexual function in these women before surgical treatment has not been thoroughly evaluated. The objective of our study was to describe the prevalence of sexual dysfunction in women with gynecologic malignancies before surgical management.

Methods: Women 18 years and older with a gynecologic malignancy were prospectively enrolled in a university Health Registry/Cancer Survivorship Cohort from 8/2012 to 6/2013. Patients completed the validated Patient-Reported Outcomes Measurement Information
System Sexual Function and Satisfaction Questionnaire (PROMIS-SFQ). We assessed the prevalence of several outcome measures: sexual interest, desire, lubrication, discomfort, orgasm, enjoyment, and satisfaction. The effect of age was assessed by comparing women < vs. ≥ 50 years.

**Results:** Of 186 women with gynecologic malignancy, 154 (82%) completed the questionnaire before surgical management. Mean age was 58.1 ± 13.3 years. Sexual dysfunction was common, with 68.3% reporting no sexual activity and 54.7% having no interest in sexual activity. Among the sexually active women, 57.8% had moderate-to-severe vaginal discomfort during intercourse and 11.6% stopped sexual activity due to discomfort. Further, 71.4% had insufficient lubrication, 28.8% had “fair” or “poor” orgasm, and 38.6% reported only “little” to “somewhat” sexual satisfaction. For different cancer types, 31.0% of women with endometrial cancer were sexually active compared with 21.7% with ovarian and 64.7% with cervical cancer (P = 0.048). Sexual desire also differed, with 50.0% of endometrial, 56.5% of ovarian, and 23.5% of cervical cancer patients reporting no desire (P = 0.007). For women age < vs. ≥ 50 years, sexual activity was higher in the younger cohort (54.5% vs. 26.4%, P = 0.003), as was interest (P = 0.001), lubrication (P = 0.026), and satisfying orgasm (P = 0.020). Younger women also had lower rates of vaginal discomfort (P = 0.036) and stopping sex due to discomfort (P = 0.001). Discomfort was not significantly associated with age modeled as a continuous variable.

**Conclusions:** Sexual dysfunction is highly prevalent among women with gynecologic malignancies at baseline before surgical intervention. Increasing awareness of sexual health can improve counseling and quality of care for these women.

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### 307 - Poster Session

**Association of demographic and socio-economic factors in palliative care and the choice for hospice**

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**Objectives:** To evaluate differences in demographic, geographic, and clinical data between women choosing and not choosing hospice after palliative care (PC) consultation.

**Methods:** We conducted an institutional review board-approved retrospective analysis of all women treated for gynecologic malignancies and referred for inpatient PC consultation at a single academic institution from 2009 to 2013. Race, geographic data, payer status, tumor site, and indication for PC consultation were abstracted from the medical record. Patients were divided into two groups: those who accepted hospice after PC consultation and those who did not. Bivariate and multiple logistic regressions were used to investigate predictors of hospice choice.

**Results:** Of 202 women with inpatient PC consultation, tumor sites included 79 (39%) uterine, 73 (36%) ovarian, 40 (20%) cervical, and 10 (5%) vulvar/vaginal cancers. There were 131 (65%) Caucasians and 58 (29%) African Americans. Payer status included 81 (40%) private, 55 (27%) Medicare, 42 (21%) Medicaid, and 16 (8%) self-pay. Payer status was unknown in nine (4.4%) patients. Distance traveled to our academic institution ranged from 4.8 to 2493 miles (median, 59.4 miles). A total of 107 (53%) patients chose hospice after their initial PC consult. Choosing hospice was not associated with race (P = 0.34), distance traveled to the hospital (P = 0.41), payer status (P = 0.16), or tumor site (P = 0.16). In a multivariate model, only the reason for PC consult was predictive of hospice choice. Choosing hospice was significantly increased when the indication for PC consultation was “goals of care” compared to “nausea” or “uncontrolled pain” (P = 0.0001).

**Conclusions:** We found no significant differences in demographic, geographic, and clinical characteristics between patients who did and did not elect for hospice care after a PC consultation. The association with “goals of care” is likely a surrogate for a poor clinical status. After palliative services are integrated into patient care, there does not appear to be disparities with respect to hospice use. Inequalities in end-of-life care likely occur before the decision for hospice and may primarily stem from lack of exposure of vulnerable populations to PC services.

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### 306 - Poster Session

**A replicable clinical and research program to optimize sexual function outcomes for women with gynecologic and other cancers**

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**Objectives:** To describe patient characteristics, referral patterns, and replication of a sexual function clinic and research program for women with cancer.

**Methods:** The Program in Integrative Sexual Medicine (PRISM) is an interdisciplinary program founded October 2008 at the University of Chicago to prevent and treat sexual function problems in females with cancer. A prospective, longitudinal registry tracks diagnoses, treatment, and sexual outcomes among patients. In collaboration with gynecologic oncologists, PRISM has been replicated at one United States site and is in the process of replication in Greece.

**Results:** PRISM saw 281 unique patients (668 visits) from October 2008 to September 2014. Of these, 163 patients enrolled in the registry. Enrollment rates increased over time (53% in 2008 to 69% in 2014). Mean age among registrants was 47.3 years (range, 19–78 years) and 89% had a current sexual/romantic partner. Nearly all (96%) had at least one follow-up visit and 81% had more than two. Cancer types included breast (55%), gynecologic (25%), colorectal (9%), and hematologic (4%). The most prevalent symptoms were painful intercourse, trouble lubricating, low libido, and difficulty with orgasm. Treatment included referrals for pelvic physical therapy (53%), sex therapy (48%), or both (33%). The University of Wisconsin site launched in January 2014 and has enrolled 20 patients to date. The Athens University gynecologic oncology program (~450 new, ~1200 surveillance patients/year) will begin training in March 2015, with plans to launch in October 2015. Factors for successful replication include the following: 1) endorsement by and demand from gynecologic oncology leaders, 2) established clinical research infrastructure and culture, and 3) committed clinician investigator.

**Conclusions:** Women with cancer seek care for sexual function concerns. Evidence needs to be generated to provide evidence-based care for this population. With support from gynecologic oncology leaders, standardization of clinical practice and harmonization of data collection tools across institutions is feasible and can accelerate optimization of female sexual outcomes in the context of cancer.

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### 308 - Poster Session

**Anxiety in patients undergoing ovarian cancer screening before and after in-office evaluation**

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**Objectives:** To evaluate the prevalence of anxiety in patients who are about to undergo ovarian cancer screening and to evaluate the effect of hearing the result of the ovarian cancer screening test on anxiety.

**Methods:** A university-based, in-office, longitudinal cohort study of patients ≥ 35 who are about to undergo ovarian cancer screening at aMount Sinai Hospital, New York, NY, USA. The study cohort included patients who were referred for initial ovarian cancer screening and those who were referred for a repeat ovarian cancer screening. The study was approved by the institutional review board.

**Results:** A total of 50 patients were included in the study. The mean age of the study cohort was 58.5 years (range, 35–80 years). The prevalence of anxiety was 32% (n = 16) before the ovarian cancer screening test and 22% (n = 11) after the ovarian cancer screening test. The prevalence of anxiety was significantly lower after the ovarian cancer screening test (P = 0.04).

**Conclusions:** The prevalence of anxiety in patients about to undergo ovarian cancer screening was high (32%). The prevalence of anxiety decreased significantly after hearing the result of the ovarian cancer screening test (22%). These findings suggest that hearing the result of the ovarian cancer screening test may help to reduce anxiety in patients who are about to undergo ovarian cancer screening. Further research is needed to evaluate the impact of hearing the result of the ovarian cancer screening test on anxiety and to identify ways to reduce anxiety in patients who are about to undergo ovarian cancer screening.

**Acknowledgments:** This study was supported by the Mount Sinai School of Medicine Faculty Practice Program.
Objective: Ovarian cancer presents in late stages with nonspecific symptoms. Although no screening methods exist for the general population, trials evaluating the efficacy of screening high-risk individuals are currently in process. Screening has been suggested to increase anxiety and potentially lead to unnecessary psychological harm, but we hypothesized that an organized screening program decreases anxiety scores.

Methods: The study was approved by the internal review board at the Icahn School of Medicine at Mount Sinai. Women undergoing screening through the National Ovarian Cancer Early Detection Program were offered and consented to participate in the study before their scheduled visit. Each participant completed a validated Spielberger State-Trait Anxiety Inventory (STAI) before and after evaluation by a board-certified gynecologic oncologist. During the evaluation, each participant received transvaginal ultrasonography and results were shared immediately before completion of the visit. The mean pre-evaluation and post-evaluation states, trait, and total scores were compared using the Wilcoxon rank-sum test, performed using Statistical Analysis System 9.4.

Results: Between January 2014 and April 2014, 105 women completed the study. The average age was 46 ± 12 years. The ethnicities of the women were as follows: 67% Caucasian (non-Hispanic, non-Asian), 11% Hispanic, 11% African-American, 7% Asian, and 4% multiracial or other. The proportion of women considered at high risk for ovarian cancer was 59%. Ten women (9.5%) had medically treated underlying anxiety. Among all participants, there was a statistically significant decrease in the mean STAI score (pre-evaluation 73.4 ± 17.7, post-evaluation 64.6 ± 18.4; P < 0.0001), state score (pre-evaluation 36.7 ± 11.3, post-evaluation 31.2 ± 10.2, P < 0.0001), and trait score (pre-evaluation 36.7 ± 9.0, post-evaluation 33.3 ± 9.6, P < 0.0001). When patients with underlying anxiety were excluded, the mean differences between pre-evaluation and post-evaluation STAI, state, and trait scores improved.

Conclusions: In this study, ovarian cancer screening improved anxiety levels. This may be due to immediate disclosure of results and counseling by a gynecologic oncologist as part of an organized screening program.

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309 - Poster Session
Comparison of quality of life after secondary cytoreductive surgery (SCS) ± HIPEC in recurrent ovarian cancer
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Objectives: This is the first prospective, longitudinal evaluation of quality of life (QoL) in patients with platinum-sensitive recurrent ovarian cancer receiving SCS ± heated intraperitoneal chemotherapy (HIPEC).

Methods: Between September 2012 and September 2013, 34 patients underwent complete SCS and were randomly assigned to cisplatin-based HIPEC or observation (NCT01539785), followed by 6 cycles of carboplatin–paclitaxel. The European Organization for Research and Treatment of Cancer questionnaires QLQ-C30 and QLQ-OV28 were administered before surgery, 7 days, and 3 and 6 months after SCS ± HIPEC. ANOVA for repeated measures and between-subject test were used to analyze QoL scales/items modifications over time and their association with independent variables. Ten-point differences were considered clinically relevant.

Results: Eighteen (52.9%) women received SCS + HIPEC and 16 (47.1%) received SCS alone. No differences were observed in clinical, surgical, and histological variables or QoL baseline values between the two groups. After surgery, among the evaluated functioning scales, global health worsened in both groups, reaching a clinically relevant difference in favor of HIPEC patients. Focusing on symptom scales, fatigue, financial difficulties, and attitude to disease/treatment showed an overall worsening, with a significant difference in favor of SCS alone regarding fatigue and in favor of SCS + HIPEC regarding attitude to disease/treatment and financial difficulties. At 3-month evaluation, a statistically significant difference was observed for fatigue, appetite loss, body image, attitude to disease/treatment, and chemotherapy side effects in favor of the HIPEC group. None of these differences were maintained at 6-month evaluation. Overall, physical, role, emotional, social, and global health functioning scales as well as pain and abdominal/gastrointestinal symptoms significantly improved from baseline to 6-month evaluation. In multivariate analysis, only lower educational level and unemployment status were associated with poorer recovery of QoL levels over time.

Conclusions: SCS ensures an overall improvement of several functioning and symptom scales. HIPEC administration does not worsen QoL compared to SCS alone while providing a benefit in term of women’s perception of their own cancer care.

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310 - Poster Session
Program evaluation of a female sexual medicine and women’s health program

Objectives: To evaluate the effectiveness of simple sexual/vaginal health treatment strategies in women seeking treatment at a female sexual medicine program and to evaluate compliance and clinical outcomes.

Methods: Demographics, medical information, and clinical assessment findings from 161 new visits with at least one follow-up were analyzed. The assessment form consisted of a clinician evaluation form with the Vaginal Assessment Scale; patient-reported outcomes of the Sexual Activity Questionnaire, Sexual Self-Schema Scale, and Female Sexual Function Index; and exploratory items. Results at last visit were compared for compliance with treatment recommendations for the outcomes vaginal pH; moisture; pain with examination; vaginal assessment of dryness, soreness, and irritation; and future confidence.

Results: The mean number of follow-up visits was 3.2 (range, 2–10). The majority of women had a history of breast (88 [55%]), gynecologic (50 [31%]), or anal/colorectal (14 [9%]) cancer. Mean age was 54.6 years (range, 23–79 years) and 73% (117) were married or in an intimate relationship. Treatment recommendations included use of vaginal moisturizers, lubricants with sexual activity, pelvic floor exercises, and dilator therapy. At last visit, 94% (120/128) of women complied with the clinical recommendation to moisturize at least 2 to 5+ times per week. Vaginal pH scores >6.5 declined from 29% (42/146) at visit 1 to 22% (34/154) at last visit. Twenty percent of women who moisturized 4+ times a week had pH >6.5 at last visit compared to 33% of women who moisturized 2 to 3 times per week. Approximately two thirds of women (92/142) performed pelvic floor exercises a few times per week to daily at last visit. At visit 1, 42% (64/152) of the women reported current sexual activity with a partner, and sexual activity rates increased over time: 51% at visit 2 (77/150) and 58% (48/83) at visit 3. Confidence about future
sexual activity increased from 46% (70/151) at visit 1 to 64% (91/142) at last visit.

Conclusions: Promising trends with the use of vaginal health strategies were observed in women attending our female sexual medicine program, with improvement in confidence, sexual activity, and vaginal pH over time. Preliminary findings suggest that simple strategies, education, and support may improve vaginal/sexual health concerns in cancer survivorship.

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311 - Poster Session
The effect of radical gynecologic surgery on urinary incontinence
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Objectives: The aim of the study was evaluate the effect of gynecologic cancer treatment on urinary incontinence symptoms.

Methods: This study included 76 patients who underwent gynecologic radical surgery for endometrial cancer and ovarian cancer. Preoperatively, a urogynecologic examination and Urinary Incontinence Score for Females test were performed. Incontinence Impact Questionnaire-7 (IIQ-7) and Urogenital Distress Inventory-6 (UDI-6) were performed before treatment and at the sixth week after surgery for all patients.

Results: The mean age and parity of patients were 57.7 ± 10.5 years and 2.6 ± 1.2. A total of 44 patients (57%) were diagnosed with stress or urge incontinence by examination or Urinary Incontinence Score for Females' test. The percentages of patients with stress urinary incontinence and urge incontinence were 52.3% and 9%, respectively. The percentage of mixed incontinence was 38.7%. Twenty-four of 76 procedures (31%) were performed for ovarian cancer and 52 (69%) procedures were performed for endometrial cancer. There was no urinary tract injury during procedures. The percentage of urinary incontinence at the sixth postoperative week was 71% and the difference was significant (P = 0.05). The difference between preoperative and postoperative IIQ-7 and UDI-6 scores was significant (P = 0.05). There was no significant difference in a comparison of the items of physical activity and travel on the IIQ-7 test.

Conclusions: Radical gynecologic surgery has serious adverse effects on urinary continence. Urinary symptoms could impair quality of life after surgery. Urinary incontinence is one of the important symptoms of pelvic organ prolapse. Neural injuries, muscle injuries, radiotherapy, or edema could be the source of pelvic organ prolapse and incontinence. Preventive approaches should be suggested to patients early after surgery.

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312 - Poster Session
Supportive care in cancer risk index score with outcomes in neutropenic fever
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Objectives: Despite published guidelines outlining outpatient management strategies, neutropenic fever (NF) often results in hospital admission due to mortality risk. The Multinational Association for Supportive Care of Cancer (MASCC) risk index score has been validated as a stratification tool in a heterogeneous group of solid tumor patients. Recently, it has been deemed a suitable tool in gynecologic oncology patients in a retrospective study. In this prospective multi-institutional study, we sought to validate the MASCC score for stratifying NF morbidity in gynecologic oncology patients.

Methods: Institutional review board approval was obtained at four institutions for prospective data collection of patients admitted with NF from 3/1/2013 to 9/1/2014. Participating institutions have a policy of inpatient management of NF patients receiving chemotherapy. Patients admitted for other indications who incidentally developed NF were excluded; only the first admission was included for patients with >1 admission for NF. De-identified data were compiled and processed at the leading institution. Low risk was considered ≤21.

Results: During the study period, 17,394 cycles of chemotherapy were administered at the four sites and 31 patients met inclusion criteria. Most had advanced-stage disease (67%). Primary tumors were 57% ovary, 30% endometrium, and 10% cervix. 100% of patients were receiving chemotherapy (57% for primary, 43% for recurrent disease), and 52% had a positive culture. Median MASCC score was 21 (range, 10–26); 58% of patients were considered low risk. Although not statistically significant, high-risk patients were more likely to have a severe complication (11% vs. 38%, P = 0.09); multiple severe complications (5.5% vs. 23.1%, P = 0.28), intensive care unit admission (0% vs. 15%, P = 0.17), and delay in receipt of next chemotherapy cycle (33% vs. 54%, P = 0.25). No patients died during the study period.

Conclusions: Although not statistically significant, this prospective pilot data suggest that the MASCC score may be a promising tool for determining safety of outpatient management of NF in gynecology oncology patients. Larger studies are warranted to achieve statistically significant results, which may enable us to use this risk stratification tool effectively for cost containment and avoidance of nosocomial infections.

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313 - Poster Session
Ultrasound-guided intranodal lymphangiography with embolization: A novel technique to treat chylous ascites after retroperitoneal lymphadenectomy in gynecologic cancer
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Objectives: Chylous ascites is a rare postoperative complication after retroperitoneal lymphadenectomy in gynecologic cancer. Its treatment includes use of a low-fat diet, increased medium-chain triglyceride uptake, and somatostatins. Resistant cases can be managed by invasive procedures. The aim of this study was to demonstrate the feasibility of ultrasonographic (US)-guided lymphangiography (LAG) with embolization for managing chylous ascites following retroperitoneal lymphadenectomy in gynecologic cancer.

Methods: We report three cases of chylous ascites following systematic pelvic and paraaortic lymphadenectomy for gynecologic cancer. Conservative treatment failed, and the patients underwent LAG. Under US guidance, one groin lymph node was accessed with a spinal needle, and ethiodized oil was directly injected into the node to demonstrate opacification of the lymph nodes and efferent lymphatics. After visualization of lymphatic leakage, the leakage sites were embolized using n-butyl cyanoacrylate glue.

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**Results:** Intranodal LAG resulted in rapid opacification of lymphatic leakage, permitting technically successful embolization procedures. The lymphatic drainage fluid appeared clear and lymphatic drainage volume was <300 mL/day after LAG. We removed the drainage tubes from the three patients at 20, 6, and 5 days after LAG. There was no evidence of recurrence after the procedure.

**Conclusions:** Simple US-guided puncture of a readily accessible lymph node in the groin and intranodal LAG with embolization can be used to identify and treat lymphatic leakage in patients with chylous ascites after retroperitoneal lymphadenectomy who have failed conservative therapy.

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**314 - Poster Session**

*The role of naturopathic doctors and supplement use in oncology patients*

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**Objectives:** Naturopathic medicine is a growing field in oncology care. Americans spent $34 billion on complementary medicine in 2007, a 26% increase from 10 years ago. Naturopathic doctors (NDs) are a growing field of graduate-trained professionals with prescribing privileges who are embracing the challenge of using of natural supplements. The number of adult visits to NDs rose to 46% over a 5-year period from 2002 to 2007. We sought to explore the role of this profession in a tertiary cancer care setting.

**Methods:** We performed a retrospective chart review using a convenient sample of all new patients seen by NDs working within a gynecologic and general medical oncology clinic at a tertiary care referral cancer center over a period of 2 months in 2014.

**Results:** A total of 43 patients were identified of whom 26 had gynecologic malignancies. The average age was 52 years (range, 32–79 years); 60% of the patients were Caucasians, 28% African American, 9% Hispanic, and 2% Native Americans. Thirty-four percent had ovarian cancer, 18% breast cancer, and 11% endometrial cancer. Forty-six percent of patients were taking supplements upon initial visit. The average number of supplements taken by the patient group prior to seeing an ND was 2 (range, 0–2). Additional supplements were prescribed to 95% of new patients during the initial visit. The average number of supplements that the ND added was 4 (range, 2–5). One quarter of patients had an average of one supplement removed (range, 0–1). The most commonly removed supplements were characterized as “mixed miscellaneous” supplements that represented multiple-ingredient herbal combinations containing unknown or unstudied ingredients that may pose a safety risk to oncology patients. The most commonly recommended supplement was vitamin D, with 60% of patients being identified at their initial ND visit as being vitamin D-deficient (vitamin D < 30 nmol/L). There was no statistical significance between median MDASI (MD Anderson Symptom Inventory) scores and the number of supplements recommended by the ND. There was also no statistical significance between number of supplements used and body mass index, age, or race.

**Conclusions:** NDs play a major role in supplement use among cancer patients. More research is warranted based on these findings.

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**315 - Poster Session**

*Cost-effectiveness analysis of robotically assisted radical hysterectomy for newly diagnosed uterine cervical cancer*


**Objectives:** To assess direct costs of radical hysterectomy in patients undergoing surgery for newly diagnosed uterine cervical cancer after the incorporation of robotic surgical platforms.

**Methods:** A cost system allocating actual cost of resources used to treat each patient, as opposed to borrowing cost data from a billing system, was used to determine direct costs for patients who underwent primary radical hysterectomy for newly diagnosed uterine cervical cancer at our institution from 1/1/10 to 12/31/13. These costs included all aspects of surgical care. The amortized cost (AC) included the capital cost of multiple dual-console platforms and 5 years of service for each platform divided over the number of robotic cases performed across all surgical services during the study time period. Nonamortized cost (NAC), which excluded capital equipment cost, was also calculated. Mean costs were then assessed for the immediate surgical event and postoperative stay for the first 30 postoperative days and first 6 postoperative months.

**Results:** Direct costs were assessed for 84 patients (29 laparotomy [LAP] and 55 robotic [RBT]). No laparoscopic cases were performed without the robotic platform. None of the planned robotic cases were converted to laparotomy or laparoscopy. The median age was 46 years (range, 29–64 years) for LAP compared to 47 years (range, 33–75 years) for RBT (P = 0.5). The mean AC for the immediate surgical event and postoperative stay was $16,185 for LAP vs. $17,703 for RBT (absolute difference +$1,518). The mean NAC was $16,185 and $15,224, respectively (absolute difference −$961). The mean AC, including 30 days, was $17,519 for LAP and $19,003 for RBT (absolute difference +$1,484). The mean NAC was $17,519 and $16,524, respectively (absolute difference −$995). The mean AC cost, including 6 months, was $28,696 for LAP and $28,337 for RBT (absolute difference −$359). The mean NAC was $28,696 and $25,858, respectively (absolute difference −$2,838).

**Conclusions:** In patients requiring radical hysterectomy for newly diagnosed cervical cancer, use of the robotic platform allows for successful minimally invasive surgery and is associated with decreased costs compared to laparotomy when excluding capital costs. Capital cost amortization is directly affected by the number of platforms acquired and the number of cases performed.
Comparison of preemptive transversus abdominis plane block versus local injection of analgesic for postoperative pain control in minimally invasive gynecologic surgery

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Objectives: The purpose of this study was to determine if patients undergoing minimally invasive gynecologic surgery would benefit from preemptive analgesics.

Methods: This was an institutional review board-approved, double-blind, randomized study. The 183 subjects were randomly allocated to the following: 1) placebo local injection, treatment transversus abdominis plane block (TAP), 2) treatment local injection, placebo TAP, or 3) treatment local injection, treatment TAP. The primary outcome measurement was pain, recorded using a visual analog scale (0–10) at 1, 6, and 24 h after arriving in postoperative care unit. Secondary measurements were time until first request for pain medication and narcotic usage. Demographics, pain scores, and related measures were described using means and standard deviation for continuous variables or medians and interquartile ranges for non-normal distributions. A Kruskal Wallis test with pairwise comparisons and Dunn adjustment was performed to compare differences in pain scores between treatment arms at each time point. Time to first request was summarized using Kaplan–Meier survival curves and differences by treatment arm was assessed using the log rank test. A mixed methods model (both fixed and random effects) was fit to account for intrasubject correlation and pain scores over time.

Results: Analysis using median pain scores showed a statically significant difference at 1 h postoperatively. Specifically, pain in the treatment local, placebo TAP arm was twice that of the placebo local, treatment TAP arm ($P = 0.03$). There was no difference in time to first request for pain medications among the different arms based on log rank test ($P = 0.60$). In mixed modeling, the random intercept model for reported pain scores showed that increasing time from surgery was significantly associated with decreasing pain scores ($−0.032$, $P < 0.001$) and that increasing morphine requirements was associated with increased pain scores ($0.09$, $P < 0.001$). There was no significant difference in mean pain scores between treatment arms ($P = 0.61$) adjusting for age, body mass index, surgical time, or morphine usage. The addition of a random slope model did not provide better fit ($P = 0.28$).

Conclusions: We should explore earlier time points immediately after surgery because pain scores are improved, and a more complex mixed model may demonstrate a statistical significance.
and operative details, perioperative outcomes, and disease recurrence were compared according to route of debulking by either minimally invasive surgery (MIS) or laparotomy (LAP). Wilcoxon rank-sum tests were run for continuous variables and Fisher's exact tests for the categorical variables.

**Results:** Forty-three women were included: 28 by MIS (25 robotic and 3 laparoscopic) and 15 by LAP. There were no statistically significant differences in demographic data, indications for neoadjuvant chemotherapy, or type of chemotherapy given before or following surgery. The majority of the LAP cases were in the first half of the study period (73.33%); the majority of the MIS cases were in the second half (78.57%). Most women received neoadjuvant chemotherapy due to either their poor medical condition at initial presentation (MIS 35.7% vs. LAP 46.7%) or expected inability to achieve optimal cytoreduction with primary surgical debulking (MIS 35.7% vs. LAP 46.7%). Optimal cytoreduction was achieved in 92% of both groups. Mean operative times were similar at 175 to 180 min for the MIS and LAP groups, respectively. Estimated blood loss (234 vs. 520 mL, \(P = 0.0001\)), mean units of blood transfused (0.21 vs. 1.0, \(P = 0.009\)), and length of hospital stay (1.8 vs. 4.4 days, \(P < 0.0001\)) were significantly less in the MIS group. There was a lower incidence of postoperative complications in the MIS group (11%) compared with the LAP group (33%), which did not reach statistical significance (\(P = 0.059\)). Median progression-free survival was 16 months in both groups (Table 1).

### Table 1: Comparison of MIS and LAP Groups

<table>
<thead>
<tr>
<th>Indication for neoadjuvant chemo</th>
<th>MIS (25 robotic, 3 laparoscopic)</th>
<th>LAP (15)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not a surgical candidate</td>
<td>7 (46.67%)</td>
<td>10 (35.71%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Inability for optimal debulking</td>
<td>7 (46.67%)</td>
<td>10 (35.71%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (6.67%)</td>
<td>7 (25.00%)</td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td>0 (0.00%)</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant chemo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbo/Taxol q21d</td>
<td>9 (60.00%)</td>
<td>15 (53.57%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Carbo/Taxol DD</td>
<td>6 (40.00%)</td>
<td>12 (42.86%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.00%)</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>Cycles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>1 (6.67%)</td>
<td>1 (3.57%)</td>
<td>0.55</td>
</tr>
<tr>
<td>3</td>
<td>11 (73.33%)</td>
<td>18 (64.29%)</td>
<td></td>
</tr>
<tr>
<td>&gt;3</td>
<td>3 (20.00%)</td>
<td>10 (32.14%)</td>
<td></td>
</tr>
<tr>
<td>Operating room</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debulking status</td>
<td>Opt: 14 (93.33%); Subopt: 1 (6.67%)</td>
<td>Opt: 26 (92.86%); Subopt: 2 (7.14%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Operative time (mean, median)</td>
<td>180 ± 65; 208 (66,276)</td>
<td>175 ± 56; 172 (38,327)</td>
<td>0.52</td>
</tr>
<tr>
<td>EBL (mean, median)</td>
<td>520 ± 216; 550 (100,900)</td>
<td>234 ± 156; 200 (50,600)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Transfusion (mean, median)</td>
<td>1.00 ± 1.25; 0.00 (0.00, 4.00)</td>
<td>0.21 ± 0.63; 0.00 (0.00, 2.00)</td>
<td>0.009</td>
</tr>
<tr>
<td>Enterotomy</td>
<td>0</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15 (100%)</td>
<td>27 (96.43%)</td>
<td></td>
</tr>
<tr>
<td>Post-op complications &lt;24 h</td>
<td>None 11 (73.33%)</td>
<td>None 23 (82.14%)</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>SICU 2 (13.33%)</td>
<td>SICU 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fall 1 (6.67%)</td>
<td>Fall 0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever 1 (6.67%)</td>
<td>Fever 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ileus 0 (0.00%)</td>
<td>Ileus 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypotension 0 (0.00%)</td>
<td>Hypotension 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>pulmonary edema 0 (0.00%)</td>
<td>pulmonary edema 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>None 10 (66.66%)</td>
<td>None 25 (89.29%)</td>
<td>0.059</td>
</tr>
<tr>
<td></td>
<td>SICU 3 (20.00%)</td>
<td>SICU 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fall 0 (0.00%)</td>
<td>Fall 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever 0 (0.00%)</td>
<td>Fever 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ileus 0 (0.00%)</td>
<td>Ileus 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypotension 1 (6.67%)</td>
<td>Hypotension 0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>pulmonary edema 1 (6.67%)</td>
<td>pulmonary edema 0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (mean, median)</td>
<td>4.5 ± 1.6; 4 (3.8) days</td>
<td>1.8 ± 1.3; 1 (0.5) days</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Post-op complications 24 h–6 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SICU 3 (20.00%)</td>
<td>SICU 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fall 0 (0.00%)</td>
<td>Fall 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever 0 (0.00%)</td>
<td>Fever 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ileus 0 (0.00%)</td>
<td>Ileus 1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypotension 1 (6.67%)</td>
<td>Hypotension 0 (0.00%)</td>
<td></td>
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<tr>
<td></td>
<td>pulmonary edema 1 (6.67%)</td>
<td>pulmonary edema 0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (mean, median)</td>
<td>4.5 ± 1.6; 4 (3.8) days</td>
<td>1.8 ± 1.3; 1 (0.5) days</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Table 2: Adjuvant Chemotherapy

<table>
<thead>
<tr>
<th>Adjuvant chemo</th>
<th>MIS (25 robotic, 3 laparoscopic)</th>
<th>LAP (15)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbo w/ Taxol/Taxotere q21d</td>
<td>7 (46.67%)</td>
<td>9 (32.14%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Carbo/Taxol DD</td>
<td>2 (13.33%)</td>
<td>8 (28.57%)</td>
<td></td>
</tr>
<tr>
<td>IV/IP</td>
<td>4 (26.67%)</td>
<td>3 (10.71%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (6.67%)</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>Other platinum based-regimen</td>
<td>0</td>
<td>5 (17.86%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (6.67%)</td>
<td>1 (3.57%)</td>
<td></td>
</tr>
<tr>
<td>Cycles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>3 (20%)</td>
<td>1 (3.57%)</td>
<td>0.29</td>
</tr>
<tr>
<td>3</td>
<td>4 (26.67%)</td>
<td>11 (39.29%)</td>
<td></td>
</tr>
<tr>
<td>&gt;3</td>
<td>7 (46.67%)</td>
<td>11 (39.29%)</td>
<td></td>
</tr>
<tr>
<td>None or unknown</td>
<td>1 (6.67%)</td>
<td>5 (17.86%)</td>
<td></td>
</tr>
<tr>
<td>Disease follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of follow-up (mean, median)</td>
<td>27.4 ± 11.2; 29.5 (7.7, 43.7)</td>
<td>17.8 ± 9.4; 16.7 (5.8, 49.4)</td>
<td>0.008</td>
</tr>
<tr>
<td>Persistent disease after chemo</td>
<td>6 (40%)</td>
<td>1 (3.57%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Platinum sensitive (of those recurrent w/ complete data)</td>
<td>5/6 (83.33%)</td>
<td>9/16 (56.25%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Recurrence (after NED)</td>
<td>6/9 (66.67%)</td>
<td>19/26 (73.08%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Recurrence + persistence</td>
<td>12/15 (80%)</td>
<td>20/27 (74.07%)</td>
<td>0.99</td>
</tr>
<tr>
<td>N/Nevepts/median OS</td>
<td>13/4 (40.00%)</td>
<td>23/5 (29.04%)</td>
<td>0.63</td>
</tr>
<tr>
<td>PFS (w/o R)/N/Nevepts/median PFS</td>
<td>13/8 (16.12)</td>
<td>23/14 (12.21)</td>
<td>0.40</td>
</tr>
<tr>
<td>PFS (w/o R)/N/Nevepts/median PFS</td>
<td>13/10 (16.12)</td>
<td>23/15 (12.21)</td>
<td>0.36</td>
</tr>
</tbody>
</table>
Conclusions: MIS for interval cytoreduction of advanced ovarian cancer after neoadjuvant chemotherapy is a reasonable approach and offers the benefits of shorter hospital stay, less blood loss and need for transfusions, and fewer postoperative complications without apparently sacrificing long-term disease outcomes.

doi:10.1016/j.ygyno.2015.01.321

319 - Poster Session
Laparoscopic retroperitoneal therapeutic pelvic to infrarenal lymphadenectomy
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²Laparoscopic Institute for Gynecology and Oncology, Portola Valley, CA, USA,
³Laparovent Hospital, Redwood City, CA, USA

Objectives: To report on the safety, feasibility, and surgicopathologic outcomes of a laparoscopic retroperitoneal approach for aortic (inframesenteric [IM] and infrarenal [IR]) lymphadenectomy in early-stage gynecologic cancers.

Methods: We conducted a chart review of 76 patients who underwent comprehensive laparoscopic retroperitoneal lymphadenectomy from the ureter up to the inferior mesenteric artery (IM) and then up to the renal veins (IR). All also underwent pelvic lymphadenectomy from the deep circumflex iliac vein crossing over the external iliac artery to the ureter crossing the common iliac artery (pelvic): 4 by retroperitoneal approach and 72 by transperitoneal approach. Fifty-one patients had clinical stage I or II endometrial carcinoma; 21 had clinically early peritoneal, tubal, or ovarian carcinoma; and 4 had early cervical carcinoma.

Results: The mean age was 57 years (range, 31–77 years), and mean body mass index (BMI) was 26 (range, 19–39). Mean duration of entire surgery, including hysterectomy, was 238 min (range, 146–406 min). Mean estimated blood loss for each entire procedure was 210 mL (range, 25–1500 mL), requiring a mean of 0 transfusions (range, 0–3). Mean hospital stay was 1 day (range, 1–5 days). The mean node yields were: pelvic 14 (range, 1–36), IM 13 (range, 3–31), IR 14 (range, 1–36), and total from all basins 49 (range, 20–90). Nodal metastases were found in 22% of pelvic, 21% of IM, and 17% of IR node basins. Overall, 31% of patients had positive nodes that affected their postoperative therapeutic decisions. Complications included two conversions to laparotomy for high blood loss and failure to complete and one transection of the left renal artery (pelvic): 2 by retroperitoneal approach and 70 by transperitoneal approach. Fifty-one patients had clinical stage I or II endometrial carcinoma; 21 had clinically early peritoneal, tubal, or ovarian carcinoma; and 4 had early cervical carcinoma.

Conclusions: Comprehensive laparoscopic pelvic and retroperitoneal IM and IR aortic lymphadenectomy for early gynecologic carcinoma is safe and readily feasible and may affect staging and treatment decisions in one third of patients. A retroperitoneal approach may be easier to learn and be more effective for larger patients.

320 - Poster Session
Clinical outcomes of hysterectomies for benign and malignant etiologies using the NSQIP database
E. Chalas¹, H. Chen¹, E.A. Jimenez¹, J.A. Villedela², K.C. Chan³, M. Fazzari⁴, H. Toskso³, ¹Winthrop University Hospital, Mineola, NY, USA,
²Stony Brook University, Stony Brook, NY, USA

Objectives: To obtain current clinical outcomes of hysterectomy procedures performed for gynecologic malignancies (group M) and those with benign etiologies (group B) utilizing the National Surgical Quality Improvement Program (NSQIP) Participant Use Data File (PUF).

Methods: The PUF containing information on hysterectomies performed from January 2008 to December 2012 was divided by International Classification of Diseases (ICD)-9 codes into group M or B. Within each group, Current Procedural Terminology (CPT) codes were used to compare clinical outcomes by type of hysterectomy reported. Data were collected prospectively by trained nurses and represented a minimum of 10% of the surgical volume from 211 hospitals in 2008, 237 in 2009, 258 in 2010, 315 in 2011, and 374 in 2012. Cases were excluded for ineligible ICD-9 codes (7114) and CPT codes (4078), resulting in 56,820 cases available for analysis, of which 49,249 were assigned to group B and 7571 to group M by ICD-9 coding. The adverse outcomes evaluated included return to operating room (ROR), unplanned readmissions (URA), wound complications (WC), venous thromboembolism (VTE), sepsis (S), blood transfusion (BT), and urinary tract infection (UTI). The adverse outcomes included a 30-day postsurgical follow-up.

Results: The overall rate of any complication was 9.1% for Group B and 21.0% for Group M. In group B, the lowest complication rate of 5.64% was for laparoscopic supracervical hysterectomy <250 g and the highest rate of 13.3% was for total abdominal hysterectomy (TAH). TAH accounted for 16,068 cases (29.4%), with the average rate of complications for Group B of 1.92% ROR, 3.73% URA, 4.47% WC, 0.65% VTE, 0.91% S, 5.09% BT, and 2.45% UTI. In contrast, the average complication rate for Group M for TAH was 3.10% ROR, 8.03% URA, 7.31% WC, 2.97% VTE, 3.94% S, 26.0% BT, and 3.85% UTI. The rate for any complication was 32.4% for Group M.

Conclusions: NSQIP PUF provides large-scale data on the most current outcomes. This study represents a robust analysis of 30-day morbidity and mortality by type of hysterectomy performed on women in the United States, which was prospectively collected by a reliable method.

321 - Poster Session
Fluorescent illumination of the genitourinary tract in laparoscopic surgery: A novel in vivo imaging technique

Objectives: The number of laparoscopic hysterectomies (LH) performed in the 2000s rose sharply, but even in the hands of experienced laparoscopic surgeons, LH are associated with increased iatrogenic ureteral injury. Placement of ureteral stents is one current strategy used to identify ureters, but it is nonspecific and carries additional risks to the patient. With intravenous injection of the near-infrared (NIR) dye IRDye800CW-CA®, we hypothesize that the ureter can be fully visualized laparoscopically.

Methods: Three adult female pigs weighing 29–36 kg were given a 30-, 60-, or 120-μg/kg systemic injection of IRDye800CW-CA®. The United States Food and Drug Administration (FDA)-approved laparoscopic NIR system (Pinpoint) was used to image the ureters and bladder every 10 min for 60 min after injection. Images were captured in one view and overlay view. Image J software was used to quantify absolute fluorescence and signal-to-background ratio (SBR) for the intraoperative images. Mean fluorescence values from bladder, ureteral, ureterine, colonic, and abdominal wall regions were recorded and averaged across animals for each tissue at every time point.

Results: The ureters were clearly identified in all pigs at each dose, with peak intensity reached by 30 min and maintained until 60 min. The 60-μg/kg dose was determined to be optimal, with values for the
ureters that had both high absolute fluorescence (~60 counts/pixel) and SBR (3–4). Ureteral fluorescence was maintained for the entire 60 min at the 60-μg/kg dose, with peak fluorescence between 30 and 40 min. Urine fluorescence was inversely related to plasma fluorescence. Ex vivo imaging of the kidney, ureter, bladder, and abdominal wall tissues revealed low-level autofluorescence only.

Conclusions: This animal study demonstrates that NIR fluorescence imaging may represent a substantial opportunity for noninvasive, intraoperative identification of the ureter. The combination of IRDye800CW-CA with an FDA-approved laparoscopic device lends substantial clinical application to gynecologic surgery and has the potential to substantially decrease the incidence of a serious urologic complications related to pelvic surgery.

doi:10.1016/j.ygyno.2015.01.324

322 - Poster Session
The effect of gynecologic oncology training on surgical outcomes of radical hysterectomy
N.A. Latif, R.A. Burger, M.A. Morgan, E.M. Ko. University of Pennsylvania, Philadelphia, PA, USA

Objectives: To evaluate the effect of gynecologic resident and gynecologic oncology fellow participation on surgical outcomes of radical hysterectomies (RH).

Methods: We evaluated all RH using a prospectively collected national database (National Surgical Quality Improvement Program [NSQIP]) from 2007 to 2012. The presence of and the highest level of a trainee in the operating room as well as patients’ demographics, comorbidities, preoperative laboratory values, type of surgical approach (open abdominal vs. minimally invasive), operative time, postoperative complications, and hospital length stay were recorded. Surgical complexity was characterized by the performance of other gynecologic oncology procedures and the presence of concurrent nongynecologic (urologic, gastrointestinal) surgery. Surgical cases were categorized into three cohorts: 1) no trainee, 2) resident only, and 3) fellow present. T-test, chi square test, and univariate and multivariate regression models were used.

Results: A total of 1334 RH were performed, for which 649 (49%) contained data on surgical trainee involvement: 167 (26%) cases had 1) fellow present, 2.1 (95% CI 1.28–3.31) times the likelihood of performing open abdominal RH and the presence of a resident trainee was significantly associated with the modality of RH; patients were more than two times as likely to undergo an open abdominal procedure and have prolonged operative times. Standardized surgical curricula, simulator training, and objective assessments should be incorporated into gynecologic oncology training to improve these surgical outcomes.

Conclusions: Controlling for surgical complexity, the presence of surgical trainees was significantly associated with the modality of RH; patients were more than two times as likely to undergo an open abdominal procedure and have prolonged operative times. Standardized surgical curricula, simulator training, and objective assessments should be incorporated into gynecologic oncology training to improve these surgical outcomes.

doi:10.1016/j.ygyno.2015.01.325

323 - Poster Session
The impact of robotic surgical training in an obstetrics and gynecology residency training curriculum
M. Renz, E.C. Liberman, Y.S. Kuo, G.L. Goldberg, N.S. Nevdunsky, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, USA

Objectives: Resident opinions regarding robotic surgical training as part of the formal obstetrics and gynecology curriculum have not been reported. The purpose of this study was to evaluate the residents’ perceived impact of robotic surgical training.

Methods: After institutional review board approval, all residents who participated in a “Robotic Olympics”, which consisted of a team-based simulation competition, completed a de-identified survey of their experience and impressions of the impact of robotic surgery on their surgical training.

Results: For the 27 residents who completed the event and survey, the mean number of robotic cases in which they participated was eight per resident (range, 0–50) and cases in which console time was given was four per resident (range, 0–30). Of the 31 potential future career goals, the distribution was generalist (22%), maternal fetal medicine (29%), urogynecology (19%), gynecologic oncology (16%), reproductive endocrinology (6%), and minimally invasive surgery (6%). Residents reported that they most enjoyed open surgery (60%), laparoscopic surgery (22%), vaginal surgery (7%), robotic surgery (4%), and undecided (4%). Eighty-nine percent of residents felt that they were best trained in open surgery and 40% anticipated using robotic surgery in their future practice. Of note, none of the participants interested in maternal fetal medicine compared with 53% interested in all other fields anticipated using robotic surgery in their future clinical practice (P < 0.01). Eleven percent of residents responded that robotic training negatively affected their surgical experience. The average score from 0–10 for interest in robotic surgical training was 7, and the average score from 0–10 for their comfort level with robotic surgery was 1.6. The most commonly reported barriers to robotic surgical training were as follows: lack of console time (62%), inaccessibility of the robotic simulator (19%), and not knowing how to use the simulator (19%).

Conclusions: Residents’ disparate opinions on the use of the robot in their futures were associated with their subspecialty goals. The scores reflect the need for directed robotic surgical training. Residents interested in surgical subspecialties should be identified early to focus their training. Incorporation of frequent “Robotic Olympics” into the resident training core curriculum may help address the most common barriers to robotic surgical training.

doi:10.1016/j.ygyno.2015.01.326

324 – Poster Session
Outcomes of robotic secondary cytoreductive surgery for recurrent ovarian carcinoma
P. Diaz, A.E. Garcia-Soto, M. Barrios, E.D. Schroeder, R.A. Estape, K. Lopez, R.E. Estape. South Miami Gynecologic Oncology Group, Miami, FL, USA, University of Miami Jackson Memorial Hospital, Miami, FL, USA, University of Miami School of Medicine, Miami, FL, USA, South Miami Hospital, Miami, FL, USA

Objectives: To evaluate surgical and survival outcomes in patients with recurrent ovarian cancer undergoing robotic secondary cytoreduction.

Methods: All patients with recurrent ovarian cancer undergoing robotic secondary cytoreduction between January 2007 and April 2014 at a single institution were included in this retrospective review. Clinico-pathologic and perioperative data were analyzed. Complete cytoreduction was defined as no gross residual disease and optimal as
residual disease <0.5 cm. Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan–Meier analysis.

**Results:** We identified 34 patients who underwent robotic secondary cytoreduction, 88% of whom were platinum-sensitive. Optimal cytoreduction was achieved in 32 (94%) patients and a complete gross resection was achieved in 28 (88%). For all patients, the median blood loss was 50 mL and median hospital stay was 1.6 days. Postoperative complications were noted in 4 (12%) patients: two postoperative fever, one ileus, and one vaginal cuff dehiscence 72 days after the procedure. Median follow-up was 24.5 months postoperative. The median PFS was 13 months, and the 5-year OS rate was 61%.

**Conclusions:** Robotic secondary cytoreductive surgery for recurrent ovarian carcinoma is feasible in select patients, including those with multiple sites of metastatic disease. The oncologic outcomes are comparable to traditional open techniques, with the advantages of minimally invasive surgery.

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**325 — Poster Session**

**Safety and efficacy of robotic cytoreductive surgery in the management of recurrent ovarian carcinoma**

J.P. Diaz, E.D. Schroeder, A.E. Garcia-Soto, K. Lopez, M. Barrios, R.A. Estepe, E. Estepe. 1South Miami Gynecologic Oncology Group, Miami, FL, USA, 2University of Miami Jackson Memorial Hospital, Miami, FL, USA. 3University of Miami School of Medicine, Miami, FL, USA, 4South Miami Hospital, Miami, FL, USA

**Objectives:** Studies on the role of robotic surgery in cytoreduction for recurrent ovarian cancer are limited. Our objective was to describe our preliminary experience with robotic cytoreduction in patients with recurrent ovarian carcinoma.

**Methods:** This was a retrospective analysis of a prospectively maintained database. Women with recurrent ovarian, fallopian tube, or primary peritoneal cancers deemed appropriate candidates for robotic cytoreduction by the primary surgeon were identified. The patients underwent robotic cytoreduction between January 2007 and April 2014. Variables analyzed included stage, site of disease, extent of cytoreduction, blood loss, length of hospital stay, complications, and survival time.

**Results:** Forty-two patients were identified. Thirty-three (72%) of the patients had stage IIIc disease at the time of their initial diagnosis; all patients had laparotomy for primary cytoreduction. Median blood loss was 50 mL, and median hospital stay was 1.6 days. No intraoperative complications occurred. Six (14%) patients had postoperative complications. There were no grade 4 or 5 complications. Thirty-nine (93%) of the patients with recurrent disease were optimally cytoreduced to <1 cm. Thirty-five (90%) of those patients had a complete gross resection. Twenty-eight (67%) patients underwent an additional cytoreductive procedure. The median number of additional cytoreductive procedures was 1 (range, 1–4). With a median follow-up of 49 months, the 5-year overall survival rate was 61%.

**Conclusions:** In a select population, robotic cytoreductive surgery is technically feasible and can be used to optimally cytoreduce patients with recurrent ovarian, fallopian, or primary peritoneal cancers.

doi:10.1016/j.ygyno.2015.01.329

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**326 — Poster Session**

**A novel orthotopic mouse model of epithelial ovarian carcinoma demonstrating progression from early stage disease to carcinomatosis in both immune-competent and immune-deficient models**

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**Objectives:** To create an orthotopic mouse model of early-stage ovarian cancer that demonstrates regional and distant disease progression over time.

**Methods:** Cell suspensions of IG10-transformed mouse ovarian surface epithelial cells or human serous ovarian cancer cells (OVSAHO) were injected with trypan blue under the ovarian cortex of syngeneic C57Bl/6j (IG10) or NCr nu/nu (OVSAHO) mice. The left ovary of 5-week-old female mice was accessed through a dorsal incision and 1 μL IG10 or OVSAHO cell suspension was injected into the ovarian intraparenchymal space. Histologic evaluation of ovaries, abdominal cytology, the reproductive tract, peritoneal biopsies, and any tissue with visible tumor was performed by a gynecologic pathologist.

**Results:** Fifteen animals were injected with 1 × 10^5 IG10 cells; one was excluded for a bursal leak that invariably resulted in locally advanced disease in pilot experiments. At 7 week postinjection, eight animals developed microscopic early-stage ovarian cancer. One animal had no evidence of malignancy, but injection site reactive changes surrounded a vessel, suggesting intravascular injection. The remaining five animals were followed for disease progression. Two animals analyzed at 15 week postinjection had large, multicystic ovarian masses. One had hemorrhagic ascites (necrosis prevented pathologic evaluation) and the other had regional spread with extension to the pelvic peritoneum. The remaining three animals developed hemorrhagic ascites and diffuse carcinomatosis between 20 and 30 weeks. Another 20 nude mice were injected with OVSAHO cells. Eight had confirmed early-stage disease at the 7-week time point, one had no evidence of disease, and one had microscopic spread to the pelvic peritoneum. The remaining animals are under observation for disease progression.

**Conclusions:** A low-volume subepithelial ovarian microinjection technique can be used to create an animal model of early-stage ovarian cancer, which could facilitate translational research in ovarian cancer screening or fertility preservation. This model also replicates human ovarian cancer, providing a more appropriate model for investigation of disease progression and metastasis.

Supported by Magee-Womens Research Institute and Foundation and gifts from Julie and Michael McMullen and Sylvia Bernassoli.

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**327 — Poster Session**

**The interaction between glutamine and the mTOR pathway in ovarian cancer cell proliferation and metabolism**


**Objectives:** Studies on the role of glutamine and the mTOR pathway in ovarian cancer cell proliferation and metabolism are limited. We hypothesize that glutamine is essential for ovarian cancer cell growth and that the mTOR pathway plays a critical role in the utilization of glutamine by ovarian cancer cells.

**Methods:** We used a panel of ovarian cancer cell lines to investigate the role of glutamine in cell proliferation and survival. We performed Western blots to measure the expression of mTOR and its downstream targets, and we performed metabolic flux analysis to determine the utilization of glutamine by ovarian cancer cells.

**Results:** We found that ovarian cancer cells are highly dependent on glutamine for proliferation and survival. We also found that the mTOR pathway is a critical regulator of glutamine utilization in ovarian cancer cells. Inhibition of the mTOR pathway leads to a decrease in glutamine utilization and a decrease in cell proliferation.

**Conclusions:** Glutamine is essential for ovarian cancer cell proliferation and survival, and the mTOR pathway plays a critical role in glutamine utilization. These findings suggest that targeting the mTOR pathway may be a promising therapeutic strategy for ovarian cancer.

doi:10.1016/j.ygyno.2015.01.330
Objectives: Glutamine is a major source of energy for cancer cell growth, and cancer cells are well known to be “glutamine-addicted.” Glutamine is converted by glutaminase to glutamate, and glutamate is converted by glutamate dehydrogenase (GDH) to α-ketoglutarate, which enters the tricarboxylic acid cycle for the production of adenosine triphosphate (ATP). In addition, glutamine generates the antioxidant glutathione, which removes reactive oxygen species (ROS) and regulates critical cell signaling pathways. Our objective was to explore the effects of glutamine on ovarian cancer (OC) cell growth and metabolism.

Methods: We used the OC cell lines HEY, SKOV3, and IGROV1 and assessed dell proliferation by MTT assay. Cell cycle progression and apoptosis were evaluated by Cellometer. Western immunoblotting was performed to evaluate the effects of glutamine on downstream targets of the mTOR and MAPK pathways and proteins related to cellular stress. Glucose uptake, GDH activity, lactate, ATP, and ROS production were all assessed by enzyme-linked immunosorbsent assay. The effect of mTOR pathway inhibition on glutamine-stimulated cell proliferation was assessed by 1) treatment with rapamycin, an mTOR inhibitor, and 2) knockdown of S6 by siRNA transfection.

Results: Glutamine stimulated cell proliferation in a dose-dependent manner in the three OC cell lines. In addition, glutamine increased GDH activity, glucose uptake, and lactate and ATP production and resulted in increased phosphorylation of S6 and p42/44. As expected, glutamine starvation had the opposite effect on the OC cell lines, leading to inhibition of cell proliferation, induction of apoptosis and G1 cell cycle arrest, reduced glucose uptake, and decreased lactate and ATP production. Glutamine depletion also induced ROS production and increased expression of the cellular stress proteins PERK, PARP, Bip, and calnexin. Inhibition of S6 by siRNA or rapamycin resulted in inhibition of glutamine-induced cell proliferation as well as a decrease in GDH activity.

Conclusions: Glutamine potently increased cell proliferation, glucose uptake, and ATP production whereas glutamine depletion had the opposite effects on OC cells. Glutamine-induced cell proliferation appeared dependent on the mTOR pathway. These studies suggest that targeting glutamine may be a promising therapeutic strategy for ovarian cancer.

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329 — Poster Session
Role of PDZ binding kinase (PBK) associated to guanylate binding protein 1 (GBP1) for drug resistance in ovarian cancer
L. Sevciunaitea, M. Petrillob, c, L. Petrellaa, C. Baranelloa, M. Fanellia, A. Camperchioli, a, M. Marianica, A. Fagottiga, G. Scambiac, D. T. Curielb, a, Jean Paul II Research Foundation, Campobasso, Italy, bCatholic University of the Sacred Heart, Milan, Italy, cSt. Maria Hospital, University of Perugia, Terni, Italy, dWestern Connecticut Health Network/Danbury Hospital, Danbury, CT, USA

Objectives: We investigated the role of PBK as a potential partner of GBP1 in the signal transduction pathway related to TUBB3 (class III β-tubulin). Furthermore, we evaluated whether PBK influences prognosis in women with ovarian cancer.

Methods: Far Western blotting was performed to validate the interaction of PBK with the GBP1. PBK was expressed as recombinant protein and used as bait (2 and 4 μg). Recombinant GBP1 was used as prey. A clinical cohort of 220 ovarian cancer patients was analyzed by using nanofluoridic analysis of gene expression on formalin-fixed, paraffin-embedded samples. Overall survival (OS) was calculated from the date of diagnosis to the date of death or last follow-up. Median values and life tables were computed using the product-limit estimate by the Kaplan-Meier method, employing the log-rank test to assess statistical significance of the observed differences.

Results: Far Western blotting validated the interaction of PBK protein with GBP1. A clear signal in correspondence with PBK was detected with anti-GBP1. Progression of disease occurred in 81 cases (36.9%) and disease-related death in 139 women (63.1%). The patients with higher expression levels of GBP1 had a median survival of 42 months compared with 81 months in the population characterized by low levels of GBP1 (P = 0.01, Fig. 1A). Patients with increased levels of PBK also exhibited a poorer prognosis compared with cases with lower
expression, but the difference did not reach statistical significance (P = 0.11, Fig. 1B). The double-positive patients (GBP1+/PBK+) had significantly shorter median OS (38 months) compared to single-positive (GBP1+/PBK-; GBP1-/PBK+; OS = 58 months) and double-negative cases (91 months) (P = 0.008, Fig. 1C).

Conclusions: PBK is functionally associated with GBP1. PBK seems to have a significant role in mediating the aggressive phenotype of ovarian cancer; in fact, the concomitant overexpression of both GBP1 and PBK was associated with a poorer prognosis in the investigated cohort of patients.

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330 — Poster Session
The ratio between type 1 and type 2 tumor-associated macrophages predicts prognosis in patients with locally advanced cervical cancer receiving chemoradiation
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Objectives: We investigated the prognostic role of the pretreatment ratio between type 1 (M1) and type 2 (M2) tumor-associated macrophages (TAMs) in locally advanced cervical cancer (LACC) patients treated with chemoradiation (CT/RT). Methods: Eighty-four consecutive LACC patients were accrued at the Gynecologic Oncology Unit, Catholic University, Rome and Campobasso, Italy. All women received cisplatin-based chemotherapy and concomitant external radiotherapy to the whole pelvic region for a total dose ranging from 39.6 to 50.0 Gy. Clinical responders underwent radical surgery. Double-labelling immunohistochemistry of CD163, pSTAT1, and PBK was associated with a poorer prognosis in the investigated cohort of patients.

Results: In the overall series, the median number of M1 and M2 was 4 (range, 0–21) and 5 (range, 0–33), respectively, with a median M1/M2 of 0.60 (range, 0.01–19.2). Using median M1/M2 as the cut-off value, we did not observe differences in terms of age, FIGO stage, nodal status (radiologic evaluation), and tumor histotype between women with high and low M1/M2 levels. Complete pathologic response (absence of residual tumor) to CT/RT was observed in 22 cases (55.0%) with high M1/M2 and in 13 patients (29.5%) with low M1/M2 (P = 0.026). Cases with high M1/M2 had a longer 5-year DFS (73.9% vs. 48.3%, P = 0.023) and 5-year OS (67.2% vs. 44.3%, P = 0.019) compared to cases with low M1/M2. Multivariate analysis, after correction for age, FIGO stage, nodal status, and pathologic response, confirmed the independent prognostic role of M1/M2 in the presented series (X2 = 5.550, P = 0.018).

Conclusions: Polarization of TAMs toward an M2 phenotype, expressed as a reduced M1/M2 ratio, is associated with poor response to CT/RT and unfavorable prognosis in term of DFS and OS.

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331 — Poster Session
Therapeutic targeting of c-Met in ovarian clear cell carcinoma
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Objectives: Recent reports revealed that c-Met activation is specifically associated with ovarian clear cell carcinoma (CCC) and poor prognosis. In this study, we investigated c-Met expression and the effects of its therapeutic targeting in ovarian CCC.

Methods: Expression levels of c-Met in CCCs, serous carcinomas, and normal ovarian tissues were evaluated using real-time polymerase chain reaction. To test c-Met inhibitors in cell lines, including ES2, RMG1, RMG2, OVISE, and OVSASHO, we performed an in vitro experiment that included MTT and apoptosis assay. We performed Western blots to evaluate c-Met expression and the downstream pathway. In addition, we performed in vivo therapy experiments in orthotopic CCC mice with RMG1 and patient-derived xenograft (PDX, Avatar) models of ovarian CCC to confirm these effects.

Results: The c-Met expression was significantly increased in CCCs compared with serous carcinomas and normal ovarian tissues (P < 0.05). Ovarian CCC cells treated with c-Met inhibitor (SU11274, Crizotinib) demonstrated significantly decreased cell viability and increased apoptosis. Western blot assay showed that the protein expressions for the c-Met signaling pathway were decreased by the c-Met inhibitor. Moreover, significant decrease of tumor weight was observed in both in vivo models that received SU11274 treatment compared with control (P < 0.05).

Conclusions: These results show that c-Met inhibitor has significant antitumor effects in ovarian CCC and suggest that c-Met could have the potential for providing a novel therapeutic for ovarian CCC.

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332 — Poster Session
Antibody fragments targeting the tumor marker mesothelin selectively deliver TRAIL therapeutics and cause efficient ovarian cancer cell death
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Objectives: Recent studies have identified mesothelin (MSTN) as an exciting target for ovarian cancer therapy. MSTN is present on the surface of ovarian cancer cells and is associated with aggressive tumor behavior. We have previously shown that MSTN is a potential target for therapeutic antibody therapies. In the current study, we aimed to investigate the potential of antibody fragments targeting MSTN to deliver TRAIL and cause efficient ovarian cancer cell death.

Methods: We used a panel of tumor cell lines and xenograft models to determine the effect of antibody fragments targeting MSTN on ovarian cancer cell viability. We also evaluated the ability of these antibody fragments to deliver TRAIL and induce apoptosis in ovarian cancer cells.

Results: We found that antibody fragments targeting MSTN were able to selectively deliver TRAIL to ovarian cancer cells, resulting in efficient cell death. These results suggest that antibody fragments targeting MSTN may have potential as a novel therapeutic approach for ovarian cancer.

Conclusions: These findings indicate that antibody fragments targeting MSTN may be a promising strategy for the treatment of ovarian cancer.

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Objectives: Efficient delivery of biologic cancer therapeutics remains a challenge in ovarian cancer research. TRAIL is a member of the tumor necrosis factor superfamily that induces apoptosis. TRAIL requires trimerization, and a functional soluble form cannot be produced from monomeric cDNAs (TR1) in mammalian cells. We studied the consequences of adding single-chain antibody fragments (scFvs) to TR1 cDNAs with the goal of enhancing cancer therapeutics.

Methods: We generated scFv-TR1 fusion proteins targeted against mesothelin (SSTR1) and an irrelevant mouse antigen (TTR1). The parental TR1 served as a control. Protein production was confirmed by Western blot. Functional assessments were performed using cell viability assays. For drug testing, we used Jurkat cells engineered to express human mesothelin (J-Meso) and their wild-type counterparts (J-WT) as well as an ovarian cancer cell line that expresses tumor marker mesothelin (OVCAR3).

Results: Differential killing of mesothelin-positive cells was observed, depending on the scFv. While TR1 was constitutively active on Jurkat cells (40% cell death), regardless of mesothelin receptor status, SSTR1 was only active on J-Meso cells (40% cell death) and nearly completely inactive on J-WT (1% cell death) (Fig. 1B and C). Furthermore, SSTR1 selectively eliminated the mesothelin-positive population from the mixed cell pool (Fig. 1C, inset). A similar trend was observed in mesothelin-expressing OVCAR3 cells. SSTR1 killed nearly 90% of the cells, while TTR1, which has no scFv-mediated affinity for the OVCAR3 cells, was only modestly effective (30% cell death) (Fig. 1D).

Conclusions: A limitation of TRAIL-based therapies is lack of efficiency. Antibody fragments targeting tumor-associated antigens can deliver pro-apoptotic death signals selectively to the cancer cells. TR1 cannot be produced from mammalian cells, but the incorporation of scFvs allowed for bioactivity. SSTR1 displayed favorable drug characteristics, including tumor-selective delivery with enhanced activity of a membrane-tethered TRAIL drug. Our data support biomarker-targeted TRAIL therapy but also highlight the difficulty in predicting functional consequences of TR1-based drug design. Molecular modifications can lead to functional alterations that need experimental verification.

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334 — Poster Session
Proteomic analysis of cisplatin resistance in the ovarian cancer line CaOv3
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Objectives: Our current understanding of endometrial gland morphogenesis is limited. Regulation of this complex process has been implicated not only in carcinoma formation, but also in many other processes involving female reproductive disorders. Sox17, a transcription factor, is known to interact with β-catenin and decrease Wnt target gene expression. Sox17 is dysregulated in many cancer types and through recent The Cancer Genome Atlas data analysis has been shown to be mutated or altered in a significant number of human endometrial cancers. We hypothesize that Sox17 is involved in endometrial gland formation and is overexpressed in human endometrial cancer samples.

Methods: Using conditional knockout mouse, we generated models for deletion of Sox17 in both the epithelial and stromal compartments and in just the epithelial compartment. We characterized glandular formation during early developmental time points, postnatal days (PND) 9 and 12, and in sexually mature mice. Lef-1, Wnt7a, and Foxa2 gene expression was measured in murine samples. Using human endometrial cancer samples, we measured Sox17 expression via real-time polymerase chain reaction.

Results: The epithelial and stromal Sox17-deleted mice produced few to no endometrial glands, while the epithelial-only Sox17-deleted mice produced endometrial glands in limited numbers compared to wild-type mice. Examining the dual compartment-deleted Sox17 mice, Lef-1 gene expression was decreased beginning on PND 12, as was Foxa2 gene expression (P < 0.01). Wnt7a expression was elevated beginning on PND 12 (P < 0.001). These relationships continued through PND 28. Human endometrial cancer specimens demonstrated increased Sox17 gene expression when compared to noncancer controls (P < 0.015).

Conclusions: Epithelium-specific Sox17 disruption resulted in relatively normal gland formation, while the dual compartment Sox17-deleted mice produced few to no endometrial glands, suggesting a side population of Sox17-positive stromal cells to be responsible for gland formation. Human endometrial cancer samples overexpress Sox17. Sox17 appears to play a role in endometrial gland formation and endometrial carcinogenesis.

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333 — Poster Session
The role of Sox17 in endometrial gland formation and carcinogenesis
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The role of Sox17 in endometrial gland formation and carcinogenesis

A. Guimaraes-Young, T. Neff, A. Dupuy, M.J. Goodheart. University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Objectives: Epithelial ovarian cancer causes more deaths in the United States than any other gynecologic cancer. Currently, there are limited therapeutic options for patients who develop chemoresistance to standard of care agents outside of clinical trials. Furthermore, there are no reliable biomarkers to predict or monitor development of chemoresistance. Differences in chemosensitive and chemoresistant disease are being investigated using an integrated systems biology approach to better direct future therapy and identify patients who would benefit from variations in therapy.

Methods: A cisplatin-resistant epithelial ovarian cancer cell line (CaOv3-CP) was generated through exposure of CaOv3 to sequentially increasing doses of cisplatin. Protein lysates for each cell line were prepared, resolved by 1D polyacrylamide gel electrophoresis, digested in-gel with trypsin, and analyzed by liquid chromatography-tandem mass spectrometry for peptide identification. Protein abundance measures were estimated by spectral counting and significance was determined through a Z-test.

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Results: Our quantitative proteomic analysis identified multiple differentially expressed enzymes in the cisplatin-resistant line from the aldo-keto reductase (AKR) superfamily. AKR B10 ($P = 2.72 \times 10^{-6}$), B15 ($P = 1.89 \times 10^{-3}$), C1 ($P = 1.40 \times 10^{-14}$), C2 ($P = 9.38 \times 10^{-21}$), and C3 ($P = 3.19 \times 10^{-3}$) were identified as significantly elevated in CaOv3CP compared to CaOv3. These enzymes are involved in NAD(P)H reduction of aldehydes and ketones and have a role in the metabolism of prostaglandins, retinoids, lipids, steroids, and carcinogens. Conclusions: We hypothesize that the increased abundance of this family of enzymes in the cisplatin-resistant ovarian cancer line represents a key potential target for development of therapy. Further characterization of these lines is planned, with focus on targeted inhibition of the AKRs and the cells’ response to cisplatin as well as interrogation of the mechanism of action of overexpression in chemoresistance.

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335 — Poster Session
Integrated genomic analysis of STIC-associated high-grade serous carcinoma
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Objectives: Many high-grade serous carcinomas (HGSCs) of the pelvis likely originate in the fimbriated portion of the fallopian tube. Serous tubal intraepithelial carcinoma (STIC) lesions are the putative precursor to HGSC and identifiable in ~50% of advanced-stage cases. To better understand the molecular etiology of HGSCs, we report a multicenter integrated genomic analysis of advanced-stage tumors with and without STIC lesions.

Methods: Fresh-frozen primary, untreated HGSCs were collected from 96 patients with stage IIC or IV disease at three academic centers. All patients had comprehensive processing of the fallopian tubes using the SEE-FIM protocol and pathology review by a specialty pathologist. The presence or absence of a STIC lesion in the distal fallopian tube was noted and cases without identifiable fallopian tube were excluded. Focal DNA somatic copy number alterations (SCNAS) were identified using the Affymetrix SNP 6.0 array and GISTIC 2.0 analyses. MicroRNA gene expression was quantified using the multiplexed nanoString nCounter digital microRNA assay. Gene expression was quantified using RNA sequencing after ribosomal depletion to a minimum depth of 20 million reads per sample. Unsupervised clustering and class comparison of the RNA sequencing data using the 9236 most variable genes identified 69 cases with and without STIC lesions.

Results: Nine women were enrolled and had samples collected on endometrial swabs at the time of surgery. After quality control measures, a mean of 75,663 sequences with 250 base paired-end reads were identified. Two specimens had inadequate read length, leaving seven specimens (three malignant, four benign) for analysis. A total of 3,478 different operational taxonomic units were identified. Overall, the most abundant phyla were Proteobacteria (52%), followed by Firmicutes (23%) and Bacteroidetes (10%). No differences between benign and malignant samples were found in alpha diversity (Shannon index). In the PCoA plot (based on unweighted UniFrac), the malignant samples clustered separately from the benign samples, suggesting diversity in the microbiota of both groups.

Conclusions: The endometrium contains a diverse microbial community. Differences in microbial communities between malignant and benign endometrium warrant further study.

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337 — Poster Session
Comparison of MISR2 expression in patient and successive passages of patient-derived xenografts of ovarian cancer
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Objectives: Müllerian inhibiting substance receptor type II (MISR2) is an attractive potential target for epithelial ovarian cancer (EOC) immunotherapy due to its high and relatively selective expression in EOC cells. There is growing interest in the use of patient-derived xenograft (PDX) models to test novel therapies, but little is known about the fidelity of MISR2 expression with serial passage of PDX tissue. To develop reliable models to allow preclinical testing of MISR2-targeted therapy, our objective was to compare the level of MISR2 expression in primary tumors and in successive expansions within PDX models.

Methods: PDX models were developed via the intraperitoneal injection of viable frozen tissues from consenting patients with ovarian, primary peritoneal, or fallopian tube cancers into mice and passaged. Tissue banked from human primary EOC was collected and analyzed via DNA microarray for MISR2 gene expression. Highly
expressing tumors were selected, and seven corresponding PDX models were chosen for RNA extraction. A two-step reverse transcriptase-polymerase chain reaction process was used to assess mRNA expression at various stages of tumor heterotransplantation: patient through late-passage PDX (defined as second to fourth generation). MISR2 protein expression was confirmed via immunohistochemistry (IHC).

Results: MISR2 mRNA expression ranged from 914.2 to 2.6 (ratio of MISR2 to RPL19 housekeeper expression levels) in all generations of the models with high expression. We observed that expression of MISR2 mRNA is preserved in successive passages within the PDX models. While expression varied from generation to generation, the variability did not exceed one order of magnitude from the primary tumor to the late-generation PDX. In addition, IHC demonstrated maintenance of consistent staining intensity within one scoring category within the stroma, cytoplasm, and nucleus among the PDX models and through multiple generations up to four passages.

Conclusions: Expression of MISR2 persists and remains stable throughout serial generations of PDX models. This further validates the fidelity with which tumor characteristics are maintained within PDX models relative to the primary cancer. Specifically, the finding of stable expression of MISR2 in PDX models supports their use as a reliable system to test novel therapies directed against MISR2.

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338 — Poster Session
A prospective phase 0 study on the effects of anesthetic selection on serum miRNA profiles during primary cytoreductive surgery for suspected ovarian cancer
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Objectives: To test if anesthetic selection alters serum miRNA profiles during primary cytoreductive surgery for suspected ovarian cancer.

Methods: This was a prospective phase 0 study of women with a new diagnosis of a pelvic mass and suspected ovarian cancer undergoing exploratory laparotomy and primary cytoreduction. Serum samples were drawn preoperatively, postoperative day 1, and postoperative day 3. miRNA was isolated directly from serum using Trizol prep. Sixty-eight microRNA targets were examined simultaneously from each sample in duplicate using the Firefly miRNA assay and normalized to let7i-5p, let7g-5p, and let7d-5p expression. A selection of patient sample in duplicate using the Firefly transcriptase-polymerase chain reaction process was used to assess mRNA expression at various stages of tumor heterotransplantation: patient through late-passage PDX (defined as second to fourth generation). MISR2 protein expression was confirmed via immunohistochemistry (IHC).

Results: MISR2 mRNA expression ranged from 914.2 to 2.6 (ratio of MISR2 to RPL19 housekeeper expression levels) in all generations of the models with high expression. We observed that expression of MISR2 mRNA is preserved in successive passages within the PDX models. While expression varied from generation to generation, the variability did not exceed one order of magnitude from the primary tumor to the late-generation PDX. In addition, IHC demonstrated maintenance of consistent staining intensity within one scoring category within the stroma, cytoplasm, and nucleus among the PDX models and through multiple generations up to four passages.

Conclusions: Expression of MISR2 persists and remains stable throughout serial generations of PDX models. This further validates the fidelity with which tumor characteristics are maintained within PDX models relative to the primary cancer. Specifically, the finding of stable expression of MISR2 in PDX models supports their use as a reliable system to test novel therapies directed against MISR2.

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339 — Poster Session
Sperm protein 17 is a novel biomarker for low grade serous ovarian adenocarcinoma
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Objectives: Sperm protein 17 (SP17) is expressed in fallopian tube epithelium and has been identified as a potential biomarker and therapeutic target in ovarian cancer. Our objective was to define the prevalence of SP17 protein expression in benign and malignant ovarian neoplasms.

Methods: Immunohistochemical staining with anti-SP17 antibody was performed on 407 ovarian specimens. The percent of cells staining positive was scored as 1+, 2+, or 3+, which corresponded to <5%, 5%–49%, and ≥50% of cells positive. The intensity of staining was scored as weak, moderate, or strong.

Results: A total of 191 serous neoplasms were stained: 6 serous cystadenomas, 14 low-malignant potential (LMP) serous tumors, 47 low-grade serous carcinomas (LGSCA), and 124 high-grade serous carcinomas (HGSCA). These specimens expressed SP17 in 5 (83%), 14 (100%), 25 (53%), and 19 (15%) specimens, respectively. Of the positive specimens, serous cystadenomas had 2 to 3+ SP17 expression in 100% of specimens and LMP serous tumors had 2 to 3+ expression in 11 (79%) specimens. Twenty-one (84%) of the LGSCAs were 2 to 3+ positive compared to 3 (16%) among HGSCAs (P = 0.0001). There was no significant difference in the intensity of staining across histologies. The 108 nonserous epithelial carcinoma specimens expressed SP17 in 5 (5%) specimens. Sex cord stromal tumors were positive in 2 of 2 (4%) and germ cell tumors were positive in 3 of 56 (5%) specimens.

Conclusions: Serous cystadenomas, LMP serous tumors, and LGSCA all highly express SP17. Expression is limited in HGSCA, other epithelial carcinomas, and nonepithelial ovarian neoplasms. SP17 expression is specific to low-grade serous ovarian carcinomas and its precursors and may have therapeutic and prognostic significance in this rare and challenging disease.

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Poster Session B
Sunday, March 29, 2015
340 — Poster Session
AKT survival signaling and phospho-AKT expression are associated with triple negative breast cancer development and clinical outcome
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**Objectives:** Triple-negative breast cancer (TNBC) is a heterogeneous disease. Unfortunately, because the underlying biologic characteristics of this disease are not well defined, the clinical management of patients with TNBC does not reflect this heterogeneity. Identification of a targetable therapeutic biomarker for TNBC has the potential to significantly improve outcomes. Here we evaluated AKT survival signaling and phospho-AKT (pAKT) expression as a therapeutic biomarker for TNBC.

**Methods:** Principal component analysis (PCA) was used to evaluate associations between the expression of the AKT survival-signaling pathway and pAKT protein, triple-negative phenotype, or survival from breast cancer using Affymetrix datasets composed of breast carcinomas from 794 patients. 1) Our institutional clinic-genomic database (HuRSTA genechip, n = 106), 2) The Cancer Genome Atlas (TCGA, U133A genechip, n = 344), 3) GSE45255 (U133A genechip, n = 94), and 4) GSE31448 (U133Plus genechip, n = 250) as well as breast cancer cells from the NCI60 drug screen database (U133Plus genechip, n = 250).

**Results:** Expression of the AKT survival-signaling pathway was associated with the triple-negative phenotype in primary breast cancers (mean PCA score, a summary measure of pathway expression: non-TNBC = 2.32; TNBC = 2.32, P < 0.0001) and cell lines (mean PCA: non-TNBC = 3.25; TNBC = −3.75). Analysis of gene expression data and AKT protein levels from TCGA indicated a correlation between AKT pathway and AKT protein expression (n = 344, P < 0.0003). Additional correlations were observed between AKT pathway expression and lymph node positivity (P = 0.04) and advanced-stage disease (P = 0.03). Further, AKT pathway expression was associated with overall survival in two datasets: n = 94, P = 0.002 and n = 250, P = 0.045. Targeted inhibition of the AKT resulted in decreased pAKT levels and increased sensitivity of TNBC but not non-TNBC cells to chemotherapy.

**Conclusions:** AKT survival signaling is associated with the triple-negative breast cancer phenotype and may influence overall patient survival. Our data suggest that AKT survival signaling may be an important determinant of chemoresistance in TNBC, representing an attractive therapeutic target.

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343 – Poster Session
What is the impact of distance from a comprehensive cancer center on survival in patients with cervical cancer?

Objectives: Current literature suggests that disparities exist for patients with gynecologic malignancies. Race, socioeconomic status, and distance from a high-volume hospital are risk factors that have been identified as barriers to compliance with National Comprehensive Cancer Network (NCCN) treatment guidelines. We sought to evaluate the potential impact on clinical outcomes in cervical cancer patients based on distance from our NCCN cancer center.

Methods: A retrospective cohort of cervical cancer patients from our cancer center was identified. Medical records were abstracted for demographics, clinicopathologic variables, treatment, and survival. Analyses both by quartiles and distance >100 and <100 miles from our institution were performed. Data were analyzed using Science Analysis System version 9.2.

Results: A total of 413 patients were identified. The median distance was 58.9 miles (range, 1.2–571 miles) from our cancer center. The majority of patients were white (262) and nonsmokers (240), had stage IB disease (162), were treated with surgery (243), and had squamous histology (308). Distance from the cancer center by quartile (<0 to 19.2 miles, >19.2 to 58.7 miles, >58.7 to 98.3 miles, >98.3 miles) suggested inferior outcomes for those living >100 miles away. Patients were divided into two strata: <100 and >100 miles. The strata were generally similar, although patients living further away were more likely to smoke and have early-stage tumors, while non-whites were more likely to live closer to the cancer center. Although neither progression-free survival (PFS) nor overall survival (OS) was statistically different, the median OS for patients >100 miles was less (65.9 vs. 97.0 months, P = 0.082). Non-white race appeared to confer both a higher risk for recurrence (HR = 1.59, 95% CI 0.76–3.31) and worse survival (HR = 1.57, 95% CI 0.80–3.08), although the difference was not statistically significant. Age, body mass index, and clinical stage did not significantly affect survival.

Conclusions: Although our data suggest that greater distance (>100 miles) from our cancer center was not associated with inferior PFS or OS, a difference was observed. This difference was most pronounced in non-white patients. Outreach efforts and utilization of navigators may help decrease the impact of geographic and racial disparities on outcomes.

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344 – Poster Session
Morbidity of triple modality therapy in the management of early stage cervical cancer
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Objectives: The purpose of this study was to retrospectively analyze patient compliance and rates of toxicities related to adjuvant chemoradiation (cRT) in a group of patients with early-stage cervical cancer treated with triple-modality therapy that included a type II or III hysterectomy.

Methods: In an institutional review board-approved retrospective review, patients with stage IA1 to IIA cervical cancer who underwent type II or III hysterectomy from 1995 to 2014 were identified at two academic institutions. All patients underwent type II or III hysterectomy followed by adjuvant cRT with single-agent platinum-based chemotherapy as determined by standard clinical care at that time and provider preference.

Results: A total of 116 patients who underwent a type II hysterectomy (n = 89) or type III hysterectomy (n = 27) and adjuvant cRT were identified with a median follow-up time of 52 months (range, 0–180 months). One hundred ten patients (95%) underwent external beam radiotherapy, 6 (5%) underwent intensity-modulated radiation therapy (median dose, 5040 Gy), and 36 (31%) received additional brachytherapy (median dose, 1500 Gy). Twenty-one of 116 (18%) patients had grade 3/4 treatment-related toxicities. Grade 3/4 gastrointestinal toxicities were the most common, affecting 10% of patients, followed by hematologic toxicities affecting 7% of patients. Grade 3/4 genitourinary complications were less common at 2%. There were no significant differences in grade 3/4 toxicities for patients treated with cRT when comparing potential patient predictor variables of age, disease stage, risk category, and tumor size (Table). Of the 94 patients who had documented completion times available, 92% completed cRT in <56 days, with a median treatment time of 41 days. Five cases had incomplete adjuvant treatment: four due to patient noncompliance and one because of neutropenic fever just 2 days short of completion of external beam radiation therapy. Two cases of treatment delays were related to grade 3 hematologic toxicities.

Rates of Grades 3–4 toxicities (per CTCAE v4.03 guidelines)

<table>
<thead>
<tr>
<th>Toxicities</th>
<th>Hematologic</th>
<th>Other (fatigue, skin)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2/116 (1.7%)</td>
<td>1/116 (0.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td>4 (3.6%)</td>
<td>1 (1.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>Stage</td>
<td>6 (9.2%)</td>
<td>1 (1.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Risk category</td>
<td>2 (3.8%)</td>
<td>2 (3.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Tumor size</td>
<td>5 (10.9%)</td>
<td>1 (2.2%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: A model using preoperative tumor size on MRI and SCC Ag level is highly predictive of microscopic parametrial invasion in patients with FIGO stage IB cervical cancer. However, the criteria for parametrial invasion may differ according to menopausal status.

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Conclusions: Triple therapy with single-agent platinum-based cRT for early-stage cervical cancer is overall well tolerated when stratified across various patient factors. Additional studies on patient comorbidities as well as long-term adverse effects may help to elucidate any subgroups at higher risk for toxicities or treatment noncompliance. Collectively, this information can be used to better inform patients about expected toxicities.

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345 — Poster Session
Comparison of FLT- and FDG-PET in gynecological cancers
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Objectives: Little is known about the utility of F-18-fluorothymidine (FLT) positron emission tomography (PET)/computed tomography (CT) in the evaluation of gynecologic cancers. This pilot study had two objectives: 1) compare metabolic parameters, i.e., standard uptake values (SUVs) and metabolic tumor volume (MTV) of FLT with F-18-fluorodeoxyglucose (FDG) PET in five patients with cervical cancer and one patient with vaginal cancer at diagnosis, and 2) assess if FLT uptake values are affected by inflammation immediately following external beam radiation therapy (EBRT).

Methods: Six patients treated for cervical (5) or vaginal (1) cancer underwent FLT-PET and FDG-PET scanning at diagnosis. Five underwent FLT-PET within 1 to 2 weeks after EBRT (and concurrent chemotherapy) before brachytherapy. Wilcoxon rank sum test was used to compare the FLT and FDG parameters.

Results: The median age at diagnosis was 61 years (range, 33–72 years). Cancer stages were IB2 (n = 1, 17%), IIB (n = 1, 17%), IIIB (n = 2, 33%) and IVA (n = 2, 33%). The most common histology was squamous cell carcinoma (n = 3, 50%), followed by adenocarcinoma (n = 2, 33%) and clear cell adenosquamous (n = 1, 17%). The median SUVmax at diagnosis was 7.8 on FLT-PET (range, 3.9–14.2) vs. 11.6 (range, 5.9–23.2) on FDG-PET (P = 0.15). The median MTVs were 33.0 (range, 11.0–76.7) and 31.7 (range, 15.4–62.2) (P = 0.31), respectively. In four of five patients who underwent FLT PET after EBRT, SUVmax of FLT declined moderately to markedly, i.e., 54%, 70%, and 81% decline in 3 patients, complete resolution in 1 patient, and visually significant decline in 1 patient (values could not be obtained due to technical issues). The interval decrease in FLT-MTV could not be calculated in many of these patients because the SUV values were too low for edge detection, which, however, indicates good response to therapy.

Conclusions: Overall, the SUV of FLT was lower than that of FDG, although the difference was statistically insignificant, likely due to a small sample size. While it is well known that FDG uptake is generally increased during the early post-radiation therapy period due to inflammation making it less useful, FLT values in our patients significantly decreased after EBRT even within 1 to 2 weeks. These results likely indicate no significant effect of inflammation on FLT uptake. FLT may be a more sensitive tool when assessing the effects of EBRT on tumor and planning for post-EBRT brachytherapy treatments. Future studies with larger samples are warranted.

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346 — Poster Session
Outpatient laparoscopic radical hysterectomy
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Objectives: Radical hysterectomy has been shown to be safe and feasible. We report on outpatient laparoscopic radical hysterectomy (LRH).

Methods: We performed a retrospective review of 21 patients with early-stage cervical cancer who underwent outpatient LRH at the Instituto de Cancerología — Las Americas in Medellin, Colombia, between January and August 2014. Inclusion criteria were the ability to sign informed consent, living <1 hour traveling distance from hospital, having a caretaker at home, Eastern Cooperative Oncology Group (ECOG) score of 0, and American Society of Anesthesiologists score of 1. In addition, patients had to be younger than 60 years and have a body mass index (BMI) ≤ 30. Other inclusion criteria were completing surgery before 14:00, surgical time <180 min, estimated blood loss (EBL) <200 mL, hypogastric nerve spared at least on one side, availability of transversus abdominal plane (TAP) blockade, tolerance of oral intake within 4 hours of surgery, spontaneous voiding without bladder catheter, a score of <3 on the visual pain scale, and agreeable to discharge on same day of surgery.

Results: A total of 21 patients were included and all had FIGO stage IB1 disease. The median age was 43 years (range, 29–51 years) and the median BMI was 25 (range, 19–32). The most common histology was adenosquamous in 16 patients (76.3%). The median operative time was 140 minutes (range, 120–180 min) and the median EBL was 50 mL (range, 20–150 mL). No intraoperative or postoperative transfusions were given. There were no intraoperative complications. All patients underwent a TAP block immediately after surgery. Breakdown in the pain evaluation scale at discharge was: 14 patients (66.6%) reported 0/10, four patients (19.1%) reported 1/10, and 3 patients (14.3%) reported 2/10. All patients were able to void spontaneously and tolerate oral intake before discharge. There were no readmissions in the first 72 postoperative hours. The median node count was 19 (range, 8–38). All patients had negative margins and no parametral involvement. Postoperatively, one patient (4.7%) had one positive pelvic lymph node. The median follow-up was 9.4 months (range, 1.5–19.5 months). There are no relapses to date.

Conclusions: Outpatient LRH is feasible and can be performed safely in a developing country in well-selected patients and within proposed safety selection criteria.

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347 — Poster Session
Microarray analysis of vascular endothelial growth factor (VEGF)-dependent angiogenic biomarkers in squamous cell carcinoma (SCCA) and adenocarcinoma (AC) of the cervix
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Objectives: On August 14, 2014, the United States Food and Drug Administration approved bevacizumab for advanced cervical cancer based on Gynecologic Oncology Group (GOG) protocol 240, the randomized phase III clinical trial that demonstrated significantly improved overall survival with chemotherapy plus bevacizumab compared to chemotherapy alone. Although the signal for efficacy of bevacizumab was not observed in a subgroup analysis of prognostic factors for ACs, this histologic type comprised only 20% of the GOG 240 population. We sought to determine whether VEGF pathway biomarkers were differentially expressed between SCCA and AC of the cervix.

Methods: We retrospectively examined 244 cervical cancer cases profiled by CARIS for changes in gene expression by the Agilent microarray platform. Among the biomarkers studied were VEGFA ligand, VEGF receptors (VEGFR1, VEGFR2), the positive regulator of
the VEGF-dependent angiogenic pathway, hypoxia-inducible factor 1 alpha (HIF1α), and the negative regulator von Hippel-Lindau or VHL (involved in ubiquitination and degradation of HIF1α). The two-tail Fisher’s exact test was performed to test where proportions of positive results differed by subgroup (P ≤ 0.05). JMPv10.0 (SAS Institute Inc., Cary, NC) was used for statistical analysis.

**Results:** The median age for the 158 (65%) cases of SCCA was 47 years and that of the 86 (35%) ACs was 45 years. Overexpression of VEGFR1/VEGFR2 was not observed in either cell type (0-2%). Importantly, overexpression of the VEGF ligand was found in 72% and 68% of SCCA and AC, respectively (P = ns). HIF1α was overexpressed in 52% of SCCAs and 41% of ACs (P = ns). VHL was overexpressed in only 26% of SCCAs and 35% of ACs. Co-expression of HIF1α and VEGFα was present in 75% of both SCCA and AC cases.

**Conclusions:** These data suggest that biomarkers along the VEGF-dependent pathway of tumor angiogenesis are not differentially expressed between SCCA and AC of the cervix. Ligand binding and sequestration using the monoclonal antibody, bevacizumab, is likely to inhibit angiogenesis in women suffering from advanced SCCA or AC of the cervix. The extent to which pretreatment microarray analysis can guide therapy decisions requires further investigation.

**References:**

1. NCBI PubMed: 10.1016/j.ygyno.2015.01.351

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**448 — Poster Session**

**Paving the road to personalized medicine in cervical cancer: Theranostic biomarker evaluation in a 592-specimen library**

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**Objectives:** The results from Gynecologic Oncology Group protocol 240, that chemotherapy plus bevacizumab significantly improves overall survival over chemotherapy alone among women with advanced cervical cancer, represents a proof of concept of the potential for antiangiogenesis therapy and the value of systemic therapy in this disease. To identify patients likely to derive the greatest benefit from angiogenesis blockade and non-platinum chemotherapy, predictive biomarkers are required and predicated on theranostics, the emerging field through which developing technologies and capabilities in the diagnostic sector can be applied to pharmacogenomics and personalized medicine.

**Methods:** We interrogated a database of theranostic biomarkers from the CARIS repository and evaluated 592 specimens in the cervical cancer library by a combination of sequencing (NGS), gene amplification (ISH), and protein expression (IHC).

**Results:** NGS sequencing in 224 specimens identified mutational hotspots corresponding to PI3KCA (26%), BRCA2 (21%), BRCA1 (10%), KRAS (10%), TP53 (10%), and FBXW7 (10%). Gene amplification of EGFR (11%, 20/174) and HER2 (8%, 32/395) was also observed. IHC studies were noteworthy for the following protein signatures: antiangiogenic death receptor 1 (PD1) tumor-infiltrating lymphocytes (65%, 53/82); overexpression of cMET (22%, 82/376); overexpression of estrogen receptor (20%, 118/590), progesterone receptor (8%, 48/589), and androgen receptor (4%, 22/578); gemcitabine-specific low RRM1 (44%, 256/538), topotaxel-related high TLE3 (27%, 256/537) and low TUBB3 (74%, 202/273), and pemetrexed-related low TS (48%, 256/537).

**Conclusions:** The August 14, 2014 United States Food and Drug Administration approval of bevacizumab for advanced cervical cancer constitutes a regulatory milestone that fulfills a high unmet clinical need. Our data support the inclusion of theranostic biomarkers to help guide therapy in clinical trials for patients who have progressed on antiangiogenesis therapy or who are considered otherwise incurable. Poly-ADP-ribose polymerase inhibition; MEK, cell cycle checkpoint, and PI3K/akt/mTOR pathway inhibitors; EGFR- and HER2-directed therapy; immunotherapy; hormonal therapy; and non-platinum chemotherapy may be suitable for study.

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**449 — Poster Session**

**Immediate radical trachelectomy versus neoadjuvant chemotherapy followed by radical trachelectomy for patients with stage IB1 cervical cancer with tumors ≥ 2 cm or larger: A literature review and analysis of oncological and obstetrical outcomes**

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10. **Centro Medico Docente La Trinidad, Caracas, Venezuela**

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

**Objectives:** Fertility preservation in patients with cervical cancer (>2 cm) remains an area of controversy. The goal of our study was compare the outcomes of patients with cervical tumor size >2 cm undergoing immediate radical trachelectomy with those of patients who underwent neoadjuvant chemotherapy (NACT) followed by surgery.

**Methods:** We performed a systematic literature review from January 1994 to January 2014 using the terms radical trachelectomy, vaginal, abdominal, laparoscopic, robotic, fertility preservation, fertility-sparing, tumor size, and cervical cancer. We reviewed each relevant article for information about patient and tumor characteristics, details of NACT, type of surgery, lymph node status, intraoperative and postoperative surgical outcomes, recurrences, deaths, and pregnancies. The results of the frequencies of the different variables were assessed using descriptive statistics.

**Results:** We found a total of 393 patients with cervical tumor >2 cm in size who attempted to preserve fertility. A total of 338 patients had immediate radical trachelectomy: abdominal radical trachelectomy (ART) in 200 patients, vaginal radical trachelectomy (VRT) in 99 patients, and laparoscopic radical trachelectomy (LRT) in 39 patients. The other 55 patients underwent NACT followed by radical trachelectomy. We found that fertility preservation was achieved in 79% of patients with tumor >2 cm who underwent primary ART and 89% of patients with tumors >2 cm who underwent NACT followed by radical trachelectomy. The overall pregnancy rate after NACT followed by radical trachelectomy was 32.7%. This pregnancy rate is greater than that previously reported for VRT (24%) or for ART (16.2%).

**Conclusions:** Caution must be exercised in offering VRT or LRT to patients with tumors >2 cm as a primary treatment, given the high

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risk of recurrence. NACT is associated with a pregnancy rate of 32.7% when compared to immediate radical trachelectomy. The oncologic results seems very similar between NACT followed by surgery and ART.

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350 — Poster Session
Cone biopsy can avoid overtreatment in stage IB cervical cancer patients
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Objectives: Clinical evaluation is not a reliable method to determine real tumor size of visible cervical cancer and is even less useful to evaluate deep stromal invasion (DSI). A clinically large tumor can ultimately present a small invasive component and warrant a more radical surgery than needed. The aim of this study was to evaluate whether an initial cone biopsy could avoid overtreatment of visible invasive stage IB cervical carcinoma.

Methods: Medical records of 170 patients who had undergone radical surgery for invasive cervical cancer between October 2009 and August 2014 were reviewed. Patients with invasive carcinoma diagnosed only by microscopy (IA1 or IA2), histology other than squamous cell carcinoma or adenocarcinoma, or incomplete medical records were excluded from the analysis. We tested the hypothesis that clinical management would be significantly affected if a cone instead of a regular biopsy had been performed in every single case before decision-making.

Results: Of the 170 patients, 99 were excluded from the analysis, and most of them (81%) had a cone biopsy before surgery. In 71 cases, treatment modality was defined based on clinical examination and simple cervical biopsy. Twenty-five patients presented clinically visible tumors up to 2 cm and underwent type B radical hysterectomy (RH) and pelvic lymphadenectomy. Pathology showed tumors with up to 3 mm DSI in five (20%) of those patients. This group would have a simple hysterectomy if a cone biopsy was performed. One patient (4%) had a tumor with more than 2 cm of DSI and would have had a type C1 RH. Of the 33 patients who had a type C1 RH based on clinical examination, four (12%) could have had a simple hysterectomy after a cone biopsy. Twenty-five patients (76%) would have had a type B RH and only 12% of those patients would have had the same treatment as planned based on clinical examination. Of the 13 patients with tumors bigger than 4 cm, 8 (62%) would have had type B RH once their DSI was less than 20 mm. Of all 71 patients, 59% would have had a less aggressive treatment if DSI was assessed through a cone biopsy as the guide for treatment decision.

Conclusions: Clinical examination can lead to overtreatment of visible stage IB cervical cancer patients. Cone biopsy can be an effective tool to guide a tailored procedure, and its actual impact should be further investigated.


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352 — Poster Session
Impact of positive peritoneal cytology on prognosis in patients with cervical cancer: A meta-analysis
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Objectives: The impact of positive peritoneal cytology on prognosis is controversial in cervical cancer. Thus, we performed a meta-analysis to determine its impact on recurrence and to investigate correlations between abnormal cytology and lymph node metastasis in cervical cancer.

Methods: We conducted a systematic literature review through July 2014. Odds ratio (OR) and 95% CIs were calculated by standard meta-analysis techniques with fixed-effects models, if there was no significant statistical heterogeneity across studies by using P. The utilization of EHR-based tools and other online health resources (OR 1.35, 95% CI 1.31–1.39, P < 0.001) and at least one primary care visit within the last 2 years (OR 2.85, 95% CI 2.76–2.95, P < 0.001) increased compliance.

Conclusions: We demonstrated that women who used online EHR-based tools and received care from female or gynecologic primary care providers had higher rates of cervical cancer screening compliance.


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351 — Poster Session
The use of electronic health record-based tools to improve cervical cancer screening compliance in a large community-based health care organization
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Objectives: To determine the significance of electronic health record (EHR) tools as well as patient and provider characteristics in association with cervical cancer screening compliance.

Methods: Patient demographic information, clinical data, and provider characteristics were extracted from the EHR of a large, diverse metropolitan group of insured patients in a nonprofit community medical group. Cervical cancer screening compliance was defined as having a Papanicolaou smear within the past 2 years. Hierarchical multivariate logistic regression models were used for statistical analyses.

Results: Of 174,926 women (41% non-Hispanic white, 30% Asian, 8% Hispanic, 1% black), the median age was 43 years (range, 21–65 years). A total of 1446 primary care providers were included in the sample: 56% were female, 90% were physicians, 14% were family medicine specialists, 12% internal medicine, 7% pediatrics, and 4% gynecology; 16% of providers had foreign language capability. There were no differences in compliance among the various racial groups, although analysis within Asian subgroups revealed that the Vietnamese patients had a higher compliance rate at 82% compared to 72% in the Asian Indians (P < .0001). Women receiving care from female vs. male providers were more likely to be compliant (odds ratio [OR] 1.48, 95% CI 1.38–1.59, P < 0.0001). Using internal medicine providers as a reference, patients cared for by gynecologists had a significantly higher rate of compliance (OR 2.22, 95% CI 1.77–2.8, P < .0001). There was no difference between family medicine vs. internal medicine providers (OR 0.98, 95% CI 0.92–1.05, P > 0.05). The utilization of EHR-based tools and other online health resources (OR 1.35, 95% CI 1.31–1.39, P < 0.001) and at least one primary care visit within the last 2 years (OR 2.85, 95% CI 2.76–2.95, P < 0.0001) increased compliance.

Conclusions: Hierarchical multivariate logistic regression models were used for statistical analyses.


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Conclusions: Although based primarily on retrospective observational studies, our meta-analysis indicated that abnormal peritoneal cytology may be strongly correlated with poor prognosis in patients with cervical cancer. Future research should verify this relationship through prospective observational studies over a longer term.

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353 — Poster Session
Cervical cancer epidemiology in former Soviet Union immigrants to Israel: A step towards solving the enigma
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Objectives: Cervical cancer is the second most common cancer in women worldwide, with more than 85% of the global burden occurring in developing countries. This can be partly attributed to early detection programs in high-resource countries. Curiously, cervical cancer incidence in Israel is persistently lower compared to other developed countries, despite the lack of a national screening program. Persistent oncogenic human papillomavirus (HPV) infection is obligatory for cervical cancer. Due to the sexually transmitted nature and geographic variance of the virus, an immigrant study can shed light on the environment's role in the etiology of this disease. Jews who immigrated to Israel from the former Soviet Union in the 1990s constitute a unique immigrant population of more than 1 million people at all ages and all health statuses who were collectively brought by the Israeli government and became equal citizens with public health services.

Methods: Crossing data from the national civil registry and the national cancer registration, we analyzed cervical cancer incidence in 342,581 immigrants compared with 1,140,912 matching Israeli-born Jewish women.

Results: Women who immigrated before the age of 12 years had significantly lower incidence (0.25% vs. 0.5%) and mortality rates (0% vs. 15.9%) compared to older immigrants. In a Cox regression analysis, the former was protective (HR 0.578) and the latter was hazardous (1.354) compared to Israeli-born women.

Conclusions: Women infected with HPV prior to immigration showed morbidity and mortality rates similar to their birth country. Thus, viral serotypes in Israel rather than ethnicity determine the incidence pattern of the disease.

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354 - Poster Session
Surveillance for recurrent cervical cancer: 10 years of Pap smears for cervical cancer survivors and not a single life saved by cytology
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Objectives: Recurrent cervical cancer is a grave diagnosis with a dismal prognosis, particularly for non-localized disease. Efforts to diagnose central recurrence may have merit, but the utility of cervical/vaginal cytology in meeting this aim is not clear. We hypothesized that routine cytology does not significantly alter the clinical course of cervical cancer survivors and, therefore, is not warranted.

Methods: Institutional review board approval was obtained and retrospective data collection performed on all-stage cervical cancer patients treated at our institution between 2003 and 2012. Patients who did not have at least one Papanicolaou (Pap) smear following therapy, failed to reach surveillance, or had fertility-sparing surgery were excluded. Patients with squamous cell carcinoma, adenocarcinoma, or adenosquamous histology were included.

Results: A total of 226 patients met inclusion criteria, 81% of patients were white, and the average age at diagnosis was 49 years (range, 22–83 years). Stage breakdown was: 70% stage I, 19% stage II, 10% stage III, and 1% stage IV. Seventeen percent had nodal metastases, and 38% were treated primarily with surgery. The median number of Pap smears per patient was 4.5. Eleven percent of Pap smears were unsatisfactory for evaluation, 18% were abnormal, and only 3% were atypical squamous cells of undetermined significance—cannot exclude high-grade squamous intraepithelial lesion (ASC-H) or worse. Forty-three percent of patients had at least one abnormal Pap smear, and 18% of patients had at least one colposcopy or biopsy as a result of an abnormal Pap smear. Four patients were treated for preinvasive disease diagnosed by abnormal cytology, none of whom developed a pelvic recurrence. At a median follow-up of 65 months, there were 33 recurrences; 15/33 (45%) of patients with recurrence had never had an abnormal Pap smear and 6/33 (18%) had localized disease. Five of the localized recurrences were associated with a visible or palpable lesion and vaginal bleeding; the remaining recurrence was diagnosed by computed tomography scan performed for pain. In one case, abnormal cytology led to imaging that showed non-localized disease in an asymptomatic patient who then received palliative chemotherapy.

Conclusions: Cytology is a poor modality for surveillance of cervical cancer. In this study, not a single curable recurrence was diagnosed by Pap smear. The most common symptom among women with curable pelvic recurrence was vaginal bleeding. A surveillance protocol consisting of history and physical examination alone for asymptomatic survivors is likely sufficient and safe.

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355 - Poster Session
Impact of smoking on survival among women treated with and without bevacizumab for advanced cervical cancer (CxCA): An NRG Oncology/Gynecologic Oncology Group study
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Objectives: Tobacco use is associated with worse survival in women with newly diagnosed, locally advanced CxCA. An important translational objective of Gynecologic Oncology Group protocol 240 was to evaluate the impact (if any) of smoking on survival among women with recurrent/persistent/metastatic CxCA treated with and without antiangiogenesis therapy.

Methods: A total of 452 women with advanced or recurrent CxCA were randomized to chemotherapy with and without bevacizumab. Patients completed a validated smoking questionnaire before treatment. Clinical and demographic data among smokers and nonsmokers were
compared using Pearson’s chi square test and the Wilcoxon test. Overall (OS) and progression-free survival (PFS) were estimated using the Kaplan–Meier method. The associations of smoking and of smoking + treatment (i.e., bevacizumab vs. no bevacizumab) with PFS and OS were evaluated with the Cox proportional hazards model.

Results: Smoking questionnaires were available for analysis in 99% of study participants. Two hundred eighty-six women (64%) were active or former smokers. In the entire study population, this group had significantly worse OS than never smokers (14.2 vs. 16.8 months, HR 1.29, 95% CI 1.03–1.61, P = 0.026). Smokers who received chemotherapy plus bevacizumab (n = 148, 52%) experienced significantly longer PFS (median 7.9 vs. 5.7 months, log-rank P < 0.001) and significantly longer OS (median 16.7 vs. 12.0 months, log rank P = 0.027) than smokers who received chemotherapy alone (n = 138, 48%). Overall response rate among smokers was 49.3% (chemotherapy plus bevacizumab) vs. 29% (chemotherapy alone) (P = 0.002). The median number of cycles of therapy in smokers vs. non-smokers (interquartile range, 4–10, smokers vs. 2–9, non-smokers) (P = ns). Smokers receiving bevacizumab experienced the following adverse events: grade 2 + fistula (16.2%), grade 3 + venous thromboembolism (9.5%), grade 2 + hypertension (27%), and grade 2 + proteinuria (2.7%). Cervical cancer was the reported cause of death in 74.5% of smokers.

Conclusions: Smoking is common and associated with a 29% increased risk of death among women with advanced or recurrent cervical cancer. The survival benefits conferred by antiangiogenesis therapy are sustained, even among smokers in this population. Smokers with CxCA should be informed of these results and efforts at smoking cessation strongly encouraged.

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356 - Poster Session
Neratinib, an irreversible pan-ErbB receptor inhibitor, is highly effective against primary cervical cancer cell lines harboring HER2/neu gene mutations
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357 - Poster Session
Evaluation for health care disparities in Hispanic and Non-Hispanic Whites with cervical cancer using National Cancer Database
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Objectives: Hispanic women (H) are the more likely than Non-Hispanic White women (NHW) to be diagnosed with cervical cancer. Data on access to care are limited. The National Cancer Database (NCDB) documents care provided to approximately 70% of the patients diagnosed in the United States annually. Our objective was to evaluate the database for potential disparities between these two groups.

Methods: NCDB was queried for all cervical cancers diagnosed from 2000 to 2011. Data reported on H and NHW were compared, including age and stage at diagnosis, socioeconomic status (percent without high school degree, median household income, and insurance status), management and access to care (distance traveled, first course of treatment, first-course surgery), and type of therapy (radiation and systemic treatment). “Days to treatment” were available only for 2011. Associations between race and other patient characteristics were analyzed via chi square testing, both overall and controlling for stage of disease at diagnosis.

Results: The study group consisted of 86,948 women, of whom 83% were NHW and 17% were H. H women tended to be younger at diagnosis (60% vs. 47% were <50 years of age), presented less often with stage I and stage IV disease, tended to come from areas with high percentages of people without high school degree, had lower incomes, and were more likely to have Medicaid or be uninsured (P < 0.0001 for all variables). Overall, H women had more days to treatment after diagnosis, with 26% having >46 days to treatment compared to 17% for NHW women.

Conclusions: Based on this large and highly reliable database, H women with cervical cancer appear to be economically disadvantaged and experience significant delay in initiation of therapy for cervical cancer. Long-term clinical correlation should be investigated.

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358 - Poster Session
Surgical, pathologic and survival outcomes of patients undergoing open, laparoscopic or robotic radical hysterectomy for invasive cervical cancer

Objectives: Radical hysterectomy (RH) for invasive cervical cancer can be performed both minimally invasively and by open technique. The aim of this study was to report on surgical, pathologic, and
Survival outcomes of patients undergoing RH by different surgical approaches.

**Methods:** We identified all patients who underwent RH for invasive cervical cancer at our institution between 01/2001 and 01/2013. Based on surgical approach, the patients were divided into three cohorts: RH completed by open technique (group A), RH completed laparoscopically (group B), and RH completed robotically (group C). Relevant surgical and pathologic findings were reported. Standard statistical analysis and Kaplan-Meier survival analysis were utilized.

**Results:** During the study period, 100 patients underwent RH at our institution. There were 41 patients in group A (41%), 33 (33%) in group B, and 26 (26%) in group C. The stage distribution between the groups was equal: group A: IA 20%, IB 73%, IIA 7%; group B: IA 27%, IB 67%, IIA 6%; group C: IA 19%, IB 73%, IIA 8%. The mean operating time in groups A, B, and C was 246, 293, and 296 minutes, respectively. The mean estimated blood loss was 530 mL in group A, 206 mL in group B, and 152 mL in group C. The mean number of pelvic lymph nodes removed was 21 in group A, 26 in group B, and 19 in group C. High-risk histologic features (positive margins, positive pelvic lymph nodes, or positive parametria) were present in 12% (5 patients) in group A, 6% (2 patients) in group B, and 4% (1 patient) in group C. After median follow-up of 47 months, the median overall survival (OS) for group A and group B was not reached. The median OS for group C was 84 months. The difference in OS was not statistically significant (P = 0.2659).

**Conclusions:** Surgical characteristics and pathologic findings are similar in patients with invasive cervical cancer undergoing RH by open, laparoscopic, and robotic approaches. Our limited survival analysis suggests similar survival outcomes among these cohorts of patients.

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**359 - Poster Session**

**Does use of uterine manipulator alter the rate of lymphovascular space invasion in patients with invasive cervical cancer undergoing radical hysterectomy?**

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**Objectives:** Lymphovascular space invasion (LVI) is a prognostic factor in cervical cancer and an important determinant in selecting postoperative adjuvant therapy. The purpose of this study was to investigate whether the use of a uterine manipulator alters the rate of LVI in patients undergoing radical hysterectomy (RH) for invasive cervical cancer.

**Methods:** We identified all patients who underwent RH for invasive cervical cancer between 01/2001 and 01/2013 at our institution. The use and type of manipulator were extracted from the operative record. Relevant demographic, clinical, and pathologic information were collected. The standard statistical tests were applied.

**Results:** During the study period, 100 patients underwent RH for invasive cervical cancer. The disease stage distribution was as follows: IA 22%, IB 71%, and IIA 7%. The majority of patients had squamous cell histology (58%), followed by adenocarcinoma (26%), and other histologies (16%). The mean operating time was 278 minutes. The mean estimated blood loss was 297 mL. The procedure was completed by open technique in 41% of cases. The remaining 59% of patients underwent minimally invasive RH: 33% laparoscopically and 26% robotically. The use of a uterine manipulator was documented in 42% of cases (42 patients): 17% robotically and 25% laparoscopically. We used the following manipulators: Humi 62% (26 patients), Rumi 31% (13 patients), Hulka 2% (1 patient), and unspecified 5% (2 patients). The rate of positive LVI in patients who underwent RH without use of manipulator was 43% (25/58 patients). In patients who underwent RH with use of a uterine manipulator, positive LVI was documented in 33% (14/42 patients). The difference was not statistically significant (P = 0.3228).

**Conclusions:** We did not find an association between the use of a uterine manipulator and LVI positivity in patients undergoing RH for invasive cervical cancer. These results may be used to counsel patients and may be helpful in the process of making a decision about the type of surgical approach.

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Objectives: Expression of the BCL2 antagonist of cell death (BAD) apoptosis pathway and phosphorylated BAD (pBAD) protein levels have been associated with cancer chemoresponsiveness in vitro. In this study, we evaluated the role of the BAD pathway in cervical cancer development, therapeutic response, patient survival, and as a therapeutic target.

Methods: Expression of the BAD pathway was measured in publicly available clinicogenomic cervical cancer datasets using a previously established principal component analysis (PCA)-based BAD pathway gene expression signature (BPGES). Further, siRNA depletion and pharmacologic inhibition of the BAD pathway kinases, AKT and PKA, and the BAD pathway phosphatase, PP2C, coupled with MTS cell survival assays were used to determine the influence of pBAD protein levels on chemosensitivity in a panel of cervical cancer cell lines. A non-targeting siRNA duplex was used as a control. Depletion of the target protein was confirmed by Western blot analysis.

Results: BAD pathway expression (quantified by the BPGES) was associated with cervical cancer development (n = 38, P < 0.005) and incomplete response to platinum-based therapy (n = 21, P = 0.001). Further, primary cervical cancer samples with high BAD pathway expression showed significantly decreased survival rates (n = 300, P < 0.0003). Treatment of cervical cancer cells with the AKT inhibitor MK2206 resulted in decreased pAKT expression as well as levels of the BAD pathway phosphatase, PP2C, coupled with MTS cell survival assays were used to determine the influence of pBAD protein levels on chemosensitivity in a panel of cervical cancer cell lines. A non-targeting siRNA duplex was used as a control. Depletion of the target protein was confirmed by Western blot analysis.

Conclusions: The BAD pathway and pBAD protein status are associated with cervical cancer development, therapeutic response, and patient survival. Targeted inhibition of the BAD pathway influences cervical cancer cell sensitivity to chemotherapy via modulation of the phosphorylation status of the BAD protein. The BAD pathway is a potential future therapeutic target to enhance cisplatin sensitivity.

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363 - Poster Session
Investigation of the timing of neoadjuvant chemotherapy on survival in advanced stage ovarian cancer
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Objectives: Studies have suggested that a shorter time interval from surgery to adjuvant therapy in ovarian cancer patients may improve survival. However, there is limited evidence about the timing of neoadjuvant chemotherapy (NACT) and its prognostic significance. Our primary objective was to investigate the impact of the time interval from NACT completion to surgery and surgery to adjuvant chemotherapy on survival outcomes.

Methods: All patients with advanced-stage ovarian or peritoneal cancer who received NACT in the Division of Gynecologic Oncology at the Cleveland Clinic and subsequently had interval debulking surgery were identified from 2003 to 2013. Kaplan–Meier survival curves and Cox proportional modeling were performed.

Results: A total of 116 patients were included, all of whom received a platinum-based NACT regimen. The median number of cycles was 4 (range, 2–16). Optimal cytoreduction was achieved in 85% of patients. The median time from NACT completion to surgery and from surgery to adjuvant chemotherapy was 31 days (range, 15–219 days) and 30 days (11–58 days), respectively. We showed an improvement in progression-free survival (PFS) when the time between NACT and surgery was >27 days (34.5 vs. 17.9 months, P = 0.0041), but there was no statistically significant difference in overall survival (OS) (P = 0.0579). On multivariate analysis, the timing of NACT failed to affect PFS (P = 0.3083) or OS (P = 0.8370). In addition, the time interval from surgery to adjuvant therapy in patients who had received NACT did not affect PFS (P = 0.0985) or OS (P = 0.8592). On multivariate analysis.

Conclusions: In our study, the timing of NACT in relation to surgery and adjuvant chemotherapy did not appear to have an impact on PFS or OS on multivariate analysis. This suggests that these time intervals

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may be tailored to best accommodate patient-specific considerations without considerable impact on survival.

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364 - Poster Session
Outpatient rapid desensitization for gynecologic oncology patients with moderate to severe hypersensitivity reactions to platinums
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Objectives: Half of platinum (carboplatin and cisplatin) hypersensitivity reactions (HSRs) are considered moderate to severe. Most published desensitization protocols were implemented in the inpatient settings. The objective of this study was to assess the safety and efficacy of outpatient rapid desensitization in gynecologic oncology patients with a history of moderate-to-severe HSRs to platinums.

Methods: A retrospective chart review was performed in gynecologic oncology patients with moderate-to-severe HSRs to platinums from January 2011 to June 2014. Moderate HSRs were defined as any symptoms with transient cardiovascular, respiratory, or central nervous system (CNS) involvement. Severe HSRs were defined as any symptoms with sustained cardiovascular, respiratory, or CNS involvement. Patients with mild reactions to platinum were excluded. Desensitization protocols involved premedication with antihistamines and corticosteroids followed by one-solution, 16-step titration of platinum (4.25 hours for carboplatin and 5.25 hours for cisplatin). The desensitizations were performed either in infusion center (OP-IC) or outpatient acute care observation beds (OP-AC). The primary end point was the rate of successful administration of each course of platinums in the outpatient setting.

Results: Twenty-three eligible patients were identified. Twelve patients had initial moderate HSRs and 11 patients had initial severe HSRs. All patients successfully completed 133/139 (95.7%) desensitization courses in the outpatient setting. The success rates of desensitizations conducted in OP-IC and OP-AC were 91/96 (94.8%) and 42/43 (97.7%), respectively. Of the 139 desensitization courses, 91 (65.5%) induced no reactions, 32 (23.0%) induced mild reactions, and 14 (10.1%) induced moderate reactions, with only 2 (1.4%) inducing severe reactions. Only two patients did not complete desensitizations due to moderate/severe reactions. There were no life-threatening reactions during desensitizations. All symptoms were managed successfully with antihistamines and corticosteroids without the use of epinephrine.

Conclusions: Outpatient rapid 16-step desensitization appeared safe and effective for patients with moderate-to-severe HSRs to platinums. Severe breakthrough reactions are less common.

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365 - Poster Session
Long-term follow-up of a phase II trial of multimodal therapy given in the “sandwich” method for stage III, IV, and recurrent endometrial cancer
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Objectives: 1) To determine updated progression-free survival (PFS) and overall survival (OS) following completion of a phase II study of multimodal therapy for advanced and recurrent endometrial cancer and 2) To assess long-term lymphedema rates associated with the protocol.

Methods: Women with newly diagnosed advanced-stage endometrial cancer or recurrent disease were recruited from 9/2004 and 6/2009 in our previously published phase II study. Patients received three cycles of intravenous docetaxel (75 mg/m²) followed by carboplatin AUC = 6 every 3 weeks for 3 cycles before and after radiation therapy. Radiation therapy involved 4,550 cGy to the pelvis; paraaortics, if involved, received 43 to 45 Gy. Volume of irradiation depended on extent of disease found at the time of surgery or recurrence. A retrospective medical chart review was conducted in June 2014 to update patient outcomes. Clinical data abstracted included lymphedema, disease progression and site, and death. OS and PFS estimates at 5 years were calculated using Kaplan-Meier methods.

Results: Of 41 patients enrolled, 10 (24%) had stage IIIA and 21 (51%) had stage IIIC disease; 32 (78%) had endometrioid histology; 35 (85%) completed the protocol; and 1 patient was lost to follow-up. Patients have now been followed for a median of 5 years (range: 0.5-9.6 years). Of all patients enrolled, 15 have died since the start of treatment. The Kaplan-Meier estimate and 95% CI for OS at 5 years was 0.70 (0.53, 0.82). Eleven patients had persistent or recurrent disease during follow-up, two of whom had local disease (one persistent pelvic disease; one local and distant recurrence). After excluding the two patients who enrolled at recurrence, 15 of the 39 patients progressed or died during follow-up. The Kaplan–Meier estimate and 95% CI for PFS at 5 years was 0.66 (0.48, 0.78). Fifteen patients (37%) had documented lymphedema during the follow-up period.

Conclusions: OS and PFS estimates remain high and in-field recurrences low following “sandwich” therapy. The 5-year median follow-up is the longest reported to date. These data suggest that the sandwich method remains an efficacious treatment option for women with stage III-IV or recurrent endometrial cancer. However, lymphedema rates were not insignificant and deserve further attention when deciding on treatment for women with advanced endometrial cancer.

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366 – Poster Session
Minimally invasive interval debulking surgery in AEOC: Preliminary results from the MISSION trial
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Objectives: To assess the feasibility and early complications rate of minimally invasive interval debulking surgery (MI-IDS) in stage III-IV epithelial ovarian cancer (EOC) patients after neoadjuvant chemotherapy (NACT).

Methods: This is a phase II prospective multicentric study (NCT-ID pending, MISSION trial) in women with advanced EOC (AEOC) cancer who had clinical complete/partial response (cCR/cPR) after NACT, according to Gynecologic Cancer Intergroup and Response Evaluation Criteria in Solid Tumors criteria. Institutional review board approval was obtained and all patients signed a written informed consent to be included in the protocol. Enrolled cases were preliminarily submitted to S-LPS to confirm preoperative findings and to be eligible for minimally invasive surgery. Surgical procedures included adhesiolysis; bilateral salpingo-oophorectomy; radical hysterectomy; radical omentectomy; and selective pelvic, parietal, and diaphragmatic peritoneectomy. Pelvic and aortic lymphadenectomy were not considered as standard procedures in these cases. Intra- and post-operative outcomes were registered.

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**Results:** From December 2013 to August 2014, 18 women met inclusion criteria and were enrolled in the study. In 16 of 18 (89%) cases submitted to S-LPS, we judged complete MI-IDS feasible. Median age was 58 years (range, 42–81 years) and median body mass index was 25 (range, 22–31). Median cycles of platinum-taxol NACT were 4 (range, 3–7); six patients (37.5%) received bevacizumab. Median operative time was 250 min (range, 81–428 min) and median estimated blood loss was 112.5 mL (range, 50–500 mL). The vast majority of patients (12/16 [75%]) were discharged on postoperative day 2. At definitive histologic diagnosis, microscopic residual disease was diagnosed in 15 patients (94%) at the level of the ovaries (100%), the omentum (69%), and peritoneum (53%). No conversions to laparotomy or intra- and early postoperative complications were registered. All patients started chemotherapy within 4 weeks of surgery and 10 patients have successfully completed the cycles. With a median follow-up of 5 months (range, 1–7 months), no recurrences have been observed.

**Conclusions:** MI-IDS seems feasible and safe in patients with cCR/cPR to NACT. A larger number of patients and a longer follow-up time are needed to confirm these data and definitively assess the prognostic impact of such an approach.

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**368 — Poster Session**

**Intra-operative handoffs and postoperative complications among gynecologic oncology patients**

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**Objectives:** Health care personnel handoffs have been associated with increased complications but rarely have been studied in surgery. Gynecologic cancer surgeries can be long and may include operating room personnel changes. We examined the association between personnel handoffs and surgical complications in major gynecologic cancer surgery.

**Methods:** A random sample of major gynecologic cases at a tertiary care academic center from 2010 to 2012 was identified from operating room software and linked to billing claims and the medical record. Cases were grouped by start time, case order and number of handoffs between anesthesia, nursing, and scrub tech staff. Demographic, procedural, and surgeon variables were included in multivariate modeling, with a primary outcome of 30-day postoperative complications. Bivariate and multivariate modeling was used to explore the relationship between handoffs and complications.

**Results:** We identified 666 major gynecologic cases: 50% via laparotomy, 49% via minimally invasive surgery, and 1% groin surgery. The median number of comorbidities was four (interquartile range, 2–6), with hypertension, cardiac, neuropsychiatric, and diabetes being the most common. The postoperative complication rate was 35.7%. Complications were: infectious (21%), gastrointestinal (12%), hematologic (8.7%), and electrolyte/nutrition (7.6%). Patients with postoperative complications had longer median case length (161 vs. 146 min, \(P = 0.004\)), more laparotomies (70% vs. 40%, \(P < 0.0001\)), and more comorbidities (6.4 vs. 3.5, \(P < 0.0001\)). There were no differences in case start time (AM vs. PM) and number of anesthesia, nursing, and scrub tech staff. On bivariate analysis, the number of scrub tech handoffs was significantly higher in the postoperative complication group (\(\geq 1\) handoff: 62.2% vs. 47.8%, \(P = 0.003\)). In a multivariate model controlling for age, comorbidity, procedure, case length, and case order, \(\geq 1\) scrub tech handoff remained associated with postoperative morbidity (OR 1.48, 95% CI 1.01–2.17).

**Conclusions:** Most surgical system variables, including anesthesia and nursing personnel changes, do not have an impact on postoperative patient outcomes. However, change of scrub tech is associated with postoperative complications, perhaps due to infectious exposure and/or impact on group performance as they work directly with the surgical team.

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369 — Poster Session
Cancer-related fertility education in women at a public rural institution
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Objectives: Cancer-related fertility education is an emerging unmet need for cancer patients. This study sought to characterize the current physician and nursing practice and female patient interest in cancer-related fertility education and to determine providers’ barriers in delivering education.

Methods: A multidisciplinary team developed three surveys to evaluate patients, nurses, and physicians. The institutional review board authorized the surveys as exempt. Women ages 18–45 years diagnosed with cancer in the previous 2 years were eligible. All oncology physicians and nurses received electronic surveys via Survey Monkey®.

Results: Seventy-one eligible patients ages 19–45 years completed the survey (Fig. 1A), and 77 providers participated. Forty-nine percent of patient participants received education on the risk of cancer treatment to fertility, and 32% received fertility preservation (FP) education. Forty-two percent of patients were interested in discussing their fertility, learning FP options, or receiving fertility referral and counseling. Of the 52% interested, 65% received education on the risk of cancer treatment to fertility and 43% received FP education. Of the 48% not interested, 68% did not receive education on the risk of cancer treatment to fertility and 79% did not receive FP education. Eighty-three percent of participants were aware of cancer treatment risk on fertility and 52% were aware of FP options. Seventy percent of patients who were unaware of the risk of cancer treatment on fertility did not receive education and 74% unaware of FP options did not receive education. Of the surveyed providers, 41% of nurses and 64% of physicians felt comfortable discussing FP options with patients and 85% of nurses and 52% of physicians felt they needed more information on FP options. Providers indicated patients’ ability to afford FP treatment at the greatest barrier to education (Fig. 1B).

Conclusions: The majority of patient participants did not receive comprehensive fertility education. Education and general awareness may influence a patient’s interest in cancer-related fertility issues. Providers need cancer-related fertility education to improve their ability to address these topics. Education efforts should be improved to insure that all women of child-bearing potential receive education at time of cancer diagnosis.

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370 — Poster Session
Gemcitabine and docetaxel compared to radiation or other chemotherapy regimens as adjuvant treatment for stages I–IV uterine leiomyosarcoma
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Objectives: For women with leiomyosarcoma (LMS), adjuvant therapy is often considered. However, few trials have documented active agents in this setting. A phase III Gynecologic Oncology Group trial failed to show improved progression-free (PFS) or overall survival (OS) in patients randomized to doxorubicin or observation. Gemcitabine and docetaxel (Gem/Tax) were also evaluated, but there was no control arm. Our objective was to compare survival outcomes among patients with uterine LMS who received Gem/Tax compared with other adjuvant chemotherapy (CT) or radiation (XRT).

Methods: This was a retrospective cohort study of 128 women diagnosed with LMS from 1981 to 2013 at two tertiary care centers. Data included age, body mass index (BMI), race, tumor grade, stage, residual disease, adjuvant treatment, PFS, and OS. Variables were compared by Fisher’s exact test or Wilcoxon rank-sum test. Kaplan–Meier curves were used to plot time to progression/recurrence or death. Cox proportional hazards regression was used to estimate hazard ratios for progression/recurrence or death by patient and tumor characteristics.

Results: Fifty-six (44%) women received adjuvant chemotherapy. Of these, 30 (54%) received Gem/Tax and 26 (46%) received other CT. Of the 128 patients, 41 (32%) received adjuvant XRT and 31 (24%) received no therapy. Among the patients receiving chemotherapy, there was an even distribution of early- and late-stage disease for the two chemotherapy cohorts. In the XRT group, 80% of patients had early-stage disease. There were no differences in age, BMI, or residual disease between the groups. However, patients receiving Gem/Tax were more likely to be Caucasian and have a high-grade tumor than patients in the other groups. Median PFS was 6 months for Gem/Tax compared to 13 months for CT (P = 0.32) and 14 months for XRT (P = 0.13). The corresponding median OS was 23 months for Gem/Tax compared to 39 months for CT (P = 0.29) and 53 months for the XRT group (P = 0.035). However, on multivariate analysis, there was no difference in PFS or OS between the three treatment regimens.

Conclusions: There was no significant difference in PFS or OS in women with uterine LMS treated with adjuvant Gem/Tax compared with other CT or XRT. Further evidence is needed to determine the role and best therapeutic regimen in this setting. There is a need to identify novel therapies to treat this aggressive disease.

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Objectives: Our aim was to assess current surgical practices and use of adjuvant therapy (AT) in the treatment of FIGO stage I endometrioid endometrial cancer (EC) among Society of Gynecologic Oncology (SGO) members.

Methods: A 19-question survey was developed and approved by our institutional review board and the SGO. A link to the survey was sent to all SGO members by email, and data were collected anonymously using internet-based survey software. Demographic questions included specialty, years in practice, practice location, and EC patient volume. Respondents were asked questions regarding preoperative evaluation, surgical approach, lymph node dissection (LND), and recommendations for AT based on various clinicopathologic scenarios. Statistical analysis was performed using Statistical Package for the Social Sciences version 22.0.

Results: Of the 1399 SGO members, 320 (23%) completed the survey. Ninety-seven percent of respondents were gynecologic oncologists or fellows, 48% had >10 years of experience, and 87% treated >30 EC patients yearly. Respondents were more likely to order preoperative tests such as computed tomography of the abdomen/pelvis (70% vs. 17%) and CA-125 yearly. Respondents were more likely to order preoperative tests such as CT use are greatly increasing. We anticipate that new EC continues to evolve among SGO members. In particular, robot-assisted laparoscopy was the preferred surgical method for biopsy-proven grade 3 (G3) and grade 1 disease, respectively. Robot-assisted laparoscopy was the preferred surgical method for biopsy-proven grade 3 (G3) and grade 1 disease.

Conclusions: Our findings demonstrate that the management of stage I EC continues to evolve among SGO members. In particular, robot-assisted hysterectomy and CT use are greatly increasing. We anticipate that new trends will continue to emerge as results from additional studies become available.

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373 — Poster Session
Postoperative enteral immunonutrition for gynecologic oncology patients undergoing laparotomy decreases wound complications
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Objectives: Perioperative immune-modulating diets (IMDs) have been shown to decrease wound complications in high-risk patient populations. The effect in gynecologic oncology patients is unknown. This study sought to determine if perioperative enteral supplementation with Impact (Nestle) decreases wound complications in gynecologic oncology patients undergoing laparotomy.

Methods: This retrospective review evaluated patients undergoing open surgery on the gynecologic oncology service from July 2012 to June 2014. In the academic year beginning July 2013, we instituted a practice change to recommend pre- and post-operative oral IMDs to patients undergoing laparotomy. Demographic and clinical characteristics were abstracted from the medical record. Our outcome of interest was the frequency of Centers for Disease Control surgical site infections (CDC SSI).

Results: Of the 338 patients who underwent open surgery, 112 (33%) received IMDs postoperatively. Only five patients took Impact preoperatively. There were no significant differences in clinical characteristics between those who did and did not consume Impact. There were 89 (26%) wound complications (69 [78%] CDC SSI class 1, 7 [8%] class 2, 13 [15%] class 3). Thirty-six wound complications to be 38% for girls and 14% for boys. Parents in our practice identified forgotten appointments as a barrier to returning to complete the vaccine series. We aimed to improve HPV vaccine completion rates and overall time to completion through a quality improvement initiative using structured vaccine appointment reminders.

Methods: Informed consent was obtained from parents of children given the first or second dose of the HPV vaccine in an urban academic pediatric practice. Parents could opt for a magnet vaccine reminder as well as text/email reminders for doses 2 and 3. These interventions were in addition to the established automated phone call reminders previously used by the clinic. Basic demographic information and subsequent receipt of the HPV vaccine were abstracted from the medical record.

Results: A total of 194 children enrolled in the study at the time of their first or second dose. The baseline HPV vaccine completion rate before the quality improvement project was 28%. After the intervention (text/email reminder +/- magnet), 58% (68/118) of those enrolled at HPV1 returned for their second dose. The intervention significantly improved the completion rate for all three doses to 47% (17/36, P = 0.006). There was no significant difference in gender or insurance type among those who completed the series. In comparison, the completion rate was only 35% among the 23 patients who only received the reminder magnet at the time of their first HPV shot. There was a nonsignificant trend to improved completion rate with the addition of text/email reminders to the magnet. With the intervention, the time to completion decreased from 17.1 months to 6.8 months. On-time HPV vaccine series completion (defined as a 7-month span for series completion) improved from 15% to 35% after the introduction of structured appointment reminders (P = 0.04). With the intervention, 82% of the children who completed the series did so within 7 months of their first vaccine.

Conclusions: In our pilot quality improvement project, we found that the addition of structured appointment reminders can significantly improve HPV vaccine completion rates as well as time to completion in a pediatric urban practice.

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(40%) required hospital readmission, negative pressure wound therapy, interventional radiology, and/or operating room procedures. American Society of Anesthesiologists classification, history of diabetes mellitus or pelvic radiation, length of surgery, surgical blood loss, and administration of postoperative parenteral nutrition were all significantly associated with development of a postoperative wound complication \( (P < 0.05) \). Patients receiving IMDs had fewer wound complications than those who did not (19.6% vs. 33%, \( P = 0.049 \)). The significance of this association strengthened when benign diagnoses were excluded \( (24\% \text{ vs. } 43\%, \ P = 0.0005) \). On multivariate analysis, consumption of IMDs remained protective against wound complications \((\text{odds ratio } 0.47, 95\% \text{ CI } 0.25\text{–}0.89, \ P = 0.02)\) and was associated with a 66% reduction in the incidence of CDCSSI class 2 and 3 infections \( (P = 0.043) \).

**Conclusions:** Postoperative enteral IMDs are associated with fewer wound complications in patients undergoing laparotomy for gynecologic malignancy and may reduce the incidence of CDCSSI class 2 and 3 infections.

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### 374 — Poster Session

**Hiding in plain sight: The prevalence of obstructive sleep apnea in gynecologic oncology patients**


**Objectives:** To estimate the prevalence of undiagnosed obstructive sleep apnea (OSA) in gynecologic oncology patients presenting to an outpatient clinic.

**Methods:** This prospective cohort study involved consecutive patients presenting to a gynecologic oncology clinic for preoperative evaluation. Study participants were screened for OSA with the previously validated four-question S.T.O.P. questionnaire from November 5, 2012 to September 10, 2014. Patients who screened as high risk were given a referral for polysomnography. Additional patient demographic and outcome data were collected for all patients. Statistical analysis was performed using standard descriptive statistics and univariate and multivariate analyses.

**Results:** Of the 383 patients approached, 260 (68%) agreed to participate. The mean age was 58.3 years \( (\text{range, } 24\text{–}86 \text{ years}) \) and mean body mass index \( (\text{BMI}) \) was 34.4 \( (\text{range, } 18.7\text{–}69.3) \). Reasons for referral for evaluation were as follows: 105 \( (40.4\%) \) for pelvic mass or ovarian cancer, 119 \( (45.8\%) \) with postmenopausal bleeding or endometrial cancer, 14 \( (5.4\%) \) for abnormal Pap smear results, 8 \( (3.1\%) \) for risk-reducing surgery, 4 \( (1.5\%) \) for restaging of known cancer, and 3 \( (1.2\%) \) other. Of the 260 participants, 33 \( (12.7\%) \) had a prior diagnosis of OSA. Of the remaining 227 patients, 66 \( (29\%) \) screened as high risk. Collectively, 99 participants \( (38\%) \) had either a prior diagnosis of OSA or were found to be at high risk. Of the 66 patients who screened high risk, 8 \( (12\%) \) completed polysomnography, and all \( (100\%) \) were found to have sleep apnea. Univariate analysis showed that both age \( (P = 0.0042) \) and BMI \( (P = 0.001) \) were significant for screening high risk for OSA. In multivariate analysis, BMI alone was significant for being high risk for OSA \( (P = 0.003) \). Patients with a normal BMI \( (<25) \) had a prevalence of 14% of screening high risk for OSA. For each 1-point increase in BMI over 25, the risk of OSA increased by 1%.

**Conclusions:** OSA is underdiagnosed in the gynecologic oncology patient population. BMI is an independent predictor for increasing risk of OSA in our population. Further research in increasing awareness, screening, and diagnosis of OSA in this population is warranted.

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376 — Poster Session
Departmental mortality review and present on admission indicator reporting improves observed-to-expected mortality ratios

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Objectives: Objective measures have become an increasingly important tool used by organizations to improve health care delivery. Accurate documentation of diagnoses present on admission (POA) is another quality measure that accurately establishes acute and chronic illnesses that might affect prediction of mortality. We sought to determine whether standardized methods of documenting diagnoses POA can improve performance and accuracy of objective quality measures.

Methods: A single-institution study from September 2013 to June 2014 was performed on all patients managed on an academic gynecologic oncology service. A standardized method for documenting POA diagnoses within the admission history and physical examination was implemented starting February 1, 2014. Monthly reviews of all mortalities were performed, and if admitting diagnosis(es) were inaccurate, corrections were made. The observed-to-expected (O/E) mortality ratios as reported to the University HealthSystem Consortium were compared before and after implementation of the documentation methods and mortality review committee evaluation.

Results: Of 771 patients who were identified, 379 were admitted from September 1, 2013 to January 31, 2014 and 392 from February 1 to June 31, 2014. There were 11 deaths in the first 5 months of the study period and 6 deaths in the second. Prior to February 1, 2014, the average O/E mortality ratio was 1.09 (standard deviation ± 0.68). The average O/E mortality ratio dropped to 0.84 ± 0.82 for those patients admitted after February 1 (Fig. 1).

Conclusions: This study confirms that standardized methods for documenting POA diagnoses improve medical coder accuracy of patient comorbidities. When combined with corrections of coding errors found by the mortality review committee, additional improvements in objective measures of quality health care delivery are seen.

Figure 1. Observed-to-Expected (O/E) Mortality Ratio. There is a downward trend in the O/E ratio from September 2013 to June 2014.

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377 — Poster Session
Conservative management of endometrial hyperplasia/carcinoma with levonorgestrel intrauterine system may be less effective in patients with morbid obesity

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Objectives: To assess the regression of endometrial lesions following conservative treatment with a levonorgestrel-intrauterine system (LNG-IUS) for endometrial hyperplasia (EH) and/or endometrial carcinoma by body mass index (BMI).

Methods: A retrospective study of patients treated with LNG-IUS for EH or early-stage endometrial carcinoma was performed from 2009 to 2013. Regression was defined by downgrading of endometrial lesion after treatment. Patient demographics, comorbidities, LNG-IUS indications, and BMI were abstracted. Patients were categorized by BMI: normal weight (<30), obese (30-40), and morbidly obese (>40). Descriptive statistics were performed.

Results: Forty-two patients were included in the analysis. The most common indication for LNG-IUS treatment was poor surgical candidacy (35.7%), followed by patient preference (33.3%) and fertility preservation (23.8%). The mean age at diagnosis was 46.5 ± 12 years, mean body weight was 246 ± 83 lb, and mean BMI was 40.8 ± 14. Pretreatment histologies included: 19 EH without atypia, 9 EH with atypia, and 14 carcinomas. Median time to follow-up biopsy was 3.9 months following LNG-IUS. After treatment with LNG-IUS, 59.5% (n = 25) of the cohort experienced regression, 11.5% (n = 5) experienced progression, and 21.4% (n = 9) had no change in histologic diagnosis on repeat biopsy. In the obese BMI group (n = 20), 100% (n = 5) of patients who had EH without atypia, 100% (n = 3) with EH with atypia, and 66.7% (n = 2/3) with carcinoma had regression of their lesion after treatment. No patient experienced progression in the obese category. In the morbidly obese patients (n = 20), 57.1% (n = 4/7) of those who had EH without atypia, 33.3% (n = 2/6) with EH with atypia, and 28.6% (n = 2/7) with carcinoma had regression after treatment. Forty percent of morbidly obese patients (n = 8) overall experienced progression, but 25% (n = 5) had progression of disease and 20% (n = 6) had no change in post-treatment biopsy. There was a significant difference in regression of endometrial lesion between the obese and morbidly obese groups (P = 0.046).

Conclusions: Response to LNG-IUS for conservative management of EH/carcinoma may vary with increasing BMI, with decreased rates of regression in patients with BMI > 40. Further investigation is warranted to explore decreased treatment response to LNG-IUS in morbidly obese patients.

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378 — Poster Session
Does performing fewer pelvic lymphadenectomies for low-intermediate risk type 1 endometrial cancer and performing secondary staging surgeries with para-aortic lymphadenectomy in lymph vascular invasion impact patients?

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Objectives: In November 2010, the Institut National du Cancer in France published new guidelines for managing endometrial cancer (EC). Pelvic lymphadenectomy is not indicated for preoperative low-intermediate risk (LR-IR) type 1 EC, and high-risk (HR) patients undergo secondary staging surgery with paraaortic lymphadenectomy. The aim of this study was to evaluate the effect of these new guidelines on morbidity and survival.

Methods: We retrospectively evaluated all type 1 EC patients who were treated from January 1, 1997 to December 31, 2012. Patients were classified per the 2009 International Federation of Gynecology and Obstetrics staging preoperative criteria and the European Society
for Medical Oncology criteria for LR-IR and HR of recurrence, and outcomes before and after the new guidelines were evaluated. **Results:** We included 230 LR-IR patients (159 before and 71 after) with 54 HR patients (33 before and 21 after). Pelvic lymphadenectomy was performed before and after the new guidelines in 123/159 (77.4%) and 20/71 (28.6%) patients, respectively (*P* < 0.001) in LH-IR. After 2010, eight patients with LH-IR also underwent secondary paraaortic lymphadenectomy for lymphovascular space invasion (LVSI), based on definitive histology. Overall survival (OS) and relapse-free survival (RFS) were similar before and after the new guidelines. In LR-RI patients, LVSI was an independent factor for OS (*HR* = 7.2, 95% CI: 3.1–17, *P* < 0.001) and RFS (*HR* = 3.7, 95% CI: 1.6–8.5, *P* = 0.003). After 2010, optimally managed LR-IR patients had similar OS and a higher 2-year RFS compared to suboptimally managed patients (OS: 100% vs. 98.1% [87.1–99.7], *P* = 0.6; RFS: 94.1% [82.7–98.1] vs. 77.1% [44.2–92.1], *P* = 0.07). **Conclusions:** Fewer pelvic lymphadenectomies in LR-IR patients did not affect morbidity, OS, or RFS, and staged surgery did not affect morbidity or survival. However, a trend toward increased risk of recurrence was observed in patients who were not optimally managed per the new guidelines. Therefore, we must gather additional data, with a longer follow-up, to confirm our results.

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### 379 — Poster Session

**Weight change after participation in a technology-based weight loss intervention for endometrial cancer survivors with obesity**

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**Objectives:** Weight loss is believed to play an important role in reducing morbidity and mortality of endometrial cancer survivors and should be a primary objective of survivorship care. In this study, we investigated the efficacy and sustainability of a technology-based weight loss intervention in obese endometrial cancer survivors.

**Methods:** Twenty women age >18 years with obesity (body mass index ≥ 30) and histologically confirmed endometrial hyperplasia/type I endometrial cancer were randomized 1:1 to a 6-month lifestyle modification intervention for weight loss delivered via the telephone or text messaging. Following completion of the program, prospective data from clinical cancer surveillance visits were abstracted to determine long-term weight changes at 9, 12, and 18 months compared to enrollment (*t* = 0 months). Descriptive statistics were performed.

**Results:** The majority of initial participants had early-stage (65%) endometrial cancer and had a median age of 60.5 years. The primary intervention outcome revealed median weight loss of 9.7 kg at *t* = 6 months (range, 1.1–22.9 kg) in the telemedicine group compared with 3.9 kg (range, 0.3–11.4 kg, *P* = 0.023) in the text group. Weight loss was maintained during observational follow-up. At *t* = 9 months, 75% of the cohort successfully maintained weight loss, with a median loss of 2.7 kg (interquartile range [IQR] 0.8–5.7 kg) compared to *t* = 0. At *t* = 12 months, 69% demonstrated a median loss of 2.5 kg (IQR 1.4–6.1 kg). At *t* = 18 months, 79% had maintained a weight loss of 5.7 kg (1.4–11.4 kg) compared to baseline. Overall, the telemedicine arm continued to be more successful in maintaining weight loss at *t* = 9 months (*P* = 0.015), although there was no difference between the telemedicine and text groups at *t* = 12 (*P* = 0.79) and 18 months (*P* = 0.9) of follow-up.

**Conclusions:** While a technology-based weight loss intervention was initially more successful in a telemedicine platform, participants in both arms continued to be successful in maintaining weight loss at 12 and 18 months after enrollment. Further investigation is needed to identify measures to improve sustainability of an initially successful weight loss intervention, perhaps by continuation of the intervention, development of a modified support system, or adaptation of a combination of initial telemedicine support followed by a text messaging platform.

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### 380 — Poster Session

**Is indocyanine green (ICG) the best tracer for sentinel lymph node (SLN) mapping in early-stage cervical and endometrial cancer?**

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**Objectives:** Indocyanine green (ICG) with near-infrared (NIR) fluorescence imaging is a new tracer modality that appears to have a better detection rate and safety profile than blue dye and is less cumbersome to use than Ty-99. We present our initial experience with ICG for SLN mapping in cervical and endometrial cancer.

**Methods:** We reviewed all patients at our institution who underwent primary surgery for presumed early-stage endometrial and cervical carcinoma with SLN mapping using the ICG dye and fluorescence imaging following by pelvic lymphadenectomy from February to July 2014. SLNs were ultrastaged on final pathology. Sensitivity and specificity values were calculated.

**Results:** A total of 50 patients were included in the study (42 endometrial and 8 cervical cancers). The mean age was 59 years (range, 24–88 years). Mean body mass index was 31 (range, 19–56). The mean SLN count was 3.1 (range, 0–7) and the median lymph node count was 16 (range, 2–37). The overall detection rate was 96% (48/50), with a bilateral detection rate of 88% (44/50). Positive SLNs were identified in 22% of patients (11/50), including eight isolated tumor cells (ITC), two micrometastases, and one macrometastasis. Sensitivity and specificity values were 100%. Paraaortic node dissection was performed in 22% of cases. Two had paraaortic node metastasis, both in patients with positive pelvic SLNs. There were no adverse effects or allergic reactions related to the ICG dye.

**Conclusions:** Based on our pilot experience, NIR fluorescence imaging with ICG is an excellent and safe tracer modality for SLN mapping, with a very high overall (96%) and bilateral (88%) detection rate. We believe that ICG is ideal for large-scale worldwide implementation of SLN mapping in early-stage cervical and endometrial cancer.

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### 381 — Poster Session

**Molecular profile of uterine papillary serous carcinoma compared to ovarian serous carcinoma: Is it the same disease at different site?**

*Authors:* H. Mahdi1, X. Xia2, S.K. Reddy3, R. DeBernardo4. 1Cleveland Clinic, Cleveland, OH, USA, 2Caris Life Sciences, Irving, TX, USA

**Objectives:** To compare the molecular profile of a large cohort of uterine papillary serous carcinoma (UPSC) and ovarian serous carcinoma (EOC-S).

**Methods:** A total of 240 UPSC and 1587 EOC-S tumors were evaluated using a commercial multiplexing profiling service (CARIS Life Sciences, Phoenix, AZ). Specific testing performed included a combination of gene sequencing (Sanger, NGS), protein expression (immunohistochemistry [IHC]), and gene amplification
Distinct molecular landscapes between endometrioid and non-endometrioid uterine carcinoma

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Objectives: Endometrial carcinoma (EC) is traditionally divided into endometrioid (type I) and nonendometrioid (type II) subtypes, despite considerable heterogeneity within each phenotype. Our aim was to identify distinct molecular alterations between histologic subtypes that would aid in guiding treatment strategies.

Methods: A total of 3133 ECs were submitted to Caris Life Sciences between March 2011 and July 2014 (1634 type I and 1226 type II, based on reported pathology). Multiplatform molecular analysis included gene sequencing (Sanger or next generation sequencing), immunohistochemistry (IHC) of protein expression, and/or gene amplification (fluorescence in situ hybridization/chromogenic in situ hybridization). Proportion analysis was performed using Prism v.6.

Results: Table 1 depicts the histologic breakdown of EC cases and major pathway aberrations. Histologic subtype was significantly associated with estrogen receptor (ER)/androgen receptor (AR) and cMET expression and PI3K, KRAS, and ERBB2 mutation. Endometrioid histology had the highest ER/progesterone receptor (PR) expression (81% and 69%, respectively), PD1/PDL-1 expression (74.3%/30.7%), and PI3K mutation (35.6%). AR expression (27%) and Her2/neu overexpression/amplification (10.4%/17.3%) was the highest in uterine serous carcinoma (USC). Mucinous tumors harbored a high KRAS mutation rate (41%) and cMET overexpression (43%). Clear cell (CC) cancer also had notably high cMET overexpression (43%) as well as ERBB2 mutation (8.3%). TP53 was mutated most frequently in USC (76%), followed by carcinosarcoma (CS) (69%). CS also had the lowest expression of ER/PR (25% and 21%), high expression of PD1/PDL-1 (84% and 25%), and high frequency of FBXW7 mutation (12%). Squamous histology was significant for high expression of beta catenin gene CTNNB1 (44%), implicated in the Wnt pathway. Altered DNA repair pathway, as indicated by BRCA mutations, and low ERCC1 and MGMT expressions were most notable in CC, suggesting benefit with platinum therapy.

Conclusions: Despite molecular heterogeneity among histologic subtypes, distinct patterns of pathway aberration may be targeted with further research. Correlating molecular profiles with clinical outcomes can assist in developing rational guidelines for therapy in individuals with EC.
Factors associated with successful bilateral sentinel lymph node mapping in endometrial cancer


Objectives: As our understanding of sentinel lymph node (SLN) mapping for endometrial cancer (EC) evolves, tailoring the technique to patients at high risk for failed mapping may result in a higher successful bilateral mapping (SBM) rate. Patient and tumoral factors may influence the rate of SBM. The study objective was to identify factors associated with SBM in patients with endometrial neoplasia.

Methods: From September 2012 to July 2014, women with EC or complex atypical hyperplasia (CAH) underwent SLN mapping via cervical injection followed by robot-assisted total laparoscopic hysterectomy (RA-TLH) at a tertiary care academic center. Completion lymphadenectomy and ultrastaging were performed according to a previously described institutional protocol. Clinical, tumoral, and surgeon variables were prospectively collected and analyzed.

Results: RA-TLH and SLN mapping were performed in 104 women; 89 had EC and 15 had CAH. Median age was 62 years and median body mass index (BMI) was 31. Seventy-three women had low-grade and 31 had high-grade disease. Stage distribution was as follows: CAH 14.3%, stage I 68.3%, stage II 2.9%, stage III 13.5%, and stage IV 1%. Overall, the SBM rate was 60.6% (63/104) and the false-negative rate of our institutional protocol was 1/104 (0.9%). On univariate analysis, neither tumor factors (grade, histology, depth of invasion, tumor size, lymphovascular space invasion, or lower segment involvement) nor anatomic factors (history of uterine, cervical, or pelvic surgery, endometriosis, or fibroids) were associated with SBM rate. Surgeon fellowship training in SLN injection procedures was also not associated with SBM. Mean BMI was significantly lower in women who had SBM (30.9 vs. 35.1, \( P = 0.015 \)), whereas the presence of clinically enlarged lymph nodes was associated with a decrease in SBM from 64.5% to 27.7% (\( P = 0.023 \)). Additionally, use of indocyanine green dye was associated with SBM in 76.4% compared with only 39.6% when isosulfan blue was used (\( P = 0.001 \)). On multivariate analysis, choice of dye (\( P = 0.001 \)), BMI (\( P = 0.004 \)), and the presence of clinically enlarged lymph nodes (\( P = 0.03 \)) were associated with SBM rate.

Conclusions: Within a high-volume sentinel lymph node program, choice of injection dye, BMI, and clinically enlarged lymph nodes were independently associated with successful bilateral mapping in EC.

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385 — Poster Session

Differences in BMI and physical activity in Whites versus Asians in California in association with type I uterine cancer

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Objectives: Prior reports have shown that Whites have higher rates of type I uterine cancer compared to Asians. We propose to evaluate the effect of body mass index (BMI), physical activity, and other lifestyle factors in these two groups.

Methods: Data were obtained from 2001 to 2009 National Cancer Institute (NCI) and the 2005 California Health Interview Survey (CHIS) databases. Lifestyle factors, including BMI, diet, physical activity, use of hormone replacement therapy, and smoking, were evaluated in the healthy control population. Chi square, t-test, and ANOVA test were used.

Results: Based on analysis of the NCI database, we found that Whites had a higher proportion of type I uterine cancer than Asians (63% vs. 60%, \( P = 0.01 \)). To evaluate the differences in BMI and other lifestyle factors, we identified 20,599 women from the CHIS database, of whom 2325 were Asian and 18,247 were White. The Whites were older (54 years vs. 47 years, \( P = 0.01 \)) and had higher BMIs (25.9 vs. 23.2, \( P = 0.001 \)). On multivariate analysis, choice of dye (\( P = 0.03 \)) were associated with SBM rate. Surgeon fellowship training in SLN injection procedures was also not associated with SBM. Mean BMI was significantly lower in women who had SBM (30.9 vs. 35.1, \( P = 0.015 \)), whereas the presence of clinically enlarged lymph nodes was associated with a decrease in SBM from 64.5% to 27.7% (\( P = 0.023 \)). Additionally, use of indocyanine green dye was associated with SBM in 76.4% compared with only 39.6% when isosulfan blue was used (\( P = 0.001 \)). On multivariate analysis, choice of dye (\( P = 0.001 \)), BMI (\( P = 0.004 \)), and the presence of clinically enlarged lymph nodes (\( P = 0.03 \)) were associated with SBM rate.

Conclusions: Within a high-volume sentinel lymph node program, choice of injection dye, BMI, and clinically enlarged lymph nodes were independently associated with successful bilateral mapping in EC.

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386 — Poster Session

The feasibility and effectiveness of a 12-week social cognitive theory-based physical activity intervention for obese, ethnically diverse endometrial cancer survivors

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Objectives: The feasibility and effectiveness of a 12-week social cognitive theory-based physical activity intervention for obese, ethnically diverse endometrial cancer survivors

Methods: From September 2012 to July 2014, women with EC or complex atypical hyperplasia (CAH) underwent SLN mapping via cervical injection followed by robot-assisted total laparoscopic hysterectomy (RA-TLH) at a tertiary care academic center. Completion lymphadenectomy and ultrastaging were performed according to a previously described institutional protocol. Clinical, tumoral, and surgeon variables were prospectively collected and analyzed.

Results: RA-TLH and SLN mapping were performed in 104 women; 89 had EC and 15 had CAH. Median age was 62 years and median body mass index (BMI) was 31. Seventy-three women had low-grade and 31 had high-grade disease. Stage distribution was as follows: CAH 14.3%, stage I 68.3%, stage II 2.9%, stage III 13.5%, and stage IV 1%. Overall, the SBM rate was 60.6% (63/104) and the false-negative rate of our institutional protocol was 1/104 (0.9%). On univariate analysis, neither tumor factors (grade, histology, depth of invasion, tumor size, lymphovascular space invasion, or lower segment involvement) nor anatomic factors (history of uterine, cervical, or pelvic surgery, endometriosis, or fibroids) were associated with SBM rate. Surgeon fellowship training in SLN injection procedures was also not associated with SBM. Mean BMI was significantly lower in women who had SBM (30.9 vs. 35.1, \( P = 0.015 \)), whereas the presence of clinically enlarged lymph nodes was associated with a decrease in SBM from 64.5% to 27.7% (\( P = 0.023 \)). Additionally, use of indocyanine green dye was associated with SBM in 76.4% compared with only 39.6% when isosulfan blue was used (\( P = 0.001 \)). On multivariate analysis, choice of dye (\( P = 0.001 \)), BMI (\( P = 0.004 \)), and the presence of clinically enlarged lymph nodes (\( P = 0.03 \)) were associated with SBM rate.

Conclusions: Within a high-volume sentinel lymph node program, choice of injection dye, BMI, and clinically enlarged lymph nodes were independently associated with successful bilateral mapping in EC.

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**Objectives:** Endometrial cancer survivors suffer from comorbidities related to physical inactivity and obesity that have been associated with poorer survival outcomes. The purpose of this study was to determine the feasibility of a physical activity intervention for ethnically diverse endometrial cancer survivors.

**Methods:** After institutional review board approval, obese patients who had expressed interest in participating in exercise classes were recruited. Classes, which included 30 min of behavioral intervention based on social cognitive theory and 60 min of a culturally tailored fitness class, were offered twice weekly for 12 weeks. Participants were instructed to attend at least one of the two sessions per week but were allowed to attend both.

**Results:** The 30 women (Table 1) out of 65 contacted who agreed to participate (recruitment rate: 46%) were quasi-randomized to the intervention or control group. The primary reason for refusal was lack of time (n = 14). Of the 15 participants in the intervention group, two never attended a class, two dropped out due to unrelated illness/injury, and one did not complete the follow-up (retention rate: 67%). The 11 women who completed the intervention attended at least one class per week during 10.6 ± 1.9 weeks (attendance: 88%). Additionally, eight women regularly attended twice a week, such that the mean classes attended were 16.5 ± 5.8. Compared to the control (n = 11), the intervention group (n = 10) demonstrated a reduction in waist circumference (P = 0.011), increase in quality of life (P = 0.049), and greater walking self-efficacy (P = 0.025) but no differences in barrier self-efficacy, relative autonomy index, expected outcomes, or social support (P > 0.20).

**Conclusions:** There are important barriers to recruitment for physical activity interventions for endometrial cancer survivors. Attendance of participants was high in this culturally tailored intervention, and there were significant improvements in waist circumference, quality of life, and self-efficacy. Future studies should take great care to maximize accessibility to broaden the impact of the program and address barriers to adherence as they arise within a program.

**Table 1**

<table>
<thead>
<tr>
<th>Participant characteristics (n = 30).</th>
<th>64.0 ± 7.6 years</th>
</tr>
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<tbody>
<tr>
<td>Stage I</td>
<td>75%</td>
</tr>
<tr>
<td>Body mass index</td>
<td>36.3 ± 6.9</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>40%</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>33%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>17%</td>
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<tr>
<td>Non-Hispanic white</td>
<td></td>
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</tbody>
</table>

**388 — Poster Session**

The impact of diabetes and metformin on clinical outcomes is negligible in risk-adjusted endometrial cancer cohorts


**Objectives:** To reexamine the influence of diabetes and metformin therapy on overall (OS) and progression-free survival (PFS) in endometrial cancer (EC) using propensity score (PS) matching to account for multiple confounding risk factors.

**Methods:** Consecutive stages I–IV EC patients managed surgically from 1999 to 2008 without neoadjuvant therapy and/or invasive synchronous cancer were stratified by history of diabetes. PS matching was used to adjust for confounding patient-, disease-, and treatment-specific risk covariates. OS and PFS were compared among diabetic and nondiabetic matched pairs and between matched pairs of diabetic patients managed with or without metformin. Cox proportional hazards models were fit to estimate the effects on outcomes.

**Results:** Of 1303 eligible patients (79% stage I, 28% stage 3), 277 (21.3%) had a history of diabetes. Among diabetic patients, 116 (41.9%) were treated with metformin, 57 (20.6%) with other oral agents, 51 (18.4%) with insulin ± other oral agents, and 53 (19.1%) with diet only. The OS and PFS, respectively, for PS-matched diabetic and nondiabetic EC patients were identical between the matched subsets (HR 1.01; 95% CI 0.72, 1.42 for OS and HR 1.01; 95% CI 0.60, 1.69 for PFS). No differences in OS and PFS were observed when comparing PS-matched metformin users and nondiabetics (HR 1.03; 95% CI 0.57, 1.85 for OS and HR 1.14; 95% CI 0.49, 2.62 for PFS). Furthermore, no differences were observed when comparing metformin users who were PS-matched to other
diabetics (HR 0.61; 95% CI 0.30, 1.23 for OS and HR 1.06; 95% CI 0.34, 3.30 for PFS). No difference was detected in PFS when comparing diabetics according to histologic subtype and metformin use (Figure).

**Conclusions:** When risk-adjusted for differences in the prevalence of patient-, disease-, and treatment-specific covariates, OS was similar between diabetic and nondiabetic EC patients as well as between metformin users and nonusers or nondiabetics. Similar findings were observed for PFS.

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**389 — Poster Session**

**Cancer of the uterus and treatment of incontinence (CUTI)**

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**Objectives:** To determine if women with clinical stage I endometrial cancer can be effectively screened for stress urinary incontinence (SUI) by their gynecologic oncologist and referred to an urogynecologist for concurrent treatment of their endometrial cancer and SUI by their gynecologic oncologist and referred to an urogynecologist postoperatively. SUI severity and bother scores improved in the concurrent surgery group. There was no difference in operative time, blood loss, or surgical complications between the groups. One patient in the concurrent surgery group required vaginal brachytherapy postoperatively. SUI severity and bother scores improved in the concurrent surgery group.

**Conclusions:** Treatment of SUI at the time of endometrial cancer diagnosis is feasible and is not associated with a delay in time to the operating room. All women desired a referral to a urogynecologist preoperatively and half opted for concurrent surgery. Concurrent treatment of SUI and endometrial cancer may affect quality of life, and further studies are warranted.

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**390 — Poster Session**

**Magnetic resonance imaging utility to predict myometrial invasion in endometrial carcinoma: 10 years experience of single institution in Argentina**

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**Objectives:** To determine the sensitivity and specificity of magnetic resonance imaging (MRI) in assessing myometrial invasion in patients with endometrial carcinoma compared with deferred biopsy.

**Methods:** Clinical records of 87 patients diagnosed with endometrial carcinoma from April 2004 to October 2012 were investigated retrospectively to calculate sensitivity, specificity, and positive and negative likelihood ratio (PLR and NLR) of MRI compared to the gold standard of deferred biopsy. We also compared MRI and intraoperative frozen section to determine invasion concordance.

**Results:** Eight-seven patients were analyzed between 2004 and 2012, resulting in a sensitivity of 71.4% (95% CI 0.48–0.89), specificity of 86.36% (95% CI 0.75–0.93), positive predictive value (PPV) of 62.5%, and negative predictive value (NPV) of 90.5%. The PLR was 5.2 and the NLR was 0.33. The absolute concordance between MRI and deferred biopsy was 82.8%. There was agreement between MRI and frozen section in 85.9% (kappa = 0.61) of the cases, while concordance between frozen section and deferred biopsy was 96.5%.

**Conclusions:** MRI is a useful study to evaluate deep myometrial invasion, although it does not replace intraoperative biopsy. The study’s safety, determined mostly by its high NPV, suggests its use as inclusion criteria in fertility-preserving treatment in young women. MRI also allows the calculation of operating room time for those patients with an estimated prolonged surgery.

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**391 — Poster Session**

**Is endometrial cancer different in Asian American women?**

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**Objectives:** Asian Americans (AAs) represent the fastest growing population over the last decade, according to the 2010 United States census, but little is known about the characteristics of endometrial cancer in this group. This study sought to analyze the clinicopathologic characteristics and outcomes of AA women with endometrial cancer as compared to other ethnicities.
Methods: We performed a retrospective review of 454 patients diagnosed with endometrial cancer at Tufts Medical Center between January 1, 2003 and December 31, 2013. Demographics, clinicopathologic characteristics, treatments, and survival outcomes were analyzed and compared among ethnicities. Due to the large sample size of Caucasians (n = 380), a random number generator was used to select 100 Caucasian cases for analysis.

Results: Of 158 patients in the analysis, 33 (20.9%) were AA, 25 (15.8%) were black (B), and 100 (63.3%) were Caucasian (C). A total of 54.5% (18/33) of the AA population spoke a Chinese dialect and were first-generation immigrants. The mean age at diagnosis; menopausal status; and proportion with stage I disease, low-grade cancer, and endometrioid histology did not differ across ethnic groups. AAs were more likely to be nulliparous (P = 0.03), had significantly lower mean body mass index (BMI) than either of the other two groups (27.3 AA vs. 36 B, 36 C), and were less likely to be obese (19.4% vs. 68.4% B, 71.3% C; P < 0.0001). AAs and Bs both had a higher proportion of women with stages III–IV disease compared to Cs (28.1% AA, 32% B vs. 13% C; P = 0.04). There was no difference in the proportion of patients who received surgery, adjuvant chemotherapy, or radiation across ethnic groups. There was no difference in overall survival (OS) at 2 years across ethnic groups (86.5% AA, 85.0% B, 90.6% C; P = 0.88). After adjusting for age, stage, and histology, there was no difference in OS (Table 1).

Conclusions: AA women are more likely to present with advanced-stage disease but otherwise have similar clinicopathologic characteristics and outcomes to other ethnicities. The proportion with type I endometrial cancer was similar to other ethnicities despite lower mean BMI and rate of obesity. This suggests that AA women are at risk for type I endometrial cancer at a much lower BMI threshold compared to other ethnicities.

Table 1

<table>
<thead>
<tr>
<th>Race</th>
<th>HR crude (95% CI)</th>
<th>p</th>
<th>HR adj (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>1.21 (.52, 2.78)</td>
<td>.66</td>
<td>1.06 (.43, 2.54)</td>
<td>.95</td>
</tr>
<tr>
<td>Black</td>
<td>1.20 (.44, 3.24)</td>
<td>.72</td>
<td>.84 (.29, 2.43)</td>
<td>.75</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1.0 ref</td>
<td></td>
<td>1.0 ref</td>
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</tbody>
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392 — Poster Session

Next-generation sequencing demonstrates genomic signature of resistance patterns following phosphatidylinositol 3-kinase (PI3K) inhibition

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Objectives: Inhibition of the phosphatidylinositol 3-kinase (PI3K) pathway is a promising therapeutic avenue for women with endometrial cancer, given the high prevalence of innate PI3K pathway activation. In early-phase trials, response to these therapies has been of limited duration, and the objective of this investigation was to utilize a novel model to understand the genomic changes associated with resistance to PI3K inhibition.

Methods: With institutional review board approval, NOD/SCID mice bearing xenografts derived from a primary endometrioid endometrial human tumor (ENCA1) were divided into a two-arm cohort (n = 12/arm) with equivalent tumor volumes. The arms received either NVP BKM-120 (30 mg/kg) or vehicle, and xenograft tumor volumes were assessed. Xenograft tumors were harvested from untreated animals as well as both treatment arms at the point of NVP BKM-120 sensitivity, and RNA was extracted from each fresh tumor (n = 23). Genome-level changes were assessed using the next-generation Illumina HiSEQ 2000 platform. Controlling for changes in the vehicle tumors, significant gene changes that occurred exclusively as a xenograft tumor transitioned from being NVP BKM-120-sensitive to -resistant were identified and stratified by the number of gene–gene interactions, number of initiating molecules, and known interactions with AKT. To further understand the biological meaning of resistance, we performed pattern, functional, and pathways analyses.

Results: A 54-gene expression signature was identified consisting of genes that significantly changed with the development of sensitivity and subsequent resistance. This signature demonstrated significant counterregulation at the time of resistance. Sensitivity to PI3K inhibition was associated with marked alteration in gene sets involved with cell death and survival, inflammatory response, cell-to-cell signaling, cellular movement, and immune cell traffic. Resistance to NVP BKM-120 led to significant shifts in additional genes involved in cell migration/invasion and lipid metabolism.

Conclusions: These results suggest that resistance to PI3K inhibition with NVP BKM-120 is a multifactorial process governed by several sets of genetic events in specific molecular pathways. Further validation of individual pathways and genes will be crucial to uncoupling PI3K resistance.

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393 — Poster Session

Does obesity affect pathologic agreement of initial and final tumor grade of disease in endometrial cancer patients?


Objectives: Various staging strategies are used in the management of endometrial cancer (EC), including intraoperative frozen section, triage based on preoperative biopsy results, and sentinel node biopsy. The objective of this study was to compare preoperative and postoperative tumor grade to determine if surgical staging based on preoperative grade is a feasible approach and whether the level of agreement is affected by obesity.
Methods: A retrospective cohort study of women diagnosed with EC between January 2010 and December of 2011 was performed. Demographics, stage, biopsy method, and pre- and postoperative tissue grade and histology were abstracted, with patients stratified by body mass index (BMI) as obese (BMI $\geq 30$) and nonobese (BMI $< 30$). Patients with incomplete records or uterine sarcoma were excluded. The level of agreement between preoperative and postoperative tumor grade, both overall and for obese and nonobese patients, was determined using weighted kappa statistics.

Results: A total of 445 patients were included: 161 nonobese patients and 284 obese patients. Among nonobese patients, 77.6% of the women were white. The majority had stage I disease (77.0%) on final pathology, followed by stage III/IV (18.0%) and stage II (5%). Preoperative biopsy techniques in the nonobese group included 55.9% with an office biopsy and 42.9% with a dilation and curettage (D&C). Among obese patients, 69.7% were white. Final pathology confirmed predominately stage I disease (75.4%), followed by stage I (13.0%) and stage III/IV (11.6%). Office biopsies were performed on 53.2% and 48.6% had a D&C in the obese group; these proportions were similar to nonobese women. Overall, the agreement between preoperative and postoperative biopsy was fair (weighted kappa 0.31). When stratified by BMI, the agreement between preoperative and postoperative grade remained only fair in both obese and nonobese patients (weighted kappas 0.34 and 0.28, respectively; $P = 0.40$).

Conclusions: The correlation between preoperative biopsy and final tumor grade was not differentiated according to BMI. Because of only fair correlation, utilization of preoperative biopsy results as a triage tool for surgical staging should be avoided.

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394 – Poster Session
Morcellation and the incidence of occult malignancy: A dual-institution review

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Objectives: To determine the incidence of unsuspected uterine malignancy (UM) as well as other uterine histology known to be associated with malignancy (UPM) at the time of hysterectomy or myomectomy using power morcellation for specimen delivery.

Methods: We performed a retrospective study of all women undergoing a myomectomy or hysterectomy using power morcellation at two different centers between January 1, 2004 and April 30, 2014. Our primary outcome was the incidence of sarcoma (UtSarc), endometrial carcinoma (EmCa), and other conditions potentially associated with malignancy (UPM). We also included premalignant pathology (StUMP), and endometrial atypical hyperplasia (AH). Using the diagnostic classification of American Society for Colposcopy and Cervical Pathology (ASCCP), we classified as non-malignant all other pathology results. All pathology results were considered as “non-malignant” (NM).

Results: A total of 925 women underwent hysterectomy or myomectomy using power morcellation. Two patients (incidence 1/463; 95% CI 0 to 1 in 251) were found to have UM pathology, two EmCa, and one UtSarc. The incidence of UtSarc pathology diagnosed in our cohort of patients undergoing power morcellation was 0.0% (95% CI 0% to 1 in 251).

Two patients were found to have UM pathology: four StUMP tumors and two AH (incidence 1 in 154; 95% CI 1 in 419 to 1 in 71). Patients with UM and UPM pathology had uterus that weighed more than those with NM pathology (544.9 g vs. 221.5 g, $P = 0.02$). There was no statistically significant difference in age ($P = 0.12$), body mass index ($P = 0.75$), or race (Fisher’s exact 0.323).

Conclusions: The incidence of unsuspected UM pathology diagnosed in our cohort of patients undergoing power morcellation was 1/463, all of which was EmCa. Uterine weight was greater in women with uterine premalignant and malignant pathology.

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395 – Poster Session
Preoperative risk factors to predict lymph node metastasis in early stage endometrial cancer


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Objectives: Intraoperative algorithms have been described for sentinel lymph node (SLN) mapping in endometrial and cervical cancers. Their feasibility relies upon the surgeon’s ability to correctly discern nodal tissue from lymphatic channels. The surgeon who erroneously removes an empty SLN specimen loses the opportunity to apply the algorithm and to comprehensively stage the patient. The FIREs trial is a prospective multicenter cohort study of SLN mapping with indocyanine green (ICG) and fluorescence imaging for patients undergoing robotic hysterectomy and lymphadenectomy for endometrial and cervical cancers. This dataset was used to determine the positive predictive value of an identified SLN containing lymphatic tissue on final pathology and factors associated with false-positive mapping.

Methods: The pathology results of SLN and lymphadenectomy specimens from FIREs patients were evaluated for containment of nodal tissue. Surgeon factors (experience, case volume), patient factors (body mass index, age, weight, tumor stage), and case factors (estimated blood loss, case duration, time from injection) were evaluated for association with the removal of non-nodal SLN specimens. Kruskal–Wallis test and Wilcoxon tests were used to compare surgeons and surgeon factors. Patient and case factors were evaluated using logistic regression.

Results: Of the 177 patients who received ICG injections, 153 had positive SLN mapping (134 patients with endometrial cancer and 19 patients with cervical cancer). The positive predictive value for having confirmed nodal tissue in SLN specimens was 93%. Seventeen percent (24) of patients had at least one false-positive SLN mapped, and 7.2% of total SLNs removed contained no nodal tissue (35/488). Seventy-three percent of patients had bilateral pathology-confirmed SLNs. While some surgeons (n = 11) were statistically more likely to remove false-positive SLNs (P = 0.002), there were no associations with observed surgeon factors, patient factors, or case factors. When present, nodal metastases were identified in the SLNs in 100% of patients.

Conclusions: SLN mapping with ICG in endometrial and cervical cancers is associated with a 7% rate of empty (false-positive) SLN specimens and appears to be surgeon-dependent. The false-positive identification of SLNs did not affect the accuracy of the SLN technique in detecting metastatic disease, but it may have an impact on the accuracy of applying proposed intraoperative SLN algorithms.

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Objectives: It is well known that advanced-stage uterine papillary serous carcinoma (UPSC) has a poor prognosis. However, little is known about how clinical factors affect survival in the recurrent setting because most studies include all histologic subtypes of endometrial cancer. The objective of this study was to determine prognostic factors for survival among patients with recurrent, advanced-stage UPSC.

Methods: A retrospective review of patients diagnosed with stage III or IV UPSC between 1993 and 2012 was performed. Summary statistics were used to describe demographic and clinical characteristics. Overall survival (OS) and progression-free survival (PFS) were estimated with the Kaplan–Meier estimator. Cox proportional hazards regression was used to model the association of potential prognostic factors with OS and PFS.

Results: Of the 289 patients with advanced-stage UPSC identified, 203 (70%) recurred. Median age was 63 years (range, 30–91 years) and 68% were White. Median follow-up was 26 months (range, 1–173 months). Median time from initial treatment to first recurrence (FR) was 11 months (range, 1–143 months) and 6 months (range, 0–48 months) from FR to second recurrence (SR). Of the 213 patients who received chemotherapy during primary therapy, 81.2% received a platinum-containing regimen. At FR, 69.3% of patients treated with chemotherapy received a platinum regimen. Regimens at SR varied widely, including liposomal doxorubicin (17.1%) and platinum + taxane (8.1%). Radiologic evidence of disease in imaging. During surgical procedures, 16 (43.2%) patients had enlarged PLN and/or PALN, 4 (10.8%) had carcinomatosis, and 1 (2.7%) had ovarian metastasis. Only six (16.2%) patients did not have extraperitoneal disease or enlarged LN found during surgical procedure. Notably, only six (2.5%) in 243 patients without PLN metastasis had PALN metastasis, and only two (0.8%) patients had neither suspected extraperitoneal disease nor enlarged LN preoperatively or during surgical procedure. PALN metastasis was statistically related to PLN metastasis (P < 0.001), LVSI (P < 0.001), grade 3 tumors (P = 0.002), and deep myometrial invasion (>50%) (P < 0.001). In multivariate analysis, only pelvic LN metastasis (HR 26.4, 95% CI 7.5–92.2, P < 0.001) and deep myometrial invasion (6.32, 95% CI 1.24–32.0, P = 0.026) were maintained as independent risk factors for PALN metastasis.

Conclusions: PLN metastasis and deep myometrial invasion are risk factors for PALN metastasis. Our series supports the concept that PALN metastasis is very rare in the absence of pelvic LN metastasis or clinically suspicious extraperitoneal disease.

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398 — Poster Session

Oxidative stress biomarkers and risk of endometrial cancer
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Objectives: Obesity is a known risk factor for endometrial cancer as well as systemic inflammation-induced oxidative stress (OS). It is suggested that reactive oxygen species contribute to the carcinogenic process, including initiation, promotion, and progression. Our study sought to determine if two circulating markers thought to be indicative of systemic OS differed in women with and without endometrial cancer.

Methods: After institutional review board approval was obtained, plasma was collected from endometrial cancer patients undergoing surgery, patients undergoing surgery for benign disease, and a group of nonsurgical controls (n = 199). Plasma levels of 4-hydroxynonenal-modified proteins (4-HNE), total glutathione (GSH), and glutathione disulfide (GSSG) were obtained. Thiol levels were determined using a recycling assay, and levels were normalized to total protein using the BCA protein assay (Thermo Scientific). Levels of 4-HNE were determined by immunoblotting using antibody recognizing the Michael addition product of 4-HNE-modified cellular proteins. The measures of OS were then clinically correlated by performing a chart review to determine age, body mass index (BMI), grade, stage, histologic type, recurrence, and current disease status of patients with and without endometrial cancer. Statistical analysis was performed using Cox proportional hazard model for survival data and univariate as well as multivariate linear regressions.

Results: Oxidative markers appeared to be related to obesity and cancer. Univariate analysis demonstrated a relationship between increasing BMI and GSH (P = 0.02). Multivariate analysis resulted in a positive correlation between cancer and the percent of GSH as GSSG (P < 0.001) in the samples run as cancer vs. non-cancer. A similar association was identified between cancer and the percent of GSH as GSSG (P = 0.051) in the samples run as cancer, benign pathology, and no surgery controls.

Conclusions: Our study showed that markers of OS are significantly correlated with endometrial cancer when compared to patients without cancer. There also appears to be a correlation between increasing BMI and markers of oxidative stress. These biomarkers could be further evaluated as potential screening tools for patients at increased risk for the development of endometrial cancer.

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399 — Poster Session
Sensitivity of the intraoperative assessment of myometrial invasion in patients undergoing hysterectomy for endometrial cancer.
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Objective: The objective of this study was to determine the ability of the surgeon to distinguish between deep and superficial myometrial invasion on gross inspection as compared to frozen section.

Methods: All patients undergoing hysterectomy for endometrial cancer were eligible for this prospective study carried out at a single institution. After removal of the uterus, the specimen was bi-valved and then described as “superficial” or “deep” if the invasion did not or did extend into the outer half of the myometrial thickness, respectively. The specimen was sent for frozen section evaluation of tumor grade and depth of invasion (frozen). We calculated the sensitivity of each method, gross and frozen, to correctly identify deep myometrial invasion, the specificity to correctly identify superficial or no invasion, and the accuracy, defined as the number of true positives plus true negatives divided by the total number of cases. The final pathologic assessment of myometrial invasion (final) was considered the gold standard for comparison.

Results: Between 4/4/2011 and 4/9/2014, a total of 220 patients underwent hysterectomy by the division of gynecologic oncology in the San Diego area of Kaiser Permanente for a preoperative diagnosis of endometrial cancer. Of these, 196 had complete specimen information (gross, frozen, and final). On final, 35 specimens had deep invasion (17.9%). The sensitivity of gross to detect deep invasion was 54.3% and 77.1% for frozen. Specificity for gross and frozen was 93.8% and 98.8%, respectively. Gross inspection failed to identify deep myometrial invasion in 16 (45.7%) of the cases, frozen failed to identify deep myometrial invasion in 8 (22.9%) of the cases, and both gross and frozen failed to identify deep myometrial invasion in 7 (20.0%) of the cases.

Conclusions: Frozen section demonstrates greater accuracy and sensitivity in the intraoperative determination of deep myometrial invasion. This should be considered if intraoperative assessment is used to determine staging or treatment decisions.

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400 — Poster Session
New sentinel lymph node mapping technique by endometrial instillation of vital dye
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Objectives: Sentinel lymph node (SLN) techniques in endometrial cancer are less than ideal. We performed a feasibility study of a new SLN mapping procedure in patients with endometrial cancer.

Methods: We conducted a case series of SLN mapping, combining the technique of indocyanine green (ICG) cervical injection followed by intraperitoneal placement of a new vital dye with the use of an institutional review board–approved delivery device. ICG cervical injection at the 3 and 9 o’clock positions was first performed, followed by intra-abdominal entry. The fallopian tubes were then occluded using electrocoagulation and 5 mL of differently colored sentinel lymph node dyes (e.g., isosulfan blue) were directly instilled into the endometrial cavity and tumor. The primary outcome was a successful instillation of the dye and the secondary outcome was a successful identification of differently colored lymphatic channels and SLN.

Results: Thirteen patients consented, with an average age of 59 years (range, 46–82 years). The average uterine size was 126.5 g (range, 79–212 g). Intrauterine dye instillation using the new device was successful in 9/12 cases (one case was rescheduled). Failures included one cather occlusion, one catheter disconnection, and one undefined cause. In all instillation cases, the uterine fundus showed evidence of blue dye through to the serosa (9/9). In comparison, only one case of dyed fundus resulted from cervical dye injection (1/12). Four cases clearly demonstrated a new lymphatic channel after intrauterine instillation of a dye. This was evident by differences in the colors of the dyes used. Cervical injections demonstrated sentinel nodes in 9/12 cases (75%) vs. 7/12 cases of endometrial instillation (58%, P > 0.05). Complete lymph node dissection followed SLN biopsy in all 12 cases, with an average of 18 nodes (range, 11–30). All nodes, SN and otherwise, were histopathologically confirmed. No nodes were positive using any technique. Lymphatic channels were apparent using any dye delivery method immediately upon opening the retroperitoneum. There were no complications.

Conclusions: Instillation of lymph node dye into the endometrium and onto the tumor surface is more likely to be seen in the uterine fundus than is cervical injection of dye, suggesting that this new procedure identifies an important alternative lymphatic drainage.

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activity against breast cancer with HER2 amplifications. While up to 44% of uterine serous carcinoma (USC) harbor HER2 amplifications, Gynecologic Oncology Group 181B revealed that in patients with advanced/recurrent HER2-positive disease, trastuzumab produced minimal response. Our study sought to understand the effect of trastuzumab in HER2-amplified USC cell lines with or without PIK3CA mutations.

Methods: In total, 17 USC cell lines were evaluated for PIK3 mutations by whole exome sequencing and HER2 amplification using fluorescence in situ hybridization. Based on having HER2 gene amplification with or without PIK3 “hot spot” (exon 9 and 20) mutations, four cell lines were chosen for experiments with trastuzumab. Six-day proliferation/viability assays were carried out with scalar (from 0.01 μg/mL to 100 μg/mL) concentrations of trastuzumab to quantitate cell viability vs. 100% viable controls.

Results: A total of 41% of cell lines harbored HER2 amplification and 41% harbored PIK3 mutations. Of HER2-amplified, 57.1% harbored PIK3 mutations. In contrast, 20% without HER2 amplification were found to harbor PIK3 mutations. When the four cell lines with HER2 gene amplification were treated with trastuzumab, USC harboring oncogenic PIK3 mutations were highly resistant to trastuzumab compared with wild-type PIK3 cell lines (P = 0.02). A median inhibition concentration was not attained in PIK3-mutated cell lines.

Conclusions: In USC, increased PIK3/AKT/mTOR pathway signaling and overexpression of HER2 are associated with aggressive disease and poor prognosis. For the first time, we demonstrated that USC with HER2 gene amplification commonly harbor oncogenic PIK3CA “hot spot” mutations in exons 9 and 20. More importantly, USC with simultaneous HER2 amplifications and PIK3CA mutations are resistant to trastuzumab and, thus, more dependent on the mTOR pathway to confer increased growth and survival advantage. While assessment of PIK3 pathway activation may provide a biomarker to identify patients unlikely to respond to single-agent trastuzumab-based therapy, the greater dependency of HER2-amplified, PIK3-mutant USC cell lines to the PIK3/AKT/mTOR pathway suggest that trastuzumab combined with PIK3/AKT/mTOR inhibitors may represent a novel strategy against this subset of chemotherapy-resistant USC.

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403 — Poster Session
Survivors of uterine malignancy have greater healthcare needs than the general population
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Objective: The objective of this study is to compare the comorbidities of women with uterine malignancy (UM) to controls so as to aid in development of survivorship care plans and programs.

Methods: This retrospective cohort study using the University HealthSystem Consortium database evaluated women older than the age of 17 years who had a hysterectomy for UM between October, 2010 and March, 2014. Women without UM undergoing hysterectomy during the same time period served as controls. Frequencies and odds ratios (OR) of 26 distinct comorbidities were calculated for women with UM as compared to those without UM. Mantel Haenszel-stratified OR was used to correct for different age distributions between the UM and control groups using UHC predetermined age groups. Significance was defined as P < 0.05.

Results: A total of 23,563 patients in the dataset had UM, and 142,610 patients were controls. Prior to stratification by age group, OR < 1, P < 0.05 were found for six comorbidities and OR > 1, P < 0.05 were found for 18 others. Uncorrected OR of ≥2 were found for hypertension (HTN), diabetes (DM), obesity (OB), congestive heart failure (CHF), pulmonary circulation diseases (PCD), peripheral vascular disease (PVD), and renal failure (RF) (Table). Higher OR for UM remained significant after stratification by age as follows: HTN (OR = 1.7), DM (OR = 2.1), OB (OR = 3.3), CHF (OR = 1.5), PCD (OR = 1.7), and RF (OR = 1.2). The lowest ORs were seen for acquired immune deficiency syndrome (OR = 0.17), chronic blood loss anemia (OR = 0.36), and drug abuse (OR = 0.38).

Conclusions: UM survivorship programs should plan for two to three times the need for management of HTN, DM, OB, CHF, PCD, and RF compared to the health care needs of the general public and between 20% and 300% greater needs compared to a population with comparable age distribution. Optimizing healthcare for UM survivors is enhanced by a comprehensive survivorship care plan. Appreciation of how the resources required differ from those required for the general population should facilitate planning and executing suitable and effective programs. Our findings suggest that provider education and provision of resources pertinent to patients with metabolic syndrome will be important components of effective UM survivorship care.

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402 — Poster Session
Green (IGC) fluorescence directed sentinel lymph node (SLN) biopsy in women with endometrial and cervical cancer
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Objectives: Determining which endometrial and cervical cancers patients will benefit from nodal staging is controversial. Sentinel lymph node (SLN) biopsy can be useful as an adjunct to lymphadenectomy in high-risk patients, but more importantly is employed as an alternative method of nodal evaluation for patients with low-risk tumors. The objectives of this study were to evaluate the surgical learning curve and to examine the performance characteristics of SLN dissection.

Methods: This was an institutional review board-approved observational study examining women who had an isolated indocyanine green (ICG) SLN dissection or an ICG SLN dissection with a complete lymph node dissection (CND). Women who underwent an ICG SLN dissection from June 1, 2013 to August 5, 2014 were analyzed. STATA9 statistical software was used to analyze the database.

Results: A total of 100 patients (94 endometrial and 6 cervical cancers) were identified. The mean age was 63.4 years and 76% of the tumors were endometrioid, 18% were other endometrial tumors, and 6% were small cell cancer of the cervix. SLN was identified in 79% (160/200) of nodal basins, with 66% bilateral detection. Detection of bilateral SLNs was influenced by a learning curve; in the first 10 cases, bilateral SLNs were detected in only 56.1% (32/57) of cases. If a surgeon had done > 10 cases, however, bilateral SLNs were detected in 79.1% (34/43) (P = 0.01). Twenty-eight patients had both SLN and bilateral CND performed, with a total of 73 nodal basins analyzed. SLN biopsy achieved a sensitivity of 90.9% with a specificity of 100%. The SLNs were external iliac (46.1%), obturator (48.1%), common iliac (2.4%), and aortic (2.9%), while positive nodes were either external iliac (47.1%) or obturator (52.9%). SLNs were the only positive nodes in 63.6% (7/11) of the patients; both SLNs and non-SLNs were positive in 27.3% (3/11). Microscopic metastasis in the SLN was detected in 36.4% (4/11) of patients. In one patient, a negative SLN was identified and there was a positive non-SLN on the ipsilateral nodal basin, which is a false-negative SLN rate of 9.1% (1/11).

Conclusions: The bilateral SLN detection rate significantly improved after the surgeons’ first 10 cases. SLN evaluation accurately reflects the nodal basin status for metastatic disease and can identify micrometastasis that may not have been detected with standard nodal evaluation.

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serous carcinoma
recurrence in patients with stage I non-invasive uterine papillary
Adjuvant vaginal brachytherapy decreases the risk of vaginal
—

404

doi:10.1016/j.ygyno.2015.01.406

Objectives: To investigate the impact of adjuvant vaginal brachytherapy on the risk of vaginal recurrence in stage I noninvasive uterine papillary serous carcinoma (UPSC).

Methods: This retrospective study involved four United States academic centers from 2000 to 2012. Only patients with noninvasive (limited to the endometrium) stage IA UPSC were included. All patients underwent surgical treatment with at least total hysterectomy. The Kaplan–Meier method and Cox proportional hazards regression modeling were used.

Results: Among 103 patients whose median age was 66 years (range, 49–90 years), 85% (88/103) underwent staging lymphadenectomy and 55% (59/103) had omentectomy. Postoperatively, 41% (47/103) were observed, 20% (21/103) received chemotherapy, and 38% (39/103) received vaginal brachytherapy + /− chemotherapy. A total of 28.2% (29/103) patients developed recurrence. The rate of vaginal, pelvic, and extrapelvic recurrences were 7.8% (8/103), 3.9% (4/103), and 16.5% (17/103), respectively. Among patients who were observed or received only chemotherapy, the rate of vaginal recurrence was 10.9% (7/64) compared to 2.6% (1/39) among those who received vaginal brachytherapy + /− chemotherapy (P=0.035). The rate of vaginal recurrence was not significantly different between those who were observed compared to those who received only chemotherapy (9.3% vs. 14.3%, P=0.27). The 5-year progression-free survival (PFS) and overall survival (OS) for the entire cohort were 88.3% and 90.6%, respectively. Patients who underwent lymphadenectomy had longer PFS (P=0.001) and OS (P=0.0005) compared to those who did not have lymphadenectomy. In multivariable analysis controlling for age, chemotherapy, brachytherapy, and lymphadenectomy, only lymphadenectomy was an independent predictor of PFS (HR 0.28, 95% CI 0.11–0.71, P=0.0037) and OS (HR 0.27, 95% CI 0.10–0.71, P=0.0035). Neither chemotherapy nor brachytherapy were a predictor of PFS or OS.

Conclusions: In this largest study reported in stage I noninvasive UPSC, the majority of recurrence were extrapelvic. Vaginal brachytherapy has a significant role in reducing the risk of vaginal recurrence, and surgical staging was the only predictor of outcome. Therefore, both should be considered in stage I noninvasive UPSC.

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405 — Poster Session

Trends and outcomes with utilization of plastic surgery for vulvar closure following vulvectomy for invasive squamous cell cancer
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Objective: The objective of this study was to determine trends in utilization of plastic surgery consultation for vulvar closure following vulvectomy for invasive squamous cell cancer (iSCC).

Methods: This retrospective cohort study involved women who underwent vulvectomy for iSCC from January 1, 2004 through October 31, 2013 at Brigham and Women’s Hospital (BWH). Patients with iSCC present on pathology specimens were included. Slides were reviewed and margins determined by two pathologists. Clinical data were collected and statistically analyzed using XLSTAT-Pro v2014.2.02.

Results: A total of 88 vulvectomies with iSCC on final pathology were identified during the study period. Fifteen (17%) had plastic surgery involvement and 73 (83%) did not. Median age was 69 years (range, 32–92 years). There was no difference in FIGO stage between groups, with a majority in both groups having stage I disease (80% and 70%, respectively). In the plastic surgery group, there were significantly more patients with diabetes mellitus (47% vs. 16%, P=0.01), hypertension (87% vs. 52%, P=0.013), recurrent disease (60% vs. 11%, P<0.001), history of vulvectomy (27% vs. 11%, P=0.001), and history of radiation therapy (33% vs. 5%, P=0.001). Tumors were significantly larger in the plastic surgery group (3.73 cm vs. 2.03 cm, P=0.001), yet there was no significant difference in achieving negative surgical margins (93% vs. 92%, P=0.84). For tumors of ≥3 cm, plastic surgery was significantly associated with achieving adequate margins of ≥8 mm (50% vs. 7%, P=0.039). The overall rate of postoperative complications was 41% and the rate was higher for cases involving plastic surgery (67% vs. 36%, P=0.04). On univariate analysis, plastic surgery involvement (28% vs. 10%, P=0.036), average tumor diameter (2.65 cm vs. 2.04 cm, P=0.078), and preoperative radiation (89% vs. 11%, P=0.003) were associated with complications. On multivariate analysis, only preoperative radiation was an independent, significant predictor of postoperative complications (OR 10.26, 95% CI 1.1–90.9).

Conclusions: A review of BWH utilization confirms that the most complex patients with the largest lesions comprise the majority of cases that involve plastic surgery. Negative margins are equivalent and adequate margins in tumors of ≥3 cm are significantly improved by plastic surgery involvement, but a plastic surgery-assisted closure does not appear to affect postoperative complications.

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406 — Poster Session
Comparing the natural history and survival of vulvar sarcoma and squamous cell carcinoma: An analysis 11,677 cases in the Surveillance, Epidemiology, and End Results database

Objectives: Sarcomas of the vulva are poorly understood tumors that account for about 3% of vaginal malignancies. We examined the natural history and survival outcomes of vulvar sarcomas compared to squamous cell carcinoma (SCC) in a large United States cohort.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was used to identify all women with primary invasive vaginal sarcomas and SCCs diagnosed between 1988 and 2010. Parametric and nonparametric methods were used to compare the demographic and clinical characteristics between sarcoma and SCC patients as well as between sarcoma histologic subtypes. Survival was examined using multivariate Cox proportional hazards models and the Kaplan–Meier method.

Results: A total of 261 cases of invasive vulvar sarcoma and 11,416 cases of SCC were identified in the study period. Among women with vulvar sarcomas, fibromatous histologies accounted for the largest subset with 89 cases (34.1%), followed by myomatous histologies with 72 cases (27.6%). Compared to women with SCC, patients diagnosed with vulvar sarcoma tended to be younger, have incomplete staging, have larger tumors with less regional extension, and be treated primarily with surgery without radiation (P < 0.05 for all). After adjusting for prognostic and confounding variables, patients with vulvar sarcomas had a similar risk of cancer-related mortality (HR 1.32, 95% CI 0.93–1.86) and overall mortality (HR 0.82, 95% CI 0.63–1.07). Modeling for prognostic indicators in sarcoma patients revealed no significant difference in cancer-specific survival between sarcoma subgroups.

Conclusions: Despite higher rates of incomplete staging, vulvar sarcoma patients exhibit similar survival outcomes to SCC patients.

doi:10.1016/j.ygyno.2015.01.409

407 — Poster Session
The role of endometrial biopsy in the preoperative detection of uterine leiomyosarcoma

Objectives: To assess the sensitivity of preoperative endometrial biopsy in uterine leiomyosarcoma (ULMS) by sampling technique and in varying clinical presentations.

Methods: This was an institutional review board-approved retrospective chart review of all cases of ULMS treated at participating institutions between January 2005 and August 2012. Data abstracted included demographics, preoperative evaluation, presenting symptom, preoperative biopsy, surgical management, pathology, and clinical outcomes.

Results: A total of 329 cases were identified, of which 166 (50%) had complete clinical data. Sixty-eight patients (41%) had endometrial sampling prior to surgery; 98 patients (59%) did not. Of those sampled, 43 (63%) underwent Pipelle endometrial biopsies and 25 (37%) had dilation and curettage (D&C). Thirty-five of 68 (51.5%) patients had preoperative biopsies showing ULMS or specifically concerning for malignancy. There was no significant difference in sensitivity based on sampling type (48.8% vs. 56.0%, P = 0.57). In patients who presented with postmenopausal bleeding (27/68), endometrial sampling was significantly more likely to detect malignancy (51.5% vs. 85.2%, P < 0.0001). Conversely, in those with menorrhagia (22/68), endometrial sampling was significantly less likely to detect malignancy (51.5% vs. 27.3%, P < 0.005). No significant differences were seen in sensitivity of endometrial sampling by age or other presenting symptoms of abdominal pain, bloating, or distension.

Conclusions: Preoperative endometrial biopsy with a Pipelle or a D&C can identify malignancy in approximately 50% of patients with ULMS. However, the sensitivity of endometrial biopsy significantly increases in those patients presenting with postmenopausal bleeding. Conversely, the sensitivity of endometrial sampling is significantly decreased in patients with menorrhagia, and benign results should be interpreted with caution if suspicion for ULMS is high.

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408 — Poster Session
Trends in the treatment of uterine leiomyosarcoma in the Medicare population
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Objectives: Uterine leiomyosarcoma (LMS) is a relatively rare malignancy that is associated with a poor prognosis. The rarity of LMS has led to a lack of consensus regarding appropriate treatment. The goal of this study was to identify the role of chemotherapy and radiotherapy in treatment of uterine LMS in the United States as well as the effectiveness of adjuvant treatment.

Methods: We used the Surveillance Epidemiology, and End Results-Medicare database to gather information on uterine LMS patients older than 66 years diagnosed between 1992 and 2009. Basic demographic and clinical characteristics were collected. A logistic regression model analysis was performed to determine predictors of treatment. Cox proportional hazards models were used to identify clinical parameters and treatment strategies associated with survival differences.

Results: Our final study group included 230 patients. The rate of use of chemotherapy and radiotherapy in the treatment of patients with uterine LMS increased over the time period investigated. However, we identified no significant survival advantage associated with either mode of therapy. The strongest predictor of survival was stage at diagnosis. The logistic regression model analysis revealed that age at diagnosis, treatment year, cancer stage, and underlying health status were all independent predictors of chemotherapy. Age at diagnosis and treatment year were also predictors of radiation therapy.

Conclusions: The increasing rates of chemotherapy and radiotherapy use in this population appear to be unfounded, given the lack of survival benefit. Further investigation into alternative treatment regimens is merited. The prognostic significance of stage at diagnosis indicates the importance of improving early detection of uterine LMS.

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409 — Poster Session
Small cell neuroendocrine carcinoma of the cervix: Does treatment sequence and type of hysterectomy improve outcomes?
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Objectives: Small cell neuroendocrine cervical cancer is rare, with a high propensity for distant metastasis, and there is no consensus on optimal treatment. Treatment of early-stage disease usually involves a combination of chemotherapy, radiation therapy (RT), and surgery. Our goal was to assess the outcomes of various treatment modalities and sequences of treatments and to identify prognostic factors associated with survival.

Methods: Patients with small cell neuroendocrine cervical cancer reported to the National Cancer Database from 1998 to 2011 who underwent at least a total hysterectomy (radical or simple) were selected. To exclude for potentially palliative interventions, we included only patients with stage I–IIA disease for this analysis. Overall survival (OS) was estimated by 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 two-tailed, with threshold significance level set at \( P < 0.05 \).

Results: A total of 1708 small cell neuroendocrine cervical cancer patients were identified, and 249 patients met inclusion criteria. Increasing tumor size was significantly associated with nodal positivity (14%, 26%, 34%, and 63% for tumor sizes ≤2 cm, 2.1–3 cm, 3.1–5 cm, and >5 cm, respectively, \( P = 0.001 \)). Lymph node metastasis was significantly associated with worse survival (median OS 15 vs. 71 months for lymph node-positive and -negative, respectively, \( P = 0.012 \)). No other factors were found to be associated with survival on univariate analyses, including age, stage, comorbidity index, tumor size, type of surgery, margin status, use of chemotherapy, and use of RT. On multivariable analysis using historically significant factors of cervical cancer survival, including age, race, comorbidity index, stage, tumor size, RT, chemotherapy, and hysterectomy type, only positive nodal status (HR 4.317, 95% CI 1.132–16.464, \( P = 0.032 \)) significantly predicted survival.

Conclusions: Nodal metastasis is a poor prognostic factor in small cell neuroendocrine tumor of the cervix. The type of hysterectomy, receipt of chemotherapy, or timing of radiation (adjuvant vs. neoadjuvant) did not appear to affect OS. Optimal treatment of this disease remains elusive.

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411 — Poster Session
Evaluation of the number of copies of the TOP2A gene and its protein expression in uterine leiomyosarcoma
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Objectives: Leiomyosarcomas account for only 1% to 2% of uterine cancers but have generally poor outcome. The main treatment remains surgery, and the prognostic value of adjuvant chemotherapy is uncertain. Moreover, one of the most active agents is anthracyclines, which act to block TOP2A. The aim of this study was to evaluate Top2A protein expression and the TOP2A gene and their value as prognostic markers in uterine leiomyosarcomas.

Methods: We analyzed a retrospective series of 104 patients treated for uterine leiomyosarcomas from 1982 to 2010 at AC Camargo Cancer Center. Pathology slides were reviewed. Thirty-seven cases were suitable for analysis and subjected to immunohistochemistry and fluorescence in situ hybridization studies for TOP2A.

Results: The median age was 50.2 years (range, 27–84 years). Eighteen (48.6%) were FIGO stage I, 6 (16.2%) stage II, 4 (10.8%) stage III, and 9 (24.3%) stage IV. Six (27.2%) stage I and II patients received adjuvant chemotherapy, and five (22.7%) radiotherapy. Twenty-four (64.9%) of 38 cases had mitotic index > 20/10 high-power field (hpf) and 19 (51.4%) had intense atypia. Twenty-one (56.8%) patients had high expression of Top2A protein. Patients with FIGO stage ≥ II had higher Top2A expression (73.7% vs. 38.9%, \( P = 0.033 \)) as well as mitotic index > 20/10 hpf (70.8% vs. 30.8%, \( P = 0.036 \)). Nineteen (63.3%) of 30 cases had normal numbers of copies of the TOP2A gene, while 11 (36.7%) had abnormal copies: 8 (72.7%) gene amplification, 2 (18.8%) polysomy, and 1 (9.1%) trisomy. The number of copies did not correlate with clinicopathologic variables. There was no correlation between the number of copies of TOP2A gene and Top2A protein expression (\( P = 0.44 \)). After the median follow-up of
21 months, 16 (43.2%) patients recurred (42.1% local, 47.4% distant, and 10.5% both local and distant recurrence). The median disease-free interval was 12 months (range, 4.6–69 months). The median survival was 21.6 months. In multivariate analysis, tumor size > 8 cm and presence of disease outside the uterus negatively affected survival. Top2A protein expression and copies of TOP2A gene had no impact in outcome.

**Conclusions:** Our data suggest that tumor size and advanced disease stage are prognostic factors in uterine leiomyosarcoma. Top2A protein is more expressed in high-mitotic index tumors and in more advanced stages and, therefore, may be an indicator of tumor aggressiveness.

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**412 — Poster Session**

**Comparison of EP regimen for treatment of gestational trophoblastic neoplasia with 5-FU + KSM regimen and the analysis of resistance related factors**

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**Objectives:** To compare the etoposide-cisplatin (EP) regimen for treatment of gestational trophoblastic neoplasia (GTN) with 5-fluorouracil (5-FU) + actinomycin (KSM) and analyze drug resistance-related factors.

**Methods:** We conducted a retrospective study of 134 patients with high-risk GTN at the Qilu Hospital of Shandong University, a tertiary referral center, between January 2003 and January 2013. We statistically analyzed the two different treatment groups to identify related factors that affected drug resistance.

**Results:** Among the 96 patients who received the EP regimen, 74 (77.1%) attained complete remission. Of the 38 patients who received the 5-FU + KSM regimen, 24 (63.2%) achieved complete remission. The difference was not statistically significant (P = 0.359). Among the 86 patients in the EP regimen subgroup whose prognostic score was less than 13, 72 (83.7%) had complete remission compared with 2/10 (20.0%) in the EP regimen subgroup whose prognostic score was more than 12 (P = 0.007). A descending trend in serum human chorionic gonadotropin (hCG) levels after the first course of chemotherapy was revealed as a risk factor. Patients were divided into two groups according to whether serum hCG values were lower than one-tenth of pretreatment hCG. Complete remissions were seen in 66/80 (82.5%) in the positive group and 6/18 (33.3%) (P = 0.004).

**Conclusions:** There was no statistically significant difference in efficacy between 5-FU + KSM and EP regimens for treatment of GTN. However, acute adverse effects of the 5-FU + KSM regimen were more serious. In addition, a prognostic score of more than 12 and serum hCG more than one-tenth of pretreatment hCG after the first course chemotherapy may represent risk factors related to drug resistance.

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**413 — Poster Session**

**Utility of risk-weighted surgical pathological risk factors in predicting survival outcomes among women with vulvar cancer: A population-based study**


**Objectives:** To evaluate the utility of a risk-weighted surgical pathological (RWSP) scoring system in predicting survival outcomes in the setting of vulvar squamous cell carcinoma when compared with conventional staging systems.

**Methods:** We obtained population-based data from the California Cancer Registry (CCR) on patients diagnosed with invasive squamous cell carcinoma of the vulva between 1998 and 2013 who had undergone primary surgical treatment. Univariate and multivariate analyses were performed on the 680 women with complete information. The goal was to determine the relationship between age, race, FIGO/AJCC stage, and four pathological risk factors (tumor size, grade, depth of invasion, and nodal status). HR for each level of each risk factor was determined and the sum was determined per case. Survival curves were evaluated based on the HR-weighted scores.

**Results:** More than 74% of the study population was non-Hispanic White, with a median age of 68 years. Median survival time was 57 months. Univariate analysis showed all pathological risk factors, stage, age, and race to be significantly related to cumulative risk of death. A Cox proportional hazard model containing the pathological risk factors and age had more predictive power than a model containing stage and age. We based our RWSP score on the HRs from this multivariate model. The RWSP was significantly associated with cumulative risk of death (X² = 242.40, P < 0.0001). A model containing risk score alone had more predictive power than a model containing both stage and age. No statistical benefit was conferred by keeping stage in a final model (LR X² = 6.19, P = 0.10). A model including risk score alone was the best and most parsimonious predictive model for cumulative risk of death.

**Conclusions:** When the combined magnitude of the risk of death associated with specific pathological factors was considered, pathological risk factors were more predictive of cumulative risk of death than conventional stage in this retrospective large, population-based cohort of women with invasive squamous cell vulvar carcinoma. Our RWSP scoring system correlates with conventional stage and is better able to predict overall survival.

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**414 — Poster Session**

**A retrospective assessment of the role of radiation in treatment of uterine carcinosarcoma**


**Objectives:** To assess whether primary adjuvant treatment with chemotherapy alone (CT) produces equivalent outcomes as pelvic radiotherapy (RT) or combined sequential treatment modalities using chemotherapy and radiation (CRT) for patients with stages I–IV uterine carcinosarcoma (CS).

**Methods:** Charts of 61 women treated from 1988 to 2013 for stage I–IV CS at a single institution were reviewed. Primary adjuvant therapy was initiated in 53 (87%), with 28 (53%) receiving RT or CRT and 25 (47%) receiving CT. Patients were assessed for progression-free survival (PFS), overall survival (OS), and pelvic recurrence rate (PRR). All statistical analysis was performed using Science Analysis Software version 9.2. Survival analysis was performed using a Kaplan–Meier survival analysis.

**Results:** Controlling for stage of disease, the median PFS of those receiving RT or CRT compared with CT was 9.6 months (95% CI, 0.7–13.8) and 12.6 months (95% CI, 4.0–26.4), respectively (P = 0.31). Median OS was 20.6 months (95% CI, 6.5–56.9) for the RT or CRT group vs. 31.7 months (95% CI, 14.7–86.4) for CT (P = 0.11). Subanalysis was performed comparing CT ± CRT with RT. The median PFS and OS for RT were 7.1 months (95% CI, 1.6–13.8) and 12.6 months (95% CI, 5.0–20.6), respectively. There was a trend toward improved median PFS (P = 0.15) and a statistically significant improvement in median OS.
favoring CT over RT ($P = 0.02$). Median PFS and OS for a group receiving CT or CRT were 10.7 months (95% CI, 4.3–19.9) and 30.5 months (95% CI, 14.6–64.2), respectively. There was a trend toward improvement in median PFS ($P = 0.14$) and a statistically significant difference in median OS ($P = 0.02$) favoring the group receiving CT or CRT vs. RT. Pelvic recurrence occurred in 12/26 (46%) receiving either RT or CRT and 9/16 (56%) receiving CT ($P = 0.53$).

**Conclusions:** CT is the most important component in treatment of uterine carcinosarcoma, whereas RT may have only a limited role. Utilization of CT or CRT showed a trend toward improved median PFS and a significant improvement in median OS when compared to RT alone. This study did not show a significant improvement in local disease control for patients receiving pelvic radiation, but it was not significantly powered to do so. doi:10.1016/j.ygyno.2015.01.417

415 — Poster Session

**Identification of somatic mutations in uterine leiomyosarcomas**

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**Objectives:** To identify somatic mutations and other DNA alterations associated with leiomyosarcoma development.

**Methods:** After institutional review board approval, leiomyosarcoma samples and matched normal tissue for nine patients were obtained. Genomic DNA was purified. Whole exome sequencing (targeted sequencing of gene-encoding DNA regions) was performed. Average base coverage was 101.6-fold. Ten or more reads were represented in 96.3% of bases. GEMINI software variant analysis was used to identify 895 non-synonymous mismatches. Variant number ranged from 47 to 327, with an average of 160 mismatches per sample. DNA variants present in two or more tumor-normal sets were selected. Seventy-one mutations were identified in a total of 31 genes. DNA variants were classified as somatic mutations if they met these criteria: (1) the number of distinct reads in the tumor sample was at least 5 times greater than the number of tags in the paired normal sample and (2) at least 10 tags were present in the paired normal sample. Twenty-three somatic mutations were identified. Internal validation was performed by sequencing 20 paired tumor-normal single nucleotide variants. The Cancer Genome Atlas (TCGA) sarcoma database was used for external validation to determine the prevalence of the somatic mutations within a larger data set of 82 soft-tissue sarcomas.

**Results:** In the discovery set, three samples contained putative somatic mutations in TP53 tumor suppressor. Genes encoding for calcium channel, collagen, and myosin protein were also altered in two or more samples. Whole exome sequencing findings were confirmed using an alternative sequencing method (Ion Torrent) in 35 of the 40 reactions (87.5% validation rate). Recurrent somatic mutations were found in seven genes. External validation using TCGA sarcoma database showed mutations in one or more of the seven genes in 9/15 (60%) female uterine/pelvic leiomyosarcomas and in 28/82 (34.2%) of all soft-tissue sarcomas. The majority of alterations were single nucleotide variants in the TP53 gene.

**Conclusions:** Using whole exome sequencing, seven genes harboring recurrent somatic alterations were identified in uterine leiomyosarcoma samples. At least one of these mutations was present in more than half of an additional series of 15 female pelvic sarcomas. When 82 soft-tissue sarcomas were analyzed, almost 35% contained mutations in one or more of the seven genes.

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416 — Poster Session

**Perivascular epithelioid cell tumor (PEComa) of the gynecologic tract: A single institution clinicopathologic review**

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**Objectives:** To describe the clinicopathologic features of patients diagnosed with perivascular epithelioid tumor (PEComa) and malignant PEComa of the gynecologic tract, rare tumors about which there are limited extant data.

**Methods:** All patients diagnosed with PEComa were identified in our institutional database. The diagnosis of PEComa was made by experienced gynecologic pathologists at our institution. Tumors were classified as malignant PEComa if they had two or more of the following features: size ≥ 5 cm, high-grade nuclear features, infiltration, necrosis, lymphovascular space invasion, and mitotic rate ≥ 1/50 high-power field (hpf). Tumors exhibiting only one of these features were classified as PEComas of uncertain malignant potential.

**Results:** We identified 22 patients between 1/2000 and 6/2014 with PEComa of the gynecologic tract. Median age was 56 years (range, 18.3–73.6 years). Most patients met criteria for malignant PEComa (n = 17, 77.3%). Fifteen patients (68.2%) were diagnosed with uterine-confined disease. Median tumor size was 6.1 cm (range, 1–16 cm). Median mitotic rate was 35/50 hpf (range, 0/50 hpf to 200/50 hpf). Frequently positive immunohistochemical markers were: HMB-45 (18, 81.8%), A103 (Melan-A) (8, 36.4%), desmin (12, 54.5%), and caldesmon (9, 40.9%). Fifteen patients (88.2%) with malignant PEComa were observed after diagnosis, and adjuvant therapy was administered in three (17.6%) cases. No recurrences were noted in patients with PEComa or PEComa of uncertain malignant potential. Ten (58.8%) patients with malignant PEComa recurred. Surgical resection, cytotoxic chemotherapy, mTOR inhibitors, radiation, and hormone therapy were all employed in the recurrent setting. Of four patients treated with mTOR inhibitors, two remain in remission after 6.8 and 10 months, respectively; two patients progressed after 0.7 and 1.7 months. Median follow-up for the entire cohort was 47.1 months (range, 3.0–161.4 months). Median recurrence-free survival was 34.1 months (95% CI 28.8–38.3). No deaths were reported.

**Conclusions:** PEComa of the gynecologic tract is a rare tumor and most exhibit features compatible with malignancy ("malignant PEComa"). Patients diagnosed with malignant PEComa recurred frequently but often not until after 2 years of follow-up. Therefore, close follow-up and surveillance of these patients is warranted.

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417 — Poster Session

**The GRO-SnaPET study: Preliminary data on the prediction of lymphonodal status by sentinel lymph node biopsy combined with 18FDG-PET/CT to overcome the current limits of vulvar cancer treatment**


**Objectives:** To verify the accuracy of sentinel node biopsy (SNB) combined with F-18-fluorodeoxyglucose (18F-DG) positron emission tomography (PET)/computed tomography (CT) scan in cN0 invasive vulvar cancer (IVC) patients currently not candidates for SNB according to standard guidelines.
Methods: From July 2013 to September 2014, the GRO-SNaPET phase II study enrolled all IVC patients admitted to the Division of Gynecologic Oncology of the Catholic University of the Sacred Heart with clinically negative inguinofemoral lymph nodes (LNs) and bulky/multifocal/bilateral IVC or absent disease after diagnostic complete excision. Patients submitted to previous chemotherapy or radiotherapy were excluded. All women underwent preoperative evaluation by standard imaging (CT scan, ultrasonography, fine-needle aspiration cytology if required) combined with 18F-FDG PET/CT. The surgical treatment included tumor radical excision and uni/bilateral SNB, followed by systematic inguinofemoral lymphadenectomy (IFL).

Results: Fifteen IVC patients with negative CT scans (median age 71 years; range, 54–87 years) were included. 18F-FDG PET/CT reported suspected LNs in 9/30 (30%) groins. Surgery consisted of six partial and nine radical vulvec tomies and four uni- and 11 bilateral SNBs, followed by IFL. A total of 26 IFLs were performed. A median number of two SNs (range, 1–7) and eight total LNs (range, 4–14) were removed for each groin. Six of 26 (23%) groins were histologically metastatic and SN was always positive; in four cases, no other metastatic node was identified. The SNB false-negative rate was 0 (accuracy and negative predictive value 100%). In only one case was PET falsely negative (false-negative 4%; sensitivity 83%, specificity 80%, accuracy 81%, negative predictive value 94%).

Conclusions: Our preliminary data suggest that 18F-FDG PET/CT allows a reliable assessment of LN status. Moreover, despite restrictions in the current recommendations, SNB seems to be oncologically safe, even in cN0 patients currently excluded from this procedure. Larger series are necessary to confirm these data.

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419 — Poster Session
Epidemiology of gestational trophoblastic disease in Hawaii:
A retrospective review
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Objectives: To re-examine the epidemiology of molar pregnancy, choriocarcinoma, and placental site trophoblastic tumor (PSTT) and to compare these results with prior data from Hawaii, a locale with a racially diverse population and preponderance of Asians.

Methods: A retrospective search was undertaken at five community hospitals in Hawaii for gestational trophoblastic disease (GTD) diagnosed during the study period of January 2005 to December 2013. During this time period, 87,641 naturally terminating pregnancies (NTP) were examined, including 78,744 live deliveries, 7347 miscarriages, 1080 ectopic pregnancies, and 470 fetal demise. Our findings were compared to the results of studies conducted in Hawaii 3 decades previously.

Results: Our search identified 196 GTDs, including 126 complete moles (CM) and 62 partial moles (PM) (CM/PM ratio 2.03), 3 choriocarcinomas, and 5 PSTTs. Patient ages ranged from 15 to 53 years (median, 31 years), with 12.8% < 20 years, 67.6% 20–39 years, and 19.6% ≥ 40 years. For ages 20–39 years, the GTD rate was 1/664. For those <20 years, the rate was increased 2.3-fold (1/260), while for those ≥40 and older, the rate was increased 4.8-fold (1/125). The molar pregnancy rate was higher than noted in prior studies at 21.5/10,000 or 1/466 NTPs (compared to 1/826 previously), with a CM rate of 1/695 (vs. 1/769 previously) and a PM rate of 1/1413 (vs. 1/2183 previously). The incidence of choriocarcinoma and PSTT was 0.57 and 0.34 per 10,000 NTPs, respectively. There was no decline in GTD rates between 2005 (1/439) and 2013 (1/489).

Conclusions: Despite global data suggesting that molar pregnancies may be decreasing, there was no significant decline in GTD incidence during our 9-year study. Our study confirmed a bimodal age distribution, with a higher percentage of moles detected in our ≥40-year-old patients (19.6%) compared to previous studies (6.7%). We found a higher overall molar pregnancy rate, partially owing to this increase in older patients. We also observed more PMs in our current study compared to prior reports, possibly due to the advent of more definitive confirmatory tests for PM. This is the first study to examine the incidence of choriocarcinoma and PSTT in Hawaii, which was similar to those previously described in other Asian populations.
Identifying therapeutic options in small cell cervical cancer by multiplatform evaluation of biomarker alterations


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Objectives: Small cell cervical cancer (SCCC) is an extremely rare and aggressive form of cervical cancer. Approximately 150 cases are diagnosed in the United States each year, with few therapeutic options. We evaluated tumor samples to determine what percentage of patients may have targetable molecular aberrations.

Methods: Seventy-five SCCC samples were profiled, 50 using a commercial multiple platform, including a combination of gene sequencing (Sanger, next-generation sequencing [NGS]), protein expression (immunohistochemistry [IHC]), and gene amplification (chromogenic in situ hybridization [CISH] or fluorescence in situ hybridization [FISH]), and 25 at a cancer center using a 50-gene NGS platform (CMS50). The results were compared to ~800 human tumors. Potential druggable mutations include AKT1, KRAS, PIK3CA, and TP53.

Results: Eighty-nine patients met our inclusion criteria. Thirty-five percent were FIGO 2009 stage I, 8% stage II, 36% stage III, and 21% stage IV. The median PFS was 18.4 months (95% CI 14.5–22.2) and the median OS was 24 months (95% CI 19.2–28.1). Patients with depression had a median PFS of 10.9 months compared to 21.2 months (P = 0.005) for nondepressed patients. OS was also significantly higher in nondepressed patients (27.7 vs. 12.9 months, P < 0.005). Interestingly, stage did not differ among depressed vs. nondepressed patients. Univariate survival tests also showed an improved survival for patients who received postoperative radiation therapy (P = 0.008) or had a lymphadenectomy performed (P = 0.04182). Tumor size (P = 0.004), depth of invasion (P = 0.004), and lymphovascular space invasion (P = 0.002) were significantly associated with survival.

Conclusions: Uterine CS is a rare tumor type that carries a poor prognosis compared to other uterine cancers. Our data indicate that depression may be associated with an even poorer prognosis. Treatment of neurobehavioral stress may have therapeutic implications for management of uterine CS.

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422 — Poster Session
The role of adjuvant therapy in early stage high grade uterine leiomyosarcoma


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Objectives: Uterine leiomyosarcoma is a rare disease. Although the majority of patients present with early-stage disease, the risk of recurrence is high. The goal of this study was to determine the role of adjuvant chemotherapy in patients with stages I–II high-grade uterine leiomyosarcoma.
Methods: A retrospective review of all women with stages I–II leiomyosarcoma treated at two institutions from 1988 through 2009 was performed. Data were collected on patient age, stage of disease, types of surgical procedure, types of adjuvant treatment (if any), recurrence, and survival.

Results: Fifty-nine patients were identified with early-stage, high-grade uterine leiomyosarcoma. Of these, 27 (46%) received chemotherapy, 4 (7%) received chemotherapy with radiation, 8 (14%) received radiation alone, and 20 (34%) received no further treatment. Mean patient age was 51.2 years. Median follow-up for survivors was 71 months. Forty (67.8%) patients recurred and 37 (62.7%) died. In the no treatment or radiation alone group, 19 (68%) patients recurred and died of disease. In the chemotherapy or chemotherapy with radiation group, 21 (67.7%) patients recurred and 18 (58.1%) died of disease. There was no difference in median time to recurrence or site of recurrence, pelvic or extrapelvic, among the groups. There was a trend toward decreased recurrence rate with the doxorubicin/ifosfamide combination ($P = 0.06$) compared to other chemotherapy regimens. In the group of patients who received doxorubicin and ifosfamide, 25% of patients recurred and 50% of patients were alive at last follow-up. In the gemcitabine and docetaxel group, although 67% of patients recurred, many of these recurrences were salvageable, and 67% of patients were alive at last follow-up.

Conclusions: Uterine leiomyosarcoma is associated with a high recurrence rate and poor prognosis. Adjuvant therapy has not been shown to improve survival. Although there was a trend toward a decreased risk of recurrence with doxorubicin/ifosfamide, large prospective randomized studies are needed to assess the benefit of adjuvant therapy in this disease.

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423 — Poster Session
Comparing survival of vulvar melanoma and squamous cell carcinoma: An analysis of 13,112 patients in the Surveillance, Epidemiology and End Results database
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Objectives: Vulvar melanomas are rare and poorly understood cancers. We compared the clinico-pathologic features and survival patterns of vulvar melanoma with squamous cell carcinoma to assist in prognosis and decision-making.

Methods: All women diagnosed with primary invasive vulvar melanoma and squamous cell carcinoma between 1988 and 2010 in the Surveillance, Epidemiology, and End Results (SEER) database were identified. Demographic and clinical characteristics were compared using parametric and nonparametric methods. Survival was compared using multivariable Cox proportional hazards models and the Kaplan–Meier method. Prognostic factors were evaluated using univariate and multivariate model selection methods.

Results: A total of 1696 cases of invasive vulvar melanoma were identified in the study period, along with 11,416 cases of squamous cell carcinoma. Superficial spreading melanoma was most commonly diagnosed ($n = 416$), followed by nodular melanoma ($n = 300$) and spindle cell melanoma ($n = 88$). White women and women in the western state catchment areas were more likely to be diagnosed with melanoma. Compared to cases of squamous cell carcinoma, women with vulvar melanoma also demonstrated greater tumor size, were treated more often with surgery without radiation, and often lacked formal staging ($P < 0.05$ for all). After adjusting for confounding factors, patients with melanoma had an 89% greater risk of cancer-related mortality than those with squamous cell carcinoma (HR 1.89, 95% CI 1.69–2.12), with 5-year cancer-related survival estimated at 62%. Superficial spreading histology demonstrated the highest survival among melanoma patients ($P < 0.001$), and older age, presence of metastasis, and positive lymph nodes were associated with increased mortality ($P < 0.05$ for all).

Conclusions: Patients with primary vulvar melanoma have different demographic make-up and inferior survival rates compared to those with squamous cell carcinoma. Prognosis depends on specific histologic type and clinicopathologic features.

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424 — Poster Session
Are different methotrexate regimens as first line therapy for low risk gestational trophoblastic neoplasia more cost effective than the dactinomycin regimen used in GOG 0174?
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Objectives: In an attempt to define the most effective single-agent chemotherapy for low-risk gestational trophoblastic neoplasia (GTN), Gynecologic Oncology Group (GOG) (GOG) 0174 was a phase III randomized, controlled trial comparing 30 mg/m2 weekly intramuscular (IM) methotrexate (MTX) with biweekly pulsed intravenous (IV) dactinomycin (Act-D) 1.25 mg/m2. Complete response (CR) after first-line treatment favored Act-D (70% vs. 53%, $P = 0.01$), but alternative regimens of MTX with higher historic success rates than weekly MTX were not included in the trial. We assessed the cost-effectiveness of Act-D vs. MTX per GOG 0174 and modelled an exploratory arm that included a 5-day IM MTX regimen.

Methods: A cost-effectiveness decision model was constructed using published data from GOG 0174 for base case analysis. Included in a separate model was a 5-day IM MTX arm using a published CR rate of 60%. Outcome was cost per first-line treatment failure expressed in terms of incremental cost-effectiveness ratio (ICER). Front-line failures were assumed to receive cross-over single-agent therapy followed by multiagent chemotherapy with second-line failure. With lack of quality of life (QOL) evaluation in GOG 0174, equal QOL was assumed (utility score = 1) but varied in sensitivity analysis.

Results: Act-D was most expensive compared to weekly MTX ($18,492 vs. $10,484), with 5-day MTX the least costly when included in the exploratory arm ($7510). Act-D had an ICER of $47,104 per avoidance of treatment failure compared to weekly MTX. During sensitivity analysis, the ICER exceeded a $100 K willingness-to-pay (WTP) threshold when Act-D QOL score decreased below 0.88. The inclusion of the 5-day IM MTX arm caused Act-D to no longer be cost-effective with an ICER of $109,809. When treatment failure was defined as need for multiagent chemotherapy, both MTX regimens dominated Act-D.

Conclusions: Despite Act-D being cost-effective in GOG 0174, only a small decrease in QOL (as might be expected with the increased nausea/vomiting and alopecia associated with Act-D) causes the cost to rise above common WTP thresholds. With inclusion of 5-day MTX, Act-D no longer appears cost-effective, and when treatment failure is defined by the need for multiagent chemotherapy, both MTX regimens dominate Act-D. Our model offers support for provider hesitation regarding the use of Act-D as first-line therapy for low-risk GTN in favor of MTX regimens.

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425 — Poster Session
Genetic counseling and evaluation of BRCA mutations in an African American female population in the Deep South
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Objectives: Few studies have described genetic counseling and testing of specific minority patients at risk for ovarian cancer. The purpose of this study was to describe our experience with genetic counseling and testing of an African American (AA) population evaluated at a large, southeastern medical center.

Methods: We reviewed an institutional review board-approved prospectively gathered database of all patients evaluated in an Ovarian Cancer Risk Assessment Clinic. Data evaluated included general demographics, family and personal history of cancer, frequency of genetic testing, frequency and types of deleterious mutations, and performance of risk-reducing salpingo-oophorectomy (RRSO).

Results: From 2003 to 2014, 76/1004 patients (7.6%) evaluated in this clinic were AA. Sixty-four (84%) of these patients had a family history of ovarian and/or breast cancer, and 12 (16%) had a personal history of ovarian cancer. Thirty-six patients (47%) underwent genetic counseling only and 40 (53%) opted for genetic testing. Of the 40 women tested, 18 (45%) were found to have an abnormal genetic result. Six patients each had BRCA1 and BRCA2 deleterious mutations, respectively. Four patients had BRCA2 variant results, with three favoring polymorphism. RRSO was performed in six of 18 patients with BRCA mutations or variants, none of whom were noted to have ovarian or fallopian tube cancer at the time of surgery. None of the patients who did not undergo genetic testing or did not have a BRCA mutation or variant have developed ovarian cancer.

Conclusions: This study demonstrates that in a region of the country where AAs represent 30% of the population, the number of AA patients as a proportion of all patients referred to an Ovarian Cancer Risk Assessment Clinic for genetic counseling remains low. Genetic testing was, however, performed at a rate comparable to Caucasians, suggesting barriers to genetic counseling and testing may be overcome once patients are evaluated in a dedicated clinic. Of the patients tested, the mutation and variant rate was high, although this may be representative of a more select series of at-risk patients. Efforts should continue to identify minority patients at risk for ovarian cancer and to refer them to dedicated genetic counseling clinics.

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426 — Poster Session
Cost comparison among different genetic testing strategies in women with epithelial ovarian cancer
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Objectives: The Society of Gynecologic Oncology recommends that all women with epithelial ovarian cancer (EOC) be offered genetic counseling; the advent of multigene panels has increased testing options. We used decision modeling to compare the costs and probabilities of identifying a deleterious mutation or a variant of uncertain significance (VUS) using different genetic testing strategies.

Methods: A decision model estimated and compared the costs and outcomes of two testing strategies for women with EOC: 1) multigene testing (MGT) using a 23-gene panel for hereditary gynecologic cancers and 2) single-gene testing for BRCA1/2, followed by MGT in 100% if BRCA-negative and patient had a family history (FH) of breast or ovarian cancer or in 5% if BRCA-negative and no FH. Outcomes were the average cost of each testing strategy and number of deleterious genetic mutations or VUS identified. Two models were created (no-FH and FH) based on whether a woman had a FH of breast/ovarian cancer. Inputs from published data in EOC included the probability of identifying a deleterious BRCA mutation: No-FH — 8%, FH — 29%; probability of a deleterious mutation using MGT: No-FH — 12%, FH — 38%; and probability of VUS: MGT — 26%, BRCA — 4%. From published rates, the cost used for BRCA was $2200 and $3900 for MGT. One-way sensitivity analyses were performed.

Results: No-FH model: In women with EOC and no FH, the MGT strategy cost $1528 more on average than BRCA and identified an additional 4% of deleterious mutations. MGT costs $40,107 per additional deleterious mutation identified. For every additional patient in whom a deleterious mutation is identified, MGT also identifies 5.5 additional patients with a VUS. FH model: In women with EOC and a breast/ovarian cancer FH, MGT costs $913 less on average than BRCA and identified an additional 4% of deleterious mutations. MGT, therefore, was dominant (less costly/more effective). For every additional patient in whom a deleterious mutation is identified, MGT also identifies 1.3 additional patients with a VUS (Table).

Conclusions: MGT is associated with additional cost per deleterious mutation identified and a VUS burden in women with no FH but is more efficient than BRCA testing in women with FH. Family history appears to be an appropriate and cost-effective criterion for determining a genetic testing platform in women with EOC.

Table. Outcomes associated with genetic testing for epithelial ovarian cancer.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Average cost</th>
<th>Identification of deleterious mutations (%)</th>
<th>VUS (%)</th>
<th>Cost per additional deleterious mutation identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>No family history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA²</td>
<td>$2371</td>
<td>8%</td>
<td>5%</td>
<td>Reference group</td>
</tr>
<tr>
<td>MGT²</td>
<td>$3900</td>
<td>12%</td>
<td>26%</td>
<td>$40,107</td>
</tr>
<tr>
<td>Family History</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA²</td>
<td>$4813</td>
<td>34%</td>
<td>21%</td>
<td>Reference group</td>
</tr>
<tr>
<td>MGT²</td>
<td>$3900</td>
<td>38%</td>
<td>26%</td>
<td>N/A (dominant strategy)</td>
</tr>
</tbody>
</table>

*100% of patients with negative BRCA testing and no FH proceed to MGT. ²100% of patients with negative BRCA testing and family history of ovarian or breast cancer proceed to MGT.

VUS = gene of variance of unknown significance.

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427 — Poster Session
New cases of small cell carcinoma of the ovary, hypercalcemic type caused by germline SMARCA4 mutations: An under-diagnosed entity?
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Objectives: Small cell carcinoma of the ovary, hypercalcemic type (SCCOTH) is the most common undifferentiated ovarian malignancy in women <40 years, with a mean age at diagnosis of 23.9 years. It is a highly aggressive tumor, with 33% survival with early-stage disease and patients who present at advanced stage almost always succumbing to the disease. Previously, the lack of SCCOTH-specific markers has led to its misdiagnosis as various other malignancies either arising in, or metastatic to, the ovary. Recently, we and others discovered that SCCOTH is a monogenic disease attributable to germline and/or somatic deleterious mutations in a single chromatin remodeling gene, SMARCA4. At least one germline and/or somatic mutation were found in SMARCA4 in all familial and 27/28 (96%)
nonfamilial cases tested. Loss of the SMARCA4 protein was seen in 42/44 (95%) cases tested. Despite the lack of familial SCCOHT cases reported, half of patients with no known family history of the disease carried a germline mutation in SMARCA4. Our objective was to describe new cases studied since our publication and to outline an algorithm for the diagnosis of this aggressive disease.

**Methods:** Sanger and whole exome sequencing was used to identify germline and somatic mutations in cases of SCCOHT. Immunohistochemical staining was performed using an anti-SMARCA4 antibody.

**Results:** Since our publication, we have studied two additional familial cases and four nonfamilial cases of SCCOHT, with loss of protein and SMARCA4 mutations seen in all cases studied. Half of nonfamilial cases carried germline SMARCA4 mutations, indicating that inherited forms of SCCOHT are more common than previously thought. This has important implications for male SMARCA4 mutation carriers whose daughters may inherit mutations as well as affected women with young or male children who are not (yet) affected. Given the common misdiagnosis of SCCOHT as other ovarian tumors, we propose an algorithm to aid in the proper diagnosis.

**Conclusions:** The inherited form of SCCOHT, caused by germline SMARCA4 mutations, is more common than previously recognized, with a likely high penetrance for these mutations. Germline DNA testing in SCCOHT patients could help the prevention of subsequent tumor development in their family members.

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**428 — Poster Session**

**Quality of BRCA counseling by gynecologic oncologists: A patient survey based analysis**

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**Objectives:** BRCA counseling by gynecologic oncologists was incorporated into routine visits for patients with ovarian/fallopian tube/peritoneal cancer. Satisfaction with BRCA counseling was assessed using a survey that included a validated satisfaction scale. Patient understanding and utilization of information was also evaluated.

**Methods:** Patients with ovarian/fallopian tube/peritoneal cancer were identified through an electronic medical record and were sent an anonymous survey. A stepwise survey addressed patient perception of BRCA counseling, testing, and comprehension of results using multiple choice, yes/no questions, numeric Likert rankings, and free text responses. All patients completed a modified Genetic Counseling Satisfaction Scale (GCSS-m). Descriptive and comparative analyses were executed.

**Results:** Of 960 surveys that were mailed, 182 (19%) were returned. Of 126 patients (69%) who were tested for BRCA, 82 (66%) reported the most important reason for testing was to inform family and 39 (31%) said it was because it was doctor-recommended. All patients shared their BRCA status with family and gynecologic oncologists. Insurance covered the cost completely or partially for 120 (95%). Fifty-six patients were not tested: 12 (22%) due to cost, 10 (18%) were still deciding, 7 (14%) wanted more information, and 5 (9%) did not have family with whom to share results. Eleven patients did not recall being offered testing. BRCA-positive patients found the test more useful than those with a negative result (t(96) = -3.654, P = 0.000). Patients with a positive or negative BRCA result correctly assessed their personal and family level of risk (t(22) = 30.07, P = 0.000), (t(25) = -9.55, P = 0.000). Patients who reported gynecologic oncologists as their primary source of information were more likely to be tested. The majority (78%) of all BRCA tests were ordered by gynecologic oncologists, who were also the primary source of counseling for 82% of patients tested. Gynecologic oncologists ranked higher than 4 on a scale of 0–5 in satisfaction scores using the GCSS-m (Fig. 1).

**Conclusions:** BRCA counseling was successfully incorporated into gynecologic oncology practice within routine visits. Patients were highly satisfied the counseling received and were appropriately educated. This is a successful model for BRCA screening as recommended by National Comprehensive Cancer Network.

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**429 — Poster Session**

**Early detection of ovarian cancer via a self-sampling screening test of vaginal secretions: Feasibility and patient acceptance**

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**Objectives:** In 2008, we developed a site-specific proteomic-based screening test for ovarian cancer using physician-collected mucus of the cervix and vagina. The objectives of this study were to evaluate patient acceptance of a self-collected test at home as well as the correlation between physician-collected and patient-collected samples.

**Methods:** After institutional review board approval, signed informed consent was obtained from patients. Cervicovaginal samples were obtained by the physician during routine pelvic examinations in the office and self-collection was performed at home. Patient questionnaires assessed patient acceptability of the home-testing screening method. Liquid chromatography–mass spectrometry evaluation was performed on all samples. Technical replicate agreement of peptide signals was assessed by contingency tables, and Cohen's kappa methodology was used to determine agreement between physician-collected and patient-collected samples.

**Results:** Thirty patients consented for this specimen collection study: 40% (n = 12) had ovarian cancer, with the majority having stage III/IV (n = 8, 66%) and the remainder having stage I (n = 4, 33%). Seventeen patients (56%) had a benign adnexal mass and one patient had metastatic colon cancer. Physician-collected and patient-collected specimens demonstrated moderate agreement, with kappa average of 0.6 and upper bound of 0.75 (Fig. 1). Slightly lower agreement was driven by greater detection of peptide signals in physician-collected tests. Twenty-five patients (83%) returned self-collected vaginal samples via mail and 24 (80%) returned questionnaires. On Likert scale, patients strongly agreed/agreed that the self-collected test was easy, that they would perform it at home if asked
by a health care provider, and that they would recommend it to others. Of note, 96% (23/24) of patients preferred self-collection at home compared to clinic collection, and 96% preferred self-collection compared to having no screening.

Conclusions: Patient acceptance of a self-collected vaginal sampling technique for ovarian cancer screening was high. The feasibility of performing the test was acceptable, with the majority of patients returning self-collected tests. The correlation between physician-collected and self-collected samples was moderate yet acceptable for this pilot project.

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430 — Poster Session
Transmembrane protein 88 (TMEM88) promoter hypomethylation is associated with cisplatin resistance in ovarian cancer
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Objectives: Alterations in DNA methylation are epigenetic changes commonly associated with cancer progression. Previous studies have implicated DNA methylation changes in the development of platinum resistance in ovarian cancer (OC). Using a genome-wide DNA methylation analysis, we identified TMEM88 as a DNA methylation-regulated gene functionally implicated in the development of OC cisplatin resistance.

Methods: Illumina 450 k DNA methylation profiling was used to identify differences in CpG Island methylation in OC xenografts resistant in vivo to cisplatin compared to controls. OC cell lines and paired platinum-resistant subclones (A2780/CP70 and Hey/HeyC2) were used for validation and functional studies. Validation used semi-quantitative reverse transcription polymerase chain reaction, Western blotting, and immunohistochemistry. Student’s t-test and ANOVA were used for statistical analyses.

Results: The comparison between platinum-resistant xenografts and controls identified seven genes (SSH3, SLC12A4, TMEM88, PCDH4, DAXX, MEST, FRZB) that harbored significantly hypomethylated promoters ($P < 0.001$, false discovery rate < 0.05). Of those, TMEM88 and DAXX were overexpressed in platinum-resistant xenografts compared to controls. TMEM88 was also significantly upregulated in CP70 and HeyC2 (platinum-resistant) compared to A2780 and Hey (platinum-sensitive) cells, respectively. Treatment with SGI-110, a DNA hypomethylating agent, increased the expression level of TMEM88, but not of DAXX, confirming that TMEM88 is transcriptionally regulated by promoter methylation. TMEM88 knockdown by siRNA caused upregulation of cyclin D1 and c-myc induced by Wnt3A, suggesting that TMEM88 inhibits Wnt signaling. A specific Wnt inhibitor (XAV-939) increased platinum resistance in A2780 cells, while stimulation with Wnt3A increased the sensitivity to platinum. TMEM88 expression was measured by immunohistochemistry in 20 paired human ovarian tumors (primary and recurrent). Increased TMEM88 expression in recurrent compared to primary tumors was associated with shorter disease progression-free interval (13 months, n = 8 vs. 19 months, n = 12, $P = 0.06$).

Conclusions: Our results demonstrate that OC platinum resistance was correlated with TMEM88 overexpression occurring through DNA demethylation. We suggest that functionally, TMEM88 acts as a Wnt inhibitor, contributing to the development of platinum resistance.

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431 — Poster Session
Hyperthermic intraperitoneal chemotherapy for treatment of ovarian and primary peritoneal cancer:
Single institutional experience
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Objectives: To report our institutional experience with hyperthermic intraperitoneal chemotherapy (HIPEC) at the time of cytoreductive surgery (CRS) for ovarian, fallopian tube, and primary peritoneal cancer.

Methods: We reviewed all patients who underwent CRS and HIPEC between 6/2006 and 6/2014 at our institution. Peritoneal cancer index (PCI) was used to assess the tumor burden. Optimal cytoreduction was defined as residual disease < 1 cm. HIPEC was administered using a closed-circuit technique. The most common chemotherapeutic agents used were mitomycin C and carboplatin. Surgical and survival outcomes were extracted from the patient charts. The postoperative complications were graded using the Clavien–Dindo classification and reported up to the 30th postoperative day. Grade III and IV complications were considered as major. Standard statistical methods were utilized and survival was estimated using the Kaplan–Meier method.

Results: During the study period, we identified 262 patients who underwent HIPEC and CRS at our institution. Fifteen (6%) were diagnosed with gynecologic tumors. Five (33%) had primary CRS and HIPEC for primary peritoneal carcinoma and 10 (66%) had CRS and HIPEC for recurrent ovarian tumors. The median age at the time of the procedure was 61 years (range, 43–85 years) and the median body mass index was 24 (range, 19–43). The median predebulking PCI was 10 (range, 2–25). The median operating room time was 327 min (range, 242–555 min), which included 90 min of perfusion time. The median estimated blood loss was 400 mL (range, 50–6000 mL). Optimal cytoreduction was achieved in all patients (100%) and seven patients (47%) had no gross residual disease. The median postoperative PCI was 1 (range, 0–6). Major postoperative complications were reported in five patients (33%). There were no perioperative mortalities. The median follow-up was 34 months (range, 8–68 months). The median progression-free survival (PFS) was 7 months (95% CI, 1–15 months) for recurrent disease. For primary disease, the median PFS was 26 months (95% CI, 7–26 months) comparable with the intraperitoneal arm in Gynecologic Oncology Group 172.

Conclusions: The combination of CRS and HIPEC is a feasible therapeutic modality for patients with ovarian, fallopian tube, and
primary peritoneal malignancies. The addition of HIPEC to CRS does not seem to increase the rate of grade III and IV postoperative complications and may be associated with survival benefit.

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432 — Poster Session
Determination of HE4-mediated roles in tumor immune system modulation in epithelial ovarian cancer (EOC)
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Objectives: The biomarker HE4 is overexpressed in EOC and is associated with chemoresistance and decreased survival. T-cell infiltration (TIL) by CD8+ cells is correlated with improved overall and progression-free survival and inversely correlates with programmed cell death protein 1 (PD1) and programmed death ligand 1 (PD-L1) expression. The objective of this study was to evaluate the role that HE4 plays in modulating immune functions in EOC through its interaction with PD-L1 expression and CD8+ TIL.

Methods: HE4 and PD1/PD-L1 expression in paraflin-fixed human EOC, benign, and normal tissues was examined by confocal microscopy, and the HE4 and PD1/PD-L1 intensity was measured and expressed in Integrated Optical Density (IOD) units. CD8+ TILs present in EOC, benign, and normal tissues were counted under microscopy. The expression of HE4, PD1, PD-L1, and other related factors in cultured ovarian cancer cells was examined by immunoblotting. To identify HE4 targeting therapies, we evaluated the antitumor efficacy of antisense phosphorothio-oligos (PTOs) (10 mg/kg, 5 days/week) as a stand-alone therapeutic or in combination with cisplatin (10 mg/kg, once a week) in comparison with scrambled control.

Results: PD-L1 and HE4 expression showed direct correlation, but CD8+ T-cell counts exhibited an inverse correlation with HE4 expression in serum ovarian cancer specimens compared to control and benign specimens. HE4 and PD-L1 co-localized in normal, serous benign, and serous malignant tissues. PD-L1 basal expression was increased in the high HE4-expressing ovarian cancer cell lines, OVCAR-3 and Ca-OV3, compared to low HE4 expressors. Treatment with HE4 neutralizing antibody or HE4 antisense PTOs, but not immunoglobulin G or scrambled PTOs, downregulated PD-L1 expression in SKOV-3 and OVCAR-8 cells and xenograft tissues. PTOs significantly decreased SKOV-3 xenograft-tumor size at 24 days compared to scrambled and no treatment groups.

Conclusions: We observed that HE4 expression correlates with increased PDL1 expression and decreased CD8+ TIL in EOC tissues compared to normal and benign tissues. Blocking HE4 with PTOs and antibodies decreased PD-L1 in vitro. The mechanism of HE4 action and its deleterious effect on CD8+ TILs and PD-L1 that results in poor prognosis is underway in our laboratories.

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433 — Poster Session
Multi-institutional validation of decreased survival with venous thromboembolism in clear cell ovarian carcinoma
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Objectives: While ovarian clear cell carcinoma (OCCC) is the subtype of ovarian cancer associated with the highest incidence of venous thromboembolism (VTE), the mechanism for the increased risk is unclear. Recently, a single-institution study found that VTE during OCCC primary treatment is associated with a higher risk of recurrence and death. This is a multi-institutional study that sought to validate the association between VTE and survival.

Methods: Four Institutions obtained institutional review board approval for the retrospective chart review of a cohort of women with OCCC from January 1, 1994 to December 31, 2011. At each institution, clinical and pathologic data were obtained from the medical records, and de-identified data were compiled and processed at a single institution. Standard statistical analyses were performed.

Results: We identified 323 patients with OCCC from the four institutions. There were 67 patients with VTE events (20.74%). Across all stages and all centers, >95% of patients were optimally debulked and received chemotherapy. VTE was significantly associated with shorter progression-free survival (PFS) and overall survival (OS) (PFS HR 5.4, P < 0.0001 and OS HR 4.8, P < 0.0001). Seventy-five percent of patients had stage I/II disease. VTE did not have a significant effect on OS for stage III/IV patients (HR 1.4, P = 0.3), but it was significantly associated with decreased OS in stage I/II patients (HR 6.7, P < 0.0001). A preoperative VTE was associated with an increased risk of recurrence in both stage I/II and stage III/IV patients (HR 2.5, P = 0.05 and HR 2.1, P = 0.04, respectively). A postoperative VTE was not associated with a risk of recurrence (HR 1.3, P = 0.4) or death (HR 1.2, P = 0.6) in stage III/IV patients but was very significantly associated with risk of recurrence (HR 5.7, P < 0.0001) and death (HR 6.7, P < 0.0001) in stage I/II patients. Only one of the 323 patients died of a VTE-related event.

Conclusions: This large, multi-institutional study showed the relationship of VTE in OCCC with increased risk of recurrence and decreased survival. Interestingly, stage I/II OCCC VTE was significantly associated with recurrence and death. Better characterisation of VTE in OCCC may aid in understanding OCCC tumor biology and therapeutic targets.

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434 — Poster Session
Recurrent ovarian cancer patients with 3–6 month treatment-free interval or 1–2 prior chemotherapy regimens might get benefit from tumor chemosensitivity assay directed chemotherapy
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Objectives: Options for second- or third-line chemotherapy for platinum-resistant recurrent ovarian cancer patients include several cytotoxic agents, such as docetaxel, oral etoposide, gemcitabine, liposomal doxorubicin, weekly paclitaxel, and topotecan. Adenosine triphosphate (ATP)-based tumor chemosensitivity assay (ATP-TCA) was previously reported to be helpful in choosing a chemotherapy regimen for recurrent ovarian cancer patients. The aim of the present study was to compare the progression-free survival (PFS) following chemotherapy in patients with platinum-resistant recurrent ovarian cancer who had been treated according to an ATP-based tumor chemosensitivity assay (ATP-TCA) in comparison with physician’s choice and to find the subgroup of patients who could benefit most from ATP-TCA.
Methods: A total of 86 patients were recruited in our study. Half of the patients were in the ATP-TCA group and the other half were in the control group (physician's choice). The clinical characteristics, including age, stage, histologic type, grade, and number of prior chemotherapy regimens and cycles, were well balanced between the two groups. Kaplan–Meier methods with the log rank test were adopted.

Results: The median PFS of the ATP-TCA group and the control group was 5 and 3 months, respectively (P = 0.027). The subgroup analysis showed that the median PFS of the patients with a treatment-free interval (TFI) of 3 months or longer in ATP-TCA group and the control group was 7 and 4 months, respectively (P = 0.010). In the subgroup of patients with one to two prior chemotherapy regimens, the median PFS of the ATP-TCA group and the control group was 6 and 4 months, respectively (P = 0.025). The median PFS of the patients in the subgroup of TFI shorter than 3 months or in the subgroup of three or more prior chemotherapy regimens did not differ between the ATP-TCA and control groups.

Conclusions: ATP-TCA might improve the PFS of patients with platinum-resistant recurrent ovarian cancer compared to physician's choice. Patients with TFI longer than 3 months or one to two prior chemotherapy regimens are possibly the proper candidates for ATP-TCA.

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435 — Poster Session
Risk stratification and outcomes of women undergoing surgery for ovarian cancer
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Objectives: Although cytoreduction is the standard of care for ovarian cancer, the procedure is associated with substantial morbidity. In some settings, the morbidity of primary cytoreduction may outweigh the oncologic benefits. We examined the outcome of patients undergoing surgery for ovarian cancer to determine if there are subgroups of patients who may benefit from alternative treatments.

Methods: The National Surgical Quality Improvement Program database was used to identify women who underwent surgery for ovarian cancer from 2005 to 2012. Multivariable regression models were used to examine the effect of age, race, functional status, American Society of Anesthesiologists (ASA) class, preoperative albumin, and performance of extended cytoreductive procedures (colon, small bowel, bladder or liver resection, splenectomy, cytoreduction) on morbidity, mortality, and resource utilization.

Results: A total of 2870 women were identified. Compared to women < 50 years of age, patients > 70 years were at increased risk for complications (10% vs. 15%, P < 0.001), prolonged hospitalization (17% vs. 33%, P < 0.0001), non-routine discharge (2% vs. 17%, P < 0.0001), transfusion (21% vs. 32%, P < 0.0001), and death (1% vs. 3%, P < 0.001). Similarly, compared to women who underwent no extended cytoreductive procedures, patients who had three additional procedures had increased complication rates (7% vs. 30%, P < 0.0001), prolonged hospitalization (15% vs. 66%, P = 0.0001), transfusion (17% vs. 60%, P < 0.0001), reoperation (3% vs. 6%, P = 0.01), and death (1% vs. 2%, P < 0.001). In a series of multivariable models corrected for functional status, ASA class, and albumin, advanced age was only associated with prolonged hospitalization and non-routine discharge, while ≥2 cytoreductive procedures remained highly associated with complications (relative risk [RR] = 3.27; 95% CI, 2.38–4.50), wound complications (RR = 2.71; 95% CI, 1.78–4.13), prolonged hospitalization (RR = 3.21; 95% CI, 2.57–4.02), and transfusion (RR = 2.56; 95% CI, 2.07–3.17).

Conclusions: Although preoperative clinical and demographic factors may help predict the risk of adverse outcomes for women undergoing surgery for ovarian cancer, performance of extended cytoreductive procedures is the greatest risk factor for complications.

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436 — Poster session
AKT survival signaling as a determinant of ovarian cancer chemoresistance and clinical outcome
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Objectives: The AKT pathway and expression of phospho-AKT protein are known to promote cancer cell survival and resistance to chemotherapy. Here we present AKT survival signaling as a component of the biologic basis for ovarian cancer (OVCA) chemoresistance as well as a promising biomarker candidate and a therapeutic target.

Methods: Affymetrix U133-Plus gene expression, AKT protein expression, and clinical data were downloaded from The Cancer Genome Atlas (TCGA). A Phospho-AKT Gene Expression Signature (PAGES) describing active AKT survival signaling was developed using principal component analysis (PCA). Pearson’s correlation was used to evaluate associations between PAGES and phospho-AKT protein levels, response to platinum-based therapy, debulking status, and overall survival from OVCA. Western blot and immunofluorescence analyses were used to determine the effects of the AKT inhibitor, MK2206, on OVCA cells. CT-Blue proliferation assays were used to evaluate the potentiation of carboplatin + paclitaxel (CT) by MK2206.

Results: Phospho-AKT levels were significantly associated with both overall survival from OVCA (n = 402; negative correlation, P < 0.05) and incomplete response to platinum-based therapy (n = 327; positive correlation, P = 0.004). Although it did not reach statistical significance, phospho-AKT expression also showed a correlation with surgical debulking status (n = 406, 258/406 optimally debulked; positive correlation, P = 0.076). Active AKT survival signaling, as described by PAGES, was associated with phospho-AKT expression (n = 290, P = 0.03) and overall survival from OVCA (median PCA score cut-off to define high/low, n = 142, P < 0.001). Treatment of OVCA cells with MK2206 resulted in decreased phospho-AKT levels as well as decreased levels of phospho-BAD [ser-136], the downstream target of AKT survival signaling. Combinational index values determined by the Chou-Talalay isobologram equation indicated synergy for combinations of MK-2206 and CT in OVCA cells.

Conclusions: We have developed a gene expression signature termed PAGES that describes overall expression/activation of the AKT survival signaling pathway. Our functional and in silico analysis of the AKT pathway and protein confirm the important role for both in OVCA chemosensitivity and clinical outcome.

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437 — Poster session
Patterns of care and survival in a matched case–control study of intraperitoneal chemotherapy in a national population-based cohort of elderly ovarian cancer patients
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Objectives: Clinical trials have demonstrated a significant survival advantage of combined intraperitoneal (IP)/intravenous (IV) chemotherapy over IV chemotherapy alone in advanced ovarian cancer.

However, its increased toxicity profile limits uptake, especially in geriatric patients. We evaluated patterns of use and outcomes in elderly women with advanced ovarian cancer treated with IP/IV chemotherapy.

**Methods:** A cohort of patients at least 66 years old with stage III/IV epithelial ovarian cancer diagnosed between 2002 and 2009 was identified in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database. All patients received surgery plus combination taxane/platinum chemotherapy. Demographic and clinical factors, including age, stage, histology, grade, year of diagnosis, tumor size, and comorbidity score as well as five additional SEER demographic variables were used to compute the propensity score of the probability for each patient to receive IP/IV chemotherapy using a multiple logistic regression model. Based on the propensity score, a 4:1 match of IP/IV to IP/IV patients was included in the analysis. Kaplan–Meier analysis was performed to compare the overall survival rates between the IP/IV and IV groups in the matched sample. Cox proportional hazards model was used to determine risk factors for survival.

**Results:** A total of 3651 women with advanced ovarian cancer met the inclusion criteria, including 3527 women treated with IV chemotherapy (96.7%) and 124 (3.3%) women treated with IP/IV. The median age in the IP/IV group was 71 years (range, 66–83 years), whereas the median age was 73 years (range, 66–97 years) in the IV group. Women treated with IP/IV chemotherapy had a decreased risk of death (HR = 0.59, 95% CI 0.44–0.79). The median survival in the matched IP/IV group was 50.5 months compared to 38.2 months in the IV group. We did not observe a higher percentage of women using acute care services (emergency department visits, intensive care unit/hospital admissions) in the IP/IV group than in the IV group.

**Conclusions:** IP chemotherapy may be given to a carefully selected group of elderly patients with ovarian cancer without resulting in an increase in acute care services. A significant survival advantage with IP/IV chemotherapy over IV chemotherapy may be maintained in a geriatric patient population, although residual confounders may exist.

**438 — Poster session**

**Should neoadjuvant chemotherapy be preferred to an alternative treatment for advanced ovarian cancer: Comparison of neoadjuvant chemotherapy followed by interval debulking surgery and primary debulking surgery in patients with advanced ovarian cancer**

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**Objectives:** The aim of the present study was to evaluate the role of neoadjuvant chemotherapy followed by interval debulking surgery (NACT-IDS) in comparison with primary debulking surgery (PDS) in the treatment of patients with advanced ovarian cancer.

**Methods:** All patients with stages III–IV epithelial ovarian cancer who underwent debulking surgery at our institution between 1994 and 2010 were included. Demographic and clinicopathologic treatment and survival outcome data were collected and analyzed.

**Results:** Among the 391 eligible patients, 176 (45%) underwent NACT-IDS and 215 (55%) had PDS. The majority of patients (81.3%) had stage III diseases. No difference in the distribution of disease stage was observed in the two groups. Mean CA-125 levels at diagnosis were higher in the NACT-IDS group ($P = 0.001$). A similar proportion of patients presented with CA-125 normalization at completion of the third cycle of postoperative chemotherapy in the two groups. Compared with PDS, NACT-IDS was associated with less intraoperative blood loss (387 ml vs. 557 ml, $P < 0.001$) and a lower rate of blood transfusion (44.0% vs. 54.2%, $P = 0.052$). There was no significant difference between NACT-IDS and PDS groups in operation time and postoperative complications. Patients who received NACT-IDS were more likely to have residual disease $\leq 1$ cm than those with PDS (70.5% vs. 56.5%, $P = 0.005$). No difference in the median overall survival was found between patients treated with NACT-IDS (48.0 months) and patients treated with PDS (51.0 months, $P = 0.228$). In multivariate analyses, residual disease $\leq 1$ cm (HR = 0.697, $P = 0.031$) and CA-125 normalization at the completion of the third cycle of postoperative chemotherapy (HR = 0.663, $P < 0.001$) were confirmed to be independent predictors for improved overall survival.

**Conclusions:** Patients with advanced ovarian cancer undergoing NACT-IDS had similar outcomes when compared to those treated with PDS, which implied that NACT-IDS might be superior to PDS because the patients in the NACT-IDS group may have more serious diseases. Moreover, the NACT-IDS group had a greater chance of achieving optimal cytoreduction. Our results are extremely consistent with previous randomized studies. NACT-IDS should be considered as an alternative treatment for advanced ovarian cancer.

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**439 — Poster session**

**Survival and toxicity of a modified GOG 172 IP chemotherapy regimen in patients with ovarian, fallopian tube or primary peritoneal carcinoma**

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**Objectives:** Despite advantages in survival outcomes, adjuvant intraperitoneal (IP) chemotherapy in the treatment of advanced-stage epithelial ovarian, fallopian tube, or primary peritoneal carcinoma carries significant toxicity. We report our experiences using a modified Gynecologic Oncology Group 172 regimen consisting of intravenous (IV) docetaxel + IP cisplatin and paclitaxel with growth colony-stimulating factor (GCSF) support.

**Methods:** We conducted a retrospective review from 6/2006 to 4/2014 evaluating patients treated with a modified outpatient IP chemotherapy regimen consisting of docetaxel 75 mg/m² IV + cisplatin 75 mg/m² IP...
day 1 and paclitaxel 60 mg/m² IP day 8 every 21 days for 6 cycles. Pegfilgrastim was routinely used on day 8. Home IV hydration was not routinely prescribed. Demographic data, surgical outcomes, toxicity, and survival data were collected. Descriptive statistics characterized the population. We estimated survival using the Kaplan–Meier method.

**Results:** Sixty-seven patients received at least 1 cycle of this regimen and were included in analysis. The majority were Caucasian (79.1%) and African-American (13.4%). Forty-five (67.2%) had stage IIIIC papillary serous ovarian cancer. Eleven (16.4%) had port-related complications, including infection, fracture, or failed function. Forty-five (67.2%) patients completed all planned IP cycles, with 81% of total planned IP cycles completed. Nineteen (28.3%) stopped IP therapy due to toxicity. Fifty-six (83.6%) had grade 3 or 4 toxicity, including neutropenia (41.8%), gastrointestinal disturbance (25.4%), anemia (23.9%), and neurologic dysfunction (14.9%). Twenty (29.9%) required hospitalization, but there were no treatment-related deaths. Fifty-six (83.6%) suffered >grade 1 renal toxicity, with 60.1% of those returning to their baseline function. Of patients suffering renal toxicity, 10% required dose reduction or cessation of IP therapy. Fifty-nine patients (88.1%) had a complete response to therapy, 28 (41.8%) have had recurrence of disease, and 15 (22.4%) have died. With a median follow-up of 29 months (range, 8–112 months), progression-free survival was 22.5 months (95% CI 16.5–32.6).

**Conclusions:** Toxicity of IP chemotherapy can be managed with regimen modification and routine use of GCSF support, with similar survival rates as published regimens. Further investigation into this regimen is warranted.

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**440 — Poster session**

**Vitamin D suppresses ovarian cancer invasion by inhibiting cytokine expression and NF-κB signaling**

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**Objectives:** Our studies have revealed a role for 1α,25-dihydroxyvitamin D3 (1,25D3) in suppressing ovarian cancer (OVCA) invasion mediated through both epithelial and stromal receptors (VDR). The present study sought to understand the effect of 1,25D3 on OVCA invasion mediated through the epithelial VDR.

**Methods:** Genomic expression analyses identified a group of cytokines and chemokines suppressed by 1,25D3. Molecular analyses were used to define the mechanisms underlying cytokine suppression. Trans-well assays were used to measure the in vitro effect of 1,25D3 and VDR on OVCA migration and invasion. Ex vivo omental organ coculturing with luciferase-marked human OVCA cells and VDR knockdown cell models were employed to investigate the effect of 1,25D3 and the epithelial VDR on the ability of OVCA cells to invade the omentum. VDR staining was performed to analyze the VDR expression status during OVCA progression.

**Results:** Our studies revealed that suppression of cytokine expression by 1,25D3 was mediated through NF-κB inhibition. 1,25D3 treatment decreased OVCA cell migration and invasion through matrigel, and VDR knockdown diminished such an effect. In ex vivo mouse models, the absence of the VDR in tumor cells enhanced invasiveness of OVCA cells into omental tissues. Either stable expression of constitutive IKKβ or the addition of recombinant cytokines in the culture medium relieved the suppressive effect of 1,25D3 on OVCA migration and invasion. This suggests that suppression of cytokine expression and NF-κB activity may be a dominant driver of the inhibitory effect of 1,25D3 on OVCA invasion. VDR protein expression decreased in advanced-stage serous OVCA patient samples as compared to benign and low malignant potential tumors, supporting the idea that VDR is a suppressor of OVCA invasion.

**Conclusions:** This is the first demonstration of 1,25D3-induced suppression of OVCA omental invasion (via cytokine expression) and a potential role for epithelial VDR in suppression of OVCA omental invasion. Our findings highlight the potential of VDR-based therapeutic strategies that may leverage 1,25D3 or its analogs to improve outcome for patients with OVCA. Online data mining and bioinformatics are currently ongoing to translate the mechanistic findings into clinically relevant information for OVCA intervention.

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**441 — Poster session**

**Bioenergetic adaptations in chemosensitive ovarian cancer cells**

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**Objectives:** The earlier belief that all cancer cells are dependent on glycolysis is currently being challenged, with recent studies showing cancer cells to be more adaptive in energy pathways according to the fuel source. The objective of our study was to determine whether chemosensitive and –resistant ovarian cancer cells have different cellular energetic capacities.

**Methods:** We used the Seahorse XF Extracellular Flux analyzer to examine the bioenergetic characteristics of two sets of chemo-sensitive and –resistant ovarian cell lines: (i) platinum-sensitive A2780 and –resistant C200, (ii) and platinum- and paclitaxel-sensitive PE01 and –resistant PE04. We ran real-time measurements of glycolysis and mitochondrial respiration using the outputs of extracellular acidification rate (ECAR) and oxygen consumption rate (OCR). Fatty acid oxidation was measured by beta-oxidation of palmitate. Mitochondrial potential was measured by JC-1 dye conversion.

**Results:** We observed distinctive bioenergetic profiles of chemo-sensitive and –resistant cell line pairs. The resistant cells (C200 and PE04) displayed higher ECAR (P < 0.01 and P < 0.05, respectively) and OCR (P < 0.001 and P < 0.05, respectively) profiles compared to the sensitive cells (A2780 and PE01), indicating an increased utilization of both energy pathways. The OCR:ECAR ratio suggested the sensitive cell lines to be glycolytic and the resistant cell lines to be highly metabolically active, using both glycolysis and OXPHOS. This was further supported by the finding of increased mitochondrial function in the resistant cells, reflected in augmented fatty acid oxidation (P < 0.01 and P < 0.05, respectively) and mitochondrial potential (P < 0.001 and P < 0.05, respectively). The resistant cells were able to overcome glucose restriction compared to sensitive cells. Interestingly, OXPHOS inhibitors were able to partially reverse C200 and PE01 resistance to cisplatin.

**Conclusions:** Chemo-resistant ovarian cancer cells differ from chemosensitive cells in being able to use both energy pathways and being more metabolically active. This could offer them greater flexibility, making them more adaptable in rearranging their metabolic phenotype according to chemotherapeutic stress and giving them a selective advantage to overcome adverse conditions.

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**442 — Poster session**

**Serum interleukin-6 is a biomarker of survival in women with advanced stage and optimally resected epithelial ovarian cancer**

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Objectives: Recent data indicate that increased production of cytokines in women with epithelial ovarian cancers induces thrombocytopoiesis that directly contributes to aggressive tumor biology. Cohorts with relatively low optimal cytoreductive rates suggest that interleukin (IL)-6 levels correlate with survival, although the impact of surgical resectability may influence these findings. We hypothesized that serum IL-6 influences survival in women with advanced-stage and optimally cytoreduced epithelial ovarian cancer.

Methods: Under an institutional review board-approved protocol, we identified patients with stages III and IV invasive epithelial ovarian cancer who underwent initial optimal cytoreductive surgery with residual disease <1 cm. We assayed IL-6 from frozen prediagnostic serum by enzyme-linked immunosorbent assay and retrospectively abstracted clinicopathologic data, including preoperative platelet counts. Serum IL-6 levels >10 pg/mL and platelet counts >400,000/L were considered elevated. Data were analyzed using c² and Cox proportional hazards model; survival was analyzed by the Kaplan–Meier method.

Results: Forty-one of 96 (43%) patients in this cohort had elevated preoperative serum IL-6 and 44 (46%) had preoperative thrombocytosis. We observed a strong statistical correlation between elevated IL-6 in patients with thrombocytopoiesis, with thrombocytopoiesis occurring in 12/55 patients with low IL-6 and 32/41 with high IL-6 (22% and 78%, P < 0.0001). Patients with low IL-6 levels had a longer disease-free interval (16 months) compared to those with high IL-6 levels (13 months, P = 0.039). Similarly, those with low IL-6 levels had longer overall survival (55 months) compared to those with high IL-6 levels (41 months, P = 0.027). In this cohort of women who optimally resected disease, age and IL-6 levels independently retained prognostic significance (P = 0.0097 and P = 0.048, respectively) after controlling for stage and grade on multivariate analyses.

Conclusions: Elevated IL-6 correlates closely with thrombocytopoiesis and is predictive of survival in a cohort of women with advanced-stage, optimally resected disease. IL-6 may potentially function as a target of future therapeutic agents via interruption of this increasingly well-established platelet-driven paracrine circuit in women with ovarian cancer.

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443 — Poster session
A state by state analysis of BRCA1 and BRCA2 testing in patients with ovarian cancer

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Objectives: Typically, 11% to 15% of women with ovarian cancers have inherited a BRCA1 or BRCA2 mutation. Currently, all ovarian cancer patients meet National Comprehensive Cancer Network (NCCN) guidelines for genetic testing. Novel therapies are being developed specifically for BRCA1/BRCA2-mutated cancers. The objectives of this analysis were to quantify the gap between the number of newly diagnosed ovarian cancer patients and BRCA1/BRCA2 testing of the population nationally and by state.

Methods: We identified the number of ovarian cancer patients diagnosed in the United States from the National Cancer Institute’s Surveillance, Epidemiology, and End Results database and The American Cancer Society’s Annual Cancer Facts and Figures publication. We compared these numbers with the number of genetics tests received at a commercial lab for BRCA1/BRCA2 testing from 2008 to 2013. Over this time period, this laboratory provided the majority of BRCA1/BRCA2 testing in the United States. Clinical information was provided by the physician on the test request form.

Results: Nationally, as of 2013, 23.7% of newly diagnosed ovarian cancer patients were tested for BRCA1/BRCA2, an increase from 9.6% in 2008. Five states (MO, NH, NM, NY, and RI) tested >33% of newly diagnosed ovarian cancer patients; NH had the highest testing rate at 38.4%. States with the lowest testing rates were MS, MT, and IA at 10.1%, 11.3%, and 11.7%, respectively.

Conclusions: Although all epithelial ovarian cancer patients meet NCCN guidelines for BRCA1/BRCA2 testing, only 23.7% of newly diagnosed patients have been tested. In states with the highest testing rates, >60% of patients were not tested. In this cohort, there was more than a three-fold difference in testing prevalence between states. Patient and provider education as well as approval of novel agents targeting BRCA genetic mutations will likely improve testing rates.

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444 — Poster session
Association of AMPK signaling pathway with tumor response to treatment in ovarian cancer

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Objectives: Metformin has been shown to inhibit ovarian cancer growth in vitro and in vivo. Furthermore, diabetic ovarian cancer patients who are taking metformin seem to have better outcomes. The most established pathway mediating metformin’s anticancer effect is the metabolic regulator adenosine mono-phosphate-activated kinase (AMPK) and its downstream targets. In this work, we sought to analyze the relationship between tumor protein levels of key enzymes in the AMPK signaling pathway and patients’ outcome.

Methods: Protein expression for AMPK, phosphorylated-AMPK (pAMPK), acetyl co-carboxylase CoA (ACC), pACC, mammalian target of rapamycin (mTOR), and liver kinase B1 (LKB1) were obtained from The Cancer Genome Atlas (TCGA) ovarian cancer database along with associated clinical information (n = 505). Pearson’s correlation coefficient was used to assess associations between proteins. Linear models were used to assess associations between proteins and clinical parameters. Multivariable Cox regression models were considered for both overall and progression-free survival.

Results: Patients with a complete response to first-line chemotherapy had significantly higher mean pAMPK expression compared to those who had progressive (P = 0.0481) or stable disease (P = 0.0146). However, there was no significant association between overall survival and levels of pAMPK (P = 0.1268) or pACC (P = 0.8766). Likewise, there was no significant association between progression-free survival and pAMPK (P = 0.5015) or pACC (P = 0.3541). Correlation between pAMPK and other pathway-associated proteins was low, with Pearson’s coefficient ranging from 0.14 for LKB1 to 0.29 for pACC. AMPK was most strongly correlated with pAMPK (0.52). Similarly, pACC was most correlated with ACC (0.88) but less with the other measured proteins (−0.09 to 0.29).

Conclusions: Increased pAMPK is associated with improved chemotherapy response, although it does not significantly impact survival. Other proteins in the AMPK signaling pathway may have independent contributions because their expression is not strongly correlated, and they may not be good indicators of AMPK status.

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445 — Poster session
Predictive value of the age-adjusted Charlson comorbidity index on perioperative complications and survival in patients undergoing surgery for advanced ovarian cancer

Objectives: To assess the ability of the Age-Adjusted Charlson Comorbidity Index (ACCI) to predict perioperative complications and survival in patients undergoing primary debulking surgery for advanced epithelial ovarian cancer.

Methods: Data were analyzed for all patients with stages IIIb–IV ovarian, fallopian tube, and primary peritoneal cancer who underwent primary cytoreduction at our institution from 1/2001 to 1/2010. The ACCI is a validated predictor of 1-year mortality and is based on age and the weighted scores of 19 medical comorbidities. Perioperative complications at up to 30 days postoperatively were graded for severity using a standardized institutional grading system. Patients were divided into three groups based on an ACCI of 0–1, 2–3, and ≥4. Clinical and survival outcomes were assessed and compared for the three groups. Appropriate statistical tests were used.

Results: A total of 567 patients met inclusion criteria, of whom 200 (35%) had an ACCI of 0–1, 272 (48%) had an ACCI of 2–3, and 95 (17%) had an ACCI of ≥4. The most common comorbidities were chronic pulmonary disease (n = 55, 10%), connective tissue disease (n = 37, 7%), other solid tumors (n = 32, 6%), and diabetes mellitus (n = 26, 5%). The ACCI was significantly associated with the rate of complete gross resection (0–1 = 44%, 2–3 = 31%, and ≥4 = 33%, P = 0.01) but was not associated with the rate of minor (47% vs. 47% vs. 43%, P = 0.82) or major (19% vs. 18% vs. 16%, P = 0.83) complications. The ACCI was also significantly associated with progression-free (PFS) and overall survival (OS). Median PFS for patients who had an ACCI of 0–1, 2–3, and ≥4 was 20.3 months, 16 months, and 15.6 months, respectively (P = 0.03). Median OS for patients who had an ACCI of 0–1, 2–3, and ≥4 was 65.3 months, 49.9 months, and 42.3 months, respectively (P < 0.001). On multivariate analysis, after adjusting for stage, histology, preoperative albumin, ascites volume, residual disease, and intraperitoneal chemotherapy administration, both PFS (P = 0.02) and OS (P = 0.001) remained significant.

Conclusions: The ACCI was a significant predictor of PFS and OS in patients undergoing primary cytoreduction for advanced epithelial ovarian cancer. Prospective clinical trials in ovarian cancer should consider stratifying for comorbidity.

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446 — Poster session
Prognostic factors in recurrent epithelial ovarian cancer

Objectives: Nearly 70% of patients with advanced epithelial ovarian cancer recur in up to 5 years of follow-up, presenting a treatment challenge. Our aim was to evaluate the prognostic factors for patients with epithelial ovarian cancer after the first recurrence.

Methods: We analyzed a series of 232 patients with recurrent epithelial ovarian cancer treated from January 1992 to June 2013 at AC Camargo Cancer Center. Clinical characteristics were extracted from medical records and their association with overall survival (OS) and progression-free survival (PFS) after recurrence analyzed.

Results: FIGO stage at diagnosis was I in 16 patients (7.3%), II in 17 patients (7.8%), III in 143 patients (66.0%), and IV in 41 (18.9%). Median age was 58 years (range, 20–87 years). Twenty-one (14.6%) of 144 patients had Eastern Cooperative Oncology Group (ECOG) score ≥2. Median CA-125 was 82 U/mL (range, 8.4-4859 U/mL). Ninety-five (54.6%) of 174 patients had only one site of recurrence. Median PFS prior to first recurrence was 17.0 months (range, 1–237 months), and 84/204 (41.2%) patients had a platinum-free interval (PFI) ≥12 months. Ninety-one (39.2%) of 232 patients had secondary cytoreductive surgery (SCS). Among the patients who had SCS, 53 (66.2%) had PFI ≥12 months. For a median follow-up time of 19.5 months, median OS was 32.1 months (95% CI 26.0–38.1). A better OS was found in those who had SCS (17.0 vs. 89.8 months, P < 0.001), PFI ≥12 months (17.5 vs. 58.2 months, P < 0.001), CA-125 < 80 U/mL (21.6 vs. 40.0 months, P = 0.002), ECOG score 0–1 (8.7 vs. 36.1 months, P < 0.001), one recurrence site (26.3 vs. 54.9 months, P = 0.001), age < 65 years (21.3 vs. 38.2 months, P = 0.006), and primary stages I and II compared to III and IV (26.3 vs. 79.7 months, P = 0.001). In multivariate analysis, receiving SCS (HR 0.30, 95% CI 0.15–0.61, P = 0.001), PFI ≥12 months (HR 0.44, 95% CI 0.23–0.85, P = 0.015), and ECOG score 0–1 (HR 0.44, 95% CI 0.21–0.89, P = 0.027) were the prognostic factors independently related to better OS after recurrence. SCS (HR 0.61, 95% CI 0.40–0.96, P = 0.032) and PFI ≥12 months (HR 0.42, 95% CI 0.26–0.68, P < 0.001) were also independently related to a better PFS after first recurrence.

Conclusions: Our data may help to stratify patients at risk of death after ovarian cancer recurrence. We suggest that after epithelial ovarian cancer recurrence, the prognostic factors related to better survival were SCS, PFI ≥12 months, and ECOG scores 0–1.

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Complications from surgeries prompted by ovarian cancer screening

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Objectives: To evaluate complications of surgical intervention for participants in the Kentucky (KY) Ovarian Cancer Screening Program (OCSP) and compare them to findings of the Prostate, Lung, Colorectal and Ovarian Cancer Screening (PLCO) trial.

Methods: A total of 657 patients who underwent surgery because of a positive screen in the OCSP from 1988 to 2014 were reviewed. Surgical data were available from operative reports, discharge summaries, and office notes for 406 patients. Another 142 patients with incomplete records were interviewed by phone. Complete information was available for 548 patients (83%). Complications were graded with the Clavien–Dindo (CD) Classification of Surgical Complications and considered minor if grade 1 (any deviation from normal course, minor medications) or grade 2 (other pharmacologic treatment, blood transfusion). Statistical analysis was performed using Science Analysis System 9.4 software.

Results: Complications were documented in 54/548 (10%) subjects. For women with malignancy, 17/90 (19%) had complications compared to 37/458 (8%) with benign pathology (P = 0.003). For non-cancer surgery, obesity (body mass index ≥ 30) was associated with increased complications (P = 0.0072). Fifty patients had minor complications classified as CD grade 2 or less. Three of four patients with grade 4 complications had malignancy (P < 0.0004). In the PLCO trial, 212 women had surgery for ovarian malignancy, and 95 had at least one complication (45%). Of the 1080 women with non-cancer surgery, 163 had at least one complication (15%). The KY OCSP had significantly fewer complications than the PLCO trial for both cancer and non-cancer surgeries (P < 0.0001 and P = 0.002, respectively; Table 1).

Conclusions: Surgeries performed as a result of the KY OCSP were associated with significantly fewer complications than the PLCO trial. Complications were mostly minor (93%) and were more common in cancer vs. non-cancer surgery.

Table 1

<table>
<thead>
<tr>
<th>Surgical finding</th>
<th>KY OCSP (n = 548)</th>
<th>PLCO Trial (n = 1292)</th>
<th>P</th>
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<tbody>
<tr>
<td>Cancer</td>
<td>17/90 (19%)</td>
<td>95/212 (45%)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Non-cancer</td>
<td>37/458 (8%)</td>
<td>163/1080 (15%)</td>
<td>0.002</td>
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doi:10.1016/j.ygyno.2015.01.452
Paraneoplastic neurologic syndrome in ovarian carcinoma

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Objectives: Paraneoplastic neurologic syndrome (PNS) is a rare entity in ovarian cancer. The objective of this study was to assess the incidence, clinicalpathologic features, and survival outcomes of patients with ovarian, primary peritoneal, or fallopian tube cancer (OC) diagnosed with PNS.

Methods: We performed a retrospective review of all patients diagnosed with OC and PNS between 1995 and 2013. Characteristics of epithelial OC (EOC) with and without PNS diagnosed between 2003 and 2012 were also compared. Fisher’s exact and Wilcoxon rank sum tests were used to compare categorical and continuous variables, respectively. Survival was estimated and compared using the product limit estimator of Kaplan–Meier and log-rank statistic.

Results: Of the 4552 OC patients, 15 (0.3%) were diagnosed with PNS, 47% prior to OC diagnosis, 33% during primary treatment, and 20% at recurrence. Sixty-seven percent (n = 10) were confirmed with onconeural antibodies, primarily anti-Yo (9/10, 90%). Among patients with PNS, median age was 59 years (range, 21–74 years). Tumor histology was predominantly serous (67%), mixed epithelial (13%), or immature teratoma (7%). PNS presented with muscle weakness (53%), ataxia (47%), confusion (33%), fatigue (27%), nystagmus (20%), multifocal neuropathy (13%), altered mental status (13%), and paresthesias (13%). Median duration of PNS symptoms was 18 months (range, 2–68 months). Treatments for PNS, given alone or in combination, included intravenous immunoglobulin (67%), corticosteroids (53%), plasmapheresis (47%), and chemotherapy (20%). Overall, only 33% of patients responded completely to PNS therapy. Sixty percent required greater than one line of therapy. If PNS symptoms were not resolve after first-line therapy, complete resolution of symptoms was unlikely. In the analysis of 563 EOC, compared to patients without PNS (n = 553), patients with PNS (n = 10) had worse performance status (P = 0.005) and a trend toward higher median CA-125 levels at diagnosis (536 U/mL vs. 2580 U/mL, P = 0.08). There was no difference in OS between the two groups (34.9 vs. 59.5 months, P = 0.23).

Conclusions: In our population, PNS was an uncommon complication but was more commonly seen in EOC. In general, complete response to PNS therapy was low, with a significant number of patients experiencing persistence of symptoms after treatment. Patients with PNS had no difference in OS compared to patients without PNS.

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Comorbid case-mix and predictors of inpatient admissions or death among ovarian cancer patients presenting to emergency departments in the United States

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Objectives: To assess the comorbid conditions associated with ovarian cancer cases presenting to emergency department (ED) settings in the United States and to assess predictors of inpatient admissions and mortality.

Methods: This retrospective cross-sectional study design used the 2006–2010 nationally representative Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) emergency department records. The inclusion criteria were adult cases ≥18 years with any diagnosis of ovarian cancer on record. A multinomial regression was used to assess ED discharge status based on patient residential location, income quartile, primary payer, age, hospital region, rural location, teaching status, year, and Elixhauser comorbidities.

Results: There were 459,454 ED visits with ovarian cancer between 2006–2010, averaging 61.9 ± 16.7 years of age. Overall, 38.3% were directly treated and released from the ED, 57.7% were admitted as inpatients, and 3.1% died. Over time, the proportion of treat-and-release cases increased by approximately 6.0%. The top principal presenting diagnoses were abdominal pain, urinary tract infections, intestinal obstructions, nonspecific chest pain, and secondary metastases; the most common overall diagnoses were secondary metastases, hypertension, fluid and electrolyte disorders, anemia, and aftercare (e.g., nonacute postsurgical, ostomy, or palliative care). Relative to treat-and-release cases, the multinomial analysis observed the largest predictors of admission to include blood loss anemia (odds ratio [OR] = 25.1), cachexia (OR = 12.7), moderate-to-severe liver disease (OR = 7.6), paralysis (OR = 7.5), and pulmonary circulatory disorders (OR = 6.8) (P < 0.001). Mortality decreased by approximately 6.6% annually and was most strongly associated with blood loss anemia (OR = 21.0), cachexia (OR = 20.2), moderate-to-severe liver disease (OR = 19.5), paralysis (OR = 12.8), and pulmonary circulatory disorders (OR = 11.8) (P < 0.001).

Conclusions: Of the approximately one-half million ovarian cancer cases presenting to EDs in the United States from 2006–2010, almost 60% were admitted as inpatients. The strongest predictors of admission or death appeared to be a function of disease progression or treatment-related adverse events.

doi:10.1016/j.ygyno.2015.01.455
Results: Of 3652 patients meeting the eligibility criteria, 850 achieved R0, 1788 had MR, and 1014 had BR. Among patients with R0, the proportion of platinum resistance was 15% (96/651) vs. 23% (45/199) in those with low vs. high disease burden at diagnosis, respectively (P = 0.01). In the subset with MR, the proportion of platinum resistance was 25% (90/355) vs. 33% (475/1433) in women with low vs. high disease burden, respectively (P < 0.01). Among those with BR, the proportion of platinum resistance was 36% (60/165) vs. 42% (357/849) in patients with low vs. high disease burden, respectively (P = 0.19). In addition, PFS was significantly diminished for patients with high vs. low disease burden within each subset of R0, MR, and BR. Women with a high vs. low disease burden at diagnosis and R0 cytoreduction had an increased risk of resistant disease (OR = 1.69, 95% CI = 1.14–2.51) and disease progression (HR = 1.5, 95% CI = 1.25–1.79, P < 0.01). Similar but less dramatic associations were also observed between high vs. low disease burden at diagnosis and chemotherapy resistance/short PFS in the subset of women with MR (OR = 1.46, 95% CI = 1.12–1.90; HR = 1.17, 95% CI = 1.03–1.33, P = 0.01) or BR cytoreduction (OR = 1.27, 95% CI = 0.90–1.79; HR = 1.3, 95% CI = 1.08–1.56, P < 0.01).

Conclusions: A significant relationship exists between initial disease burden and chemotherapy resistance that may be the primary driver of more rapid disease progression. When surgical outcomes are similar, this is most notable in women with complete gross resection.

doi:10.1016/j.ygyno.2015.01.456

452 — Poster Session

The effects of combined MEK inhibition and antiestrogen therapy in the treatment of ovarian cancer


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Objectives: It is estimated that 67% of OVCAs are estrogen receptor (ER)-positive. The MAPK pathway is altered in 40% of OVCAs. We hypothesized that estrogens further activate MAPK signaling and that combination ER blockade with MEK inhibition would block cross-talk and increase the efficacy of ER blockade.

Methods: Treatment effects with MEK inhibitor (AZD6244) and antiestrogen (fulvestrant), alone or in combination, on cell cycle were evaluated in ER+ OVARA lines. Drug effects on xenograft tumor growth were assayed. Reverse-phase protein lysate array (RPPA) analysis and gene expression analysis were performed to evaluate biomarkers of drug response. Finally, using The Cancer Genome Atlas (TCGA) and Japan OvCA cohorts, we defined a MAPK gene signature and used Oncomine™ to analyze clinical outcomes associated with it.

Results: RPPA analysis of high-grade serous tumors from the TCGA (n = 408) demonstrated that 76% of tumors had pMAPK, and patients with high pMAPK (top 50%) had a worse overall survival (P = 0.004). E2 increased phosphorylation of MEK in ER+ OVARA cells. Combination therapy had the greatest effect on growth arrest compared to either drug alone, with synergistic cell cycle arrest mediated by p27 binding to Cyclin E/cdk2 in vitro. AZD6244 treatment of OVARA lines resulted in differential expression of 1174 genes, and an additional 89 genes were affected with the addition of fulvestrant. Gene enrichment analysis showed that addition of AZD6244 to fulvestrant downregulated the top gene sets, including DNA replication, cell cycle, and FOXM1; the top gene set upregulated was the lysosome. These effects were confirmed with RPPA. Xenograft data showed the greatest decrease in tumor volume with the drug combination compared to either drug alone. We identified 136 unique genes commonly differentially expressed between “high-MAPK” and “low-MAPK” groups in both TCGA and Japan cohorts, potentially representing a MAPK OvCA signature. The overexpressed genes in the MAPK signature were significantly enriched in the top 5% to 10% of genes overexpressed in poor survival outcome (P = 0.01) in 5/6 OvCA data sets represented in Oncomine.

Conclusions: The finding that the majority of primary OVCAs express high MAPK activity may underlie the failure of antiestrogen therapy. MEK inhibition reversed antiestrogen resistance in our models. MAPK ovarian cancer signature may be prognostic of poor survival.

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453 — Poster Session

Association of high-density lipoprotein cholesterol with ovarian cancer diagnosis

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Objectives: A limited number of studies have shown an association of low cholesterol with ovarian cancer. These studies used single measures of cholesterol either at cohort entry or diagnosis. Results are mixed, depending on size of cohort, timing of measure, and type of cholesterol measured. This study used data from a single institution to evaluate serial high-density lipoprotein (HDL) cholesterol measures in the 10 years prior to diagnosis.

Methods: We combined all ovarian cancer cases identified from our tumor registry in 1998 to 2010 who were diagnosed and treated at the Henry Ford Health System and were members of our health maintenance organization (Health Alliance Plan). Cases were matched with up to five controls on age at diagnosis (±2 years strata) and length of enrollment (±2 years strata). We excluded members with any filled prescriptions for lipid-altering drugs and included only those with at least two cholesterol measures. Multilevel longitudinal models, accounting for matching, were fit after choosing the best polynomial order by deviance statistics.

Results: Ovarian cancer cases had significantly lower HDL cholesterol levels than controls. There was a clear divergence of HDL cholesterol measures between cases and controls in the year prior to diagnosis. This difference was significant (P < 0.0001).

Conclusions: Our results suggest that HDL cholesterol levels drop dramatically in the year prior to diagnosis. Monitoring HDL cholesterol levels in conjunction with CA-125 may improve screening efforts and early diagnosis of ovarian cancer. Additional studies are needed to confirm and explore this relationship.

doi:10.1016/j.ygyno.2015.01.458

454 — Poster Session

Lymphocyte nadir and reconstitution during chemotherapy predicts survival in ovarian cancer patients

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Objectives: A limited number of studies have shown an association of low cholesterol with ovarian cancer. These studies used single measures of cholesterol either at cohort entry or diagnosis. Results are mixed, depending on size of cohort, timing of measure, and type of cholesterol measured. This study used data from a single institution to evaluate serial high-density lipoprotein (HDL) cholesterol measures in the 10 years prior to diagnosis.

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doi:10.1016/j.ygyno.2015.01.458
Objectives: The optimal strategy for combining chemotherapy with immunotherapy in ovarian cancer patients is currently unknown. Increasing evidence indicates that the lymphopenia induced by chemotherapy may promote homeostatic proliferation, thereby enhancing antitumor immunity. The goals of this study were to determine the frequency of chemotherapy-induced lymphopenia and the impact of the timing of lymphopenia on clinical outcomes of ovarian cancer patients.

Methods: We performed a chart review of 115 patients identified in the electronic medical record from May 2005–2011. Identified patients were those who received at least 6 cycles of carboplatin and paclitaxel under our care for primary peritoneal, ovarian, or fallopian tube carcinoma. We focused on lymphocyte nadir for this population. For each patient’s lymphocyte count, nadir values were abstracted from weekly complete blood counts. We then split the population into two groups based on whether the nadir occurred at or after the 9-week mark (third cycle). This point was chosen because it was good for prognosis and it corresponds to patients whose trajectories bottom out.

Results: The nadir of absolute lymphocyte concentrations was associated with platinum status and clinical response (Fig. 1A). A total of 94/115 patients had a lymphocyte count nadir after the third cycle of chemotherapy and 71/94 (75.5%) were platinum-sensitive, 21/94 (22.3%) were platinum-resistant, and 2/94 (2.1%) were refractory. Of those who experienced a nadir before 3 cycles, 10 (47.6%) were -sensitive, 10 (47.6%) were -resistant, and 1 (4.7%) was refractory (P = 0.04). Considering nadir values continuously, both overall survival (OS) (P = 0.0068) and progression-free survival (PFS) (P = 0.0321) were strongly associated with late nadir points. Twenty-one of the 115 patients had a nadir value earlier than the third draw and this was associated with progressive disease, platinum resistance, poor OS, and poor PFS. The effect sizes were substantial (median OS 33 vs. 66 months; median PFS 14 vs. 38 months with early vs. late nadir, respectively [Fig. 1B]).

Conclusions: The nadir of absolute lymphocyte concentrations is an independent predictor of OS and PFS. This is an easily measurable biomarker that can be used for identifying patients who are likely to respond to immunomodulation.

<table>
<thead>
<tr>
<th>Table</th>
<th>Patient demographics regarding the lymphocyte nadir before and after the third cycle of chemotherapy.</th>
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<tr>
<td></td>
<td>≥9 weeks</td>
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<tr>
<td>n</td>
<td>94</td>
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<tr>
<td>Site</td>
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<tr>
<td></td>
<td>Ovary</td>
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<td></td>
<td>Primary peritoneal</td>
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<tr>
<td>Age</td>
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<tr>
<td>BMI</td>
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<tr>
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<tr>
<td>Stage</td>
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<td></td>
<td>III/IV</td>
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<tr>
<td>Grade</td>
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<td>2</td>
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<td></td>
<td>3</td>
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<tr>
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**Figure.** Overall survival and progression free survival in patients that had a lymphocyte count nadir before and after the third cycle.

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455 – Poster Session

The genomic landscapes of high grade serous ovarian cancers: Contrasting long term survivors and “platinum-resistant” disease

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Objectives: To explore genomic determinants of treatment sensitivity and resistance in high-grade serous ovarian carcinoma (HGSOC), we examined whole genome profiles of extreme responders: long-term survivors (LS) vs. short recurrence (SR).

Methods: Women with HGSOC with fresh frozen tissue, clinicopathologic, and outcome data across two institutions were identified as either LS >4.5 years from diagnosis or SR <9 months after diagnosis. Comprehensive whole genome sequencing (WGS), copy number, loss of heterozygosity (LOH), and rearrangements were assessed.

Results: A total of 75 cases were identified with SR <9 month relapse or LS >4.5 years. Of the 62 WGS libraries completed thus far, full analysis is available on 50 cases: 29 LS, 19 SR, and 2 SRLS (median coverage tumors 50×). Nanostring gene expression profiles were also obtained on all samples. No association was seen between extreme outcomes groups and previously established gene expression subtypes. No association was seen in relative mutation load (single nucleotide variations) between groups. Tumor protein 53 mutation frequency and distribution across protein domains were consistent with expectation of >80%. Mutations in genes involved in DNA repair mechanisms were frequent (>87%) and diverse (>29 genes), with enrichment in LS. BRCA1/2 mutations were more frequent in LS: BRCA1 germline (5 LS, 2 SR), BRCA2 germline (2 LS, 1 SR), BRCA1 somatic (1 LS), and BRCA2 somatic (1 LS, 1 SR). SR cases exhibited enrichment of PIK3CA mutations, loss of PTEN, CCNE1 high-level amplification, fewer BRCA1/2 mutations, more rearrangements in RAD51B, and enrichment of C-T nucleotide substitution patterns. LS and SR harbored different rearrangement profiles and clonal diversity profiles in LOH features, with tumors from women experiencing SR having a greater proportion of dominant clonal populations as compared to a higher proportion of subclonal in LS.

Conclusions: Amid the diverse landscape of what is classified as HGSOC, supervised analysis of extreme outcome groups identified global genomic architecture differences, largely attributable to enriched deficiency of DNA repair pathways in LS. We hypothesize that the interplay between clonal diversity and genomic instability confers inherent potential for resistance and sensitivity to platinum-based therapy and opportunities for patient stratification.

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456 – Poster Session

Hyperthermic intraperitoneal chemotherapy for epithelial ovarian cancers: Is there a role?


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Objectives: Hyperthermic intraperitoneal chemotherapy (HIPEC) is often used to treat gastrointestinal malignancies and is of interest in epithelial ovarian cancer (EOC), given the propensity for intraperitoneal spread. The role of HIPEC in the treatment of gynecologic malignancies has not been well defined. We sought to describe clinical characteristics and outcomes of our patient population treated with HIPEC.

Methods: Institutional review board approval was obtained. Patients diagnosed with EOC and treated with HIPEC during their disease course from January 2007 to December 2013 were identified using a prospectively maintained HIPEC database. Patient charts were abstracted to identify patient demographic information, treatment characteristics, and outcome data. Statistical analysis was descriptive.

Results: Twenty-eight patients were identified. Mean age at diagnosis was 56 years. The majority of cases (20 [71%]) were of serous histology. The indications for HIPEC administration were as follows: 13% primary treatment, 55% first recurrence, and 32% second recurrence. The majority of patients (17 [55%]) received mitomycin C. The other drugs administered included cisplatin (10 [32%]), oxaliplatin (2 [6%]), and carboplatin (1 [3%]). The mean number of chemotherapy regimens administered prior to HIPEC was 1.7 (range, 0–4). Mean length of hospital stay was 9 days (range, 3–25 days). Twelve (39%) patients required postoperative intensive care unit admission, most of which were planned preoperatively. The rates of postoperative bacteremia and hematologic toxicity were 3% and 39%, respectively. Seven (23%) patients developed transient renal dysfunction (all resolved by 30 days following surgery), and this was seen almost exclusively in patients who received cisplatin. There were no perioperative deaths in this cohort. Nine (32%) patients received additional chemotherapy following HIPEC administration. At median follow-up of 18 months, 8 patients are alive with disease, 8 have no evidence of disease, 12 have died of their disease, and for 3 patients the status is unknown.

Conclusions: These data support a reasonable adverse effect profile of treatment of EOC with HIPEC. Prospective studies are needed to elucidate the optimal drug and patient population that would derive the most benefit from treatment with HIPEC.

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457 – Poster Session

Impact of perioperative fluid status on surgical outcomes in patients with epithelial ovarian cancer

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Objectives: Perioperative fluid management in cytoreductive surgery for ovarian cancer requires a delicate balance because patients frequently have large-volume ascites and procedures are often lengthy, with multiple organ resections. In the non-gynecologic literature, fluid overload (FO) has been shown to be associated with postoperative morbidity. The study objective was to investigate the impact of FO, a potentially modifiable factor, in patients undergoing laparotomy for ovarian cancer.

Methods: All patients undergoing primary surgery with laparotomy for ovarian, fallopian tube, and primary peritoneal carcinoma at a comprehensive cancer center from 12/2010 to 7/2014 were identified. Demographic, perioperative, and 30-day complication data were abstracted from the medical records. Perioperative weight change, defined as the difference between preoperative weight and the maximum weight measured during the perioperative period, was used as a surrogate for FO. The time to diuresis (tD) was defined as the postoperative day that the patient’s weight began to downtrend. Standard statistical analysis was used.

Results: Ninety-one patients were identified. Median age was 63 years (range, 34–88 years) and median body mass index was 25.8 (range, 16.6–47.9). The majority were stages III–IV (59.3%). Median blood loss was 500 mL (range, 100–4000 mL) and median operative time was 303.5 min (range, 134–755 min). A median of 5000 mL of crystalloid (range, 2500–17,550 mL) was given intraoperatively. At least one bowel resection was performed in 41 cases (45%) and at least one upper abdominal procedure in 60 patients (65.9%). The median perioperative weight gain was +6 kg (range, −9.8 kg–+35.7 kg). The median tD was 3 days (range, 1–17 days). In the 5 patients with tD > 5 days, there was a 100% complication rate. On univariate analysis, FO was associated with anastomotic leak, ileus, wound infection/breakdown, and length of stay. On multivariate analysis that included known surgical risk factors, FO was independently associated with wound complications. Operative time was the only factor significantly associated with length of stay.

Conclusions: Postoperative FO is common in patients undergoing surgery for ovarian cancer and is independently associated with wound complications. Euvolemia should remain the goal of care when possible.

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458 – Poster Session

Patterns of cancer recurrence in African American patients with high grade epithelial ovarian carcinoma

S. Singh, A. Armstrong, G. Pettigrew, K.E. Resnick. University Hospitals Case Medical Center, Cleveland, OH, USA

Objectives: To compare the distribution of site of first recurrence in African American (AA) patients with high-grade epithelial ovarian, tubal, and primary peritoneal carcinoma compared to Caucasian (C) patients after primary surgical management followed by adjuvant platinum-based therapy.

Methods: Patients diagnosed with high-grade epithelial ovarian, fallopian tube, or peritoneal carcinoma at our institution between 2007 and 2013 were identified from an existing tumor registry. We included patients who underwent surgical staging and/or optimal surgical cytoreduction who also received adjuvant platinum-based chemotherapy. Demographics, tumor characteristics, and adjuvant treatment details were recorded. Time to recurrence, anatomic location of recurrence, and disease status at the last follow-up were identified. Descriptive statistics were used to analyze data, with a P = 0.05 being considered significant.

Results: Two hundred thirty-eight patients met the criteria for inclusion and were divided into groups based on race: 211 (88.7%) were C and 27 (11.3%) were AA. The groups did not differ with respect to age, body mass index, or stage at diagnosis. Most patients presented with stage III disease (82.3%) and had serous histology (84%). The majority of patients (90.4%) completed six cycles of adjuvant chemotherapy, with the number of completed cycles not significantly differing between groups. AA patients were more likely to have multiple anatomic sites of recurrence rather than a single site when compared to C patients (61.5% vs. 40.4%, P = 0.039). At time of first recurrence, AA patients were more likely to have liver involvement (23.1% vs. 7.5%, P = 0.1) and chest involvement (30.8% vs. 12.9%, P = 0.007).
Patients were identified through established pathology databases that were searched from 2000 to 2014. The inclusion criteria were a pelvic serous cancer. Of the nine patients, only two (22%) were patients with isolated STIC received adjuvant therapy, and at a median follow-up of 30 months, none of the patients had developed a pelvic serous cancer. Of the nine patients, only two (22%) were diagnosed after RR Sophia with a BRCA mutation. Of the seven patients diagnosed outside of an RR Sophia, one was diagnosed after surgery for endometrioid endometrial cancer and two had a family history of ovarian cancer. One of the non-RR Sophia patients was BRCA tested, and she was negative. During the same time period, at one of the institutions there were 6500 salpingectomies performed, 188 of which were risk-reducing, giving an isolated STIC rate of 0.06% and 1% from non-RR Sophia and RR Sophia procedures, respectively.

Conclusions: The rate of STIC in our population was extremely low. However, our study shows that STIC likely exists as an entity within non-BRCA carriers. The diagnosis of STIC outside of RR Sophia will likely increase as salpingectomy at the time of hysterectomy and salpingectomy as a method of sterilization increase. The question of how many STIC lesions are being missed due to SEE-FIM being performed selectively on RR Sophia specimens and the clinical significance of this is a topic for further study. However, it is reassuring that without adjuvant therapy, no patients in our study developed invasive cancer.

Objective: The decision to perform radical cytoreductive surgery (CRS) in patients with ovarian cancer (OC) is multifactorial. The study objective was to describe the national trends and factors associated with CRS radicality.

Methods: An analysis of the Healthcare Cost and Utilization Project-National Inpatient Sample database was performed. All single admissions for patients with OC undergoing at least laparotomy with oophorectomy and excision/destruction of peritoneal lesion from 1988 to 2011 were identified. CRS radicality was defined using International Classification of Disease-9 codes as: “Simple pelvic” (SP), “Extensive pelvic” (EP), and “Extensive upper abdominal” (EUA). Patient-specific factors, including age, race, and income, and system-specific factors, including location (rural vs. urban), region, ovarian cancer volume, hospital size, and teaching status, were examined for their associations with CRS radicality. Trends in CRS were analyzed per year and associated factors in 5-year blocks (“early” 1988–1992 vs. “late” 2007–2011).

Results: In total, 56,414 admissions were analyzed. Over time, the rate of EP resections increased from 8% to 18.1% (P < 0.001) and the rate of EUA resections increased from 1.3% to 5.4% (P < 0.001). The rate of EP resections decreased from 90.6% to 76.5% (P < 0.001). In the early time period, factors significantly associated with CRS radicality were age (P < 0.001), income (P = 0.02), urban teaching hospital (P < 0.001), and region (P < 0.001). Overall, more radical procedures were performed in patients who were younger, higher income, and at urban teaching hospitals in the Northeast and West regions. In the late time period, age (P < 0.001), income (P = 0.02), race (P = 0.02), urban teaching hospital (P < 0.001), region (P < 0.001), and hospital size (P < 0.001) were associated with radicality. Overall, more radical procedures were performed in patients who were younger, higher income, white race, at urban teaching hospitals, at large centers, and in the South.

Conclusions: The rate of radical CRS, including both EP and EUA resections, has significantly increased over the past 2 decades. Patient-specific factors such as age, race, and income as well as system-specific factors such as region, location, and hospital type and size were associated with CRS radicality. Understanding the impact of these factors is crucial in addressing disparities in the care of our changing health care environment.
women. In premenopausal women, 21.75% (87/400) had malignancy at the time of surgery, higher than comparable national statistics. Using the ACOG/SGO referral criteria, 62.1% (54/87) would be predicted to have cancer and referred to a gynecologic oncologist for surgery; however, in practice, only 55.2% (48/87) were operated on by an oncologist. Among postmenopausal women, the ACOG/SGO referral guidelines would have captured 87.5% of malignant cases. The sensitivity of oncology referral in actual practice was slightly lower (68.9%) for both pre- and postmenopausal women; there was a higher specificity (85.9%) and PPV (68.5%) compared to that predicted by the ACOG/SGO criteria (81.7% and 64.8%, respectively). Of all the ACOG/SGO criteria, CA-125 remained the only significant independent predictor of cancer in both premenopausal (relative risk [RR] 3.63, P < 0.001) and postmenopausal women (RR 1.33, P < 0.001).

Conclusions: In this population, even though there is a higher risk of malignancy compared to the national cancer statistics, the ACOG/SGO preoperative guidelines correctly identified 75.4% of all women and 62.1% of premenopausal women. Referral patterns based on actual practice maximized specificity and PPV. Further studies should focus on those patients who had malignant disease at the time of surgery but were not identified by the SGO criteria to determine what other preoperative factors are important for appropriate referral.

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462 — Poster Session
Refusal of recommended chemotherapy for ovarian cancer: Risk factors and outcomes, a National Cancer Database study
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Objectives: We sought to identify risk factors associated with refusal of recommended chemotherapy (CT) as well as its impact on patients with epithelial ovarian cancer using a large, national cancer database.

Methods: We identified patients in the National Cancer Database (NCDB) diagnosed with epithelial ovarian cancer from 1/1998 to 12/2011. Patients who refused CT were identified and compared to those who received recommended multiagent CT. Univariate and multivariable analyses were performed using chi square test with Bonferroni correction, binary logistic regression, log-rank test, and Cox proportional hazards modeling. Threshold for statistical significance was set at P < 0.05.

Results: A total of 147,713 patients were identified, of whom 2707 (1.8%) refused CT. These patients were compared with 92,212 (62.4%) patients who received multiagent CT. On multivariable logistic regression, older age (>70 vs. ≤50 years, odds ratio [OR] 4.2), more medical comorbidities (≥2 vs. 0, OR 1.8), not having insurance (OR 1.4–2.9, depending on type), later year of diagnosis (2009–2011 vs. 2002–2004, OR 1.3), lower-than-expected facility adherence to the National Comprehensive Cancer Network guidelines (OR 1.2), treatment at low-volume center (lowest vs. highest, OR 1.6), lower grade (1 vs. 3, OR 2.0), and stage (1 vs. IV, OR 2.2) were all significantly and independently associated with CT refusal, while patient race, residential urban status/income/education level, unplanned surgical readmission, and treatment facility academic status/location/distance were not. Median overall survival of patients who received multiagent CT was 43 months, while it was 4.8 months for those who refused CT. On multivariable Cox model, after controlling for known patient, facility, and disease prognostic factors, CT refusal was associated with a 189% increased risk of death (95% CI 2.56–3.26, P < 0.0005).

Conclusions: Patient frailty (age, comorbidities), lack of insurance, treatment at less-experienced facilities (volume, guideline adherence), and lower stage/grade of disease but not race/socioeconomic factors are independently associated with CT refusal, which is associated with a significantly increased risk of death, even when known prognosticators are controlled. Further research is needed to identify individualized best practices for this high-risk subgroup.

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463 — Poster Session
Survival of the fittest: Can exercise prolong the time to ovarian cancer recurrence?
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Objectives: Epidemiologic studies suggest that exercise may improve survival outcomes among women with ovarian cancer. This benefit has been seen in other cancer types, including breast, prostate, and colon cancers, where regular aerobic activity significantly reduces cancer recurrence and improves overall survival. We sought to characterize the effect of exercise on ovarian cancer growth using a syngeneic murine model of ovarian cancer recurrence.

Methods: Murine ID8 ovarian cancer cells were injected intraperitoneally into 60 C57BL/6 mice. The mice randomized to exercise were given access to a Fastrac low-profile running wheel capable of measuring distance traveled per day, whereas sedentary mice were provided with a locked wheel for a duration of 2, 4, and 8 h per day. When any one treatment group of mice became moribund, all animals were sacrificed and tumor weights were compared. Serum was collected at the time of sacrifice and biomarkers were measured using commercially available enzyme-linked immunosorbent assay kits. Once the optimal duration of exercise was established, the study was repeated to determine the optimal frequency of exercise (2, 4, or 7 days per week). Tumor weights and biomarker concentrations were compared between groups using Student’s t-tests.

Results: Overall, exercising mice had a lower tumor weight compared to sedentary mice (0.1069 g vs. 0.1353 g, P = 0.03). The optimal frequency and duration of exercise was 4 h a day, 7 days a week, demonstrating the greatest improvement in tumor...
Factors affecting ovarian cancer treatment in the octogenarian patient population


Objectives: To identify treatment patterns, treatment decision factors, associated morbidity, and survival in women aged 80 and older with newly diagnosed ovarian cancer.

Methods: A single-institution retrospective analysis of women 80 years of age and older treated for newly diagnosed ovarian cancer was performed. Data were abstracted on treatment received, comorbidities, and outcomes.

Results: Forty-seven octogenarian patients were identified with newly diagnosed ovarian cancer. Median age was 83 years (range, 80–94 years). Stage distribution was as follows: 7 stage I, 2 stage II, 22 stage III (18 stage IIC), and 11 stage IV. Five patients were not staged or incompletely staged. Ninety-one percent had at least one comorbidity, 15% with a prior malignancy or synchronous primary, colon cancer being the most common. Thirty-one patients (66%) underwent primary debulking, 4 (40%) of which were performed by non-gynecologic oncologists because of bowel obstruction or colonic perforations. Twenty-one of 31 (68%) surgical patients subsequently received adjuvant chemotherapy at a mean of 28 days (range, 15–42 days) from surgery. Four perioperative deaths were noted, two of which were associated with bowel perforations. Of the 16 neoadjuvant chemotherapy patients, the reason for treatment was most commonly related to extent/stage of disease and performance status. Age was a factor in only one case and extensive comorbidities was a factor in three cases. Only seven (44%) patients underwent interval debulking. Mean progression-free survival for this octogenarian cohort was 21 months (range, 2–43 months) and overall survival was 34 months (range, 0–122 months).

Conclusions: Octogenarians have a high perioperative death rate (10%), mostly associated with bowel perforations, and are less likely to undergo adjuvant chemotherapy after surgical resection. They are more likely to receive neoadjuvant chemotherapy because of poor performance status and advanced-stage disease.

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Cost effectiveness of primary debulking surgery when compared to neoadjuvant chemotherapy in the management of stages IIIC and IV epithelial ovarian cancer

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Objectives: To examine the cost-effectiveness of primary debulking surgery (PDS) when compared to neoadjuvant chemotherapy (NACT) in the management of epithelial ovarian cancer (EOC) using Surveillance, Epidemiology, and End Results data linked to Medicare claims (SEER-Medicare).

Methods: Using a Markov model, the cost-effectiveness of PDS was compared to that of NACT. We modeled cost and survival inputs using data from women in the SEER-Medicare database with ovarian cancer treated by either PDS or NACT between 1992 and 2009. Direct and indirect costs were discounted by an annual rate of 3%. Utility weights were obtained from published data. The incremental cost-effectiveness ratio (ICER) of PDS compared to NACT was calculated.

Results: In our model, women with stage IIIC EOC had a higher mean adjusted treatment cost for PDS when compared to NACT ($31,945 vs. $30,016) but yielded greater quality-adjusted life-years (QALYs) (1.79 vs. 1.69). The ICER was $19,359/QALY gained. Women with stage IV EOC had a higher mean adjusted treatment cost following PDS when compared to NACT ($31,869 vs. $27,338) but yielded greater QALYs (1.79 vs. 1.69). The ICER was $130,083/QALY gained. A sensitivity analysis showed that for both PDS and NACT, the ICER was sensitive to incremental changes in the utility weight.

Conclusions: PDS is significantly more cost-effective for women with stage IIIC EOC when compared to NACT. In women with stage IV EOC, PDS is also more cost-effective, although the QALYs gained are much more costly and exceed a $50,000 willingness to pay.

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Poor prognosis after conservative surgery in stage I mucinous epithelial ovarian cancer

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Conclusions: Exercise may suppress tumor growth, especially when the frequency and duration are optimized. Omentin may serve as a relevant biomarker of tumor response to exercise and may be useful in ongoing human studies. Our research supports epidemiologic studies suggesting that exercise may be beneficial for women diagnosed with ovarian cancer and may potentially prolong the time to recurrence.
Objectives: To evaluate the oncologic safety of conservative surgery and to identify prognostic factors for recurrence in premenopausal women with stage I mucinous epithelial ovarian cancer (mEOC).

Methods: We enrolled 97 patients who were premenopausal at the time of surgery and diagnosed with FIGO stage I mEOC. Conservative surgery was defined as unilateral salpingo-oophorectomy with without contralateral ovarian wedge resection, and none of the conservative surgery was completed by unilateral ovarian cystectomy alone.

Results: The median age was 33 years (range, 13–50 years) at the time of surgery. Sixty-three (64.9%) patients were stage Ia and 34 (35.1%) were Ic. Fifty-three (54.6%) patients underwent conservative surgery, and adjuvant chemotherapy was administrated to 61 (62.9%) patients. During 73.7 months (range, 7.1–243.5 months) of the median follow-up duration, 13 (13.4%) patients recurred and 8 (8.2%) of them died of the disease. Among patients who underwent conservative surgery, there were 10 recurrences, and the most common recurrence site was the intraperitoneal cavity (n = 8). In a multivariate analysis, a significantly poorer prognosis was noted for patients who underwent conservative surgery (HR 6.26, 95% CI 1.53–25.53, P = 0.011) and in patients with high preoperative CA-125 (HR 1.98, 95% CI 1.26–3.11, P = 0.003). In Cox’s proportional hazard model, patients who had high preoperative CA-125 (>35 U/ml, n = 48) and also underwent conservative surgery showed significantly worse prognosis (HR 5.73, 95% CI 1.22–27.03, P = 0.027). Five-year disease-free survival rate was significantly lower in patients who underwent conservative surgery than in patients who did not (77.7% vs. 94.2%, P = 0.047).

Conclusions: A poorer prognosis was observed in stage I mEOC patients who underwent conservative surgery. A further multicenter study with larger cohort is needed to evaluate the oncologic safety of conservative surgery in mEOC.

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467 — Poster Session

FIGO staging criteria is a meaningful clinical threshold for evaluating molecular signatures in serous ovarian cancer patients

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Methods: This study was performed in a cohort of 1183 serous ovarian cancer patients with publicly accessible FIGO stage, pathology, outcome, and Affymetrix-based transcriptome data. Data were downloaded from http://bcb.dfci.harvard.edu/ovariancancer and Combat corrected. Cox regression analysis was used to compare the prognostic impact using HR and 95% CI and the predictive accuracy using c-index ± SE for models. C-index provided a concordance probability and measure of ordinal predictive power for each model similar to AUC for a logistic regression model (C-index > 0.5 indicates a good model, C-index of 1.0 signifies a perfect model).

Results: Women diagnosed with more advanced stage or a higher RS200 calculated score had worse survival and an increased risk of death (Table 1). Evaluation of RS200 as a continuous variable or dichotomized at the median illustrated an inverse relationship between HR and C-index, with an increase in HR and corresponding reduction in predictive accuracy observed when the score was dichotomized. Integration of RS200 with stage demonstrated that each provides independent prognostic value and a significant improvement in predictive accuracy over stage alone.

Conclusions: The FIGO staging criteria is a meaningful clinical benchmark for comparing molecular signatures in serous ovarian cancer patients. The RS200 and FIGO stages provided independent prognostic value and optimal predictive accuracy for serous ovarian cancer patients.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>C-index ± SE</th>
<th>HR (95% CI)</th>
<th>C-index ± SE</th>
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</thead>
<tbody>
<tr>
<td>Univariate modeling</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Stage</td>
<td>1.6 (1.4–2.0)</td>
<td>0.551 ± 0.009</td>
<td>1.3 (1.1–1.6)</td>
<td>0.631 ± 0.013</td>
</tr>
<tr>
<td>RS200 risk score</td>
<td>1.5 (1.3–1.8)</td>
<td>0.642 ± 0.013</td>
<td>1.7 (1.5–2.1)</td>
<td>0.628 ± 0.012</td>
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<td>0.628 ± 0.012</td>
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</table>

Hazard ratio (HR), confidence interval (CI), c-index standard error (SE).

Statistical analysis:
† The FIGO 1988 stage was evaluated as I/II vs. III vs. IV.
‡ Continuous variable.
§ Dichotomized at the median as high vs. low.
¥ RS200 was calculated by i = 1/1 = 200coefficient i × transcript expression i where HR = e^coefficient

468 — Poster Session

Improving NCCN guideline-adherent care for ovarian cancer: Value of an intervention

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Objectives: To estimate the potential cost-effectiveness of an intervention to improve adherence to National Comprehensive Cancer Network (NCCN) guideline-based care for ovarian cancer.

Methods: A modified Markov model with a 5-year time horizon estimated the potential cost-effectiveness of an intervention (AD-INT) to improve NCCN guideline adherence compared to status quo (SQ) levels of adherence. Data were obtained from a population-based analysis of National Cancer Data Base records for primary epithelial ovarian cancer diagnosed from 1998 to 2002 (n = 47,160). Cohorts for survival and cost estimates were defined by race (black or white) and levels of adherence to NCCN guideline-based care (SQ: 36% black, 44% white). Costs of surgery and chemotherapy were estimated using 2014 Medicare reimbursements. Incremental cost-effectiveness ratios (ICERs) were calculated in 2014 US dollars per year of life saved (YLS) using the standard threshold of $50,000/YLS. We simulated an AD-INT that reduced nonadherence by 25% and cost at least $100 per patient. End-of-life costs were from Medicare and personal care, a reasonably effective AD-INT is also highly likely to be cost-effective. An AD-INT costing $100 per patient and reducing nonadherence by 25% is dominant (more effective and less expensive).

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compared with SQ, while interventions costing >$1000 are more expensive but still cost-effective. AD-INT remains cost-effective at a per-patient intervention cost of up to $8000 (targeting blacks) or $4000 (targeting all patients). Given approximately 20,000 new cases of ovarian cancer per year (10% in black women), an AD-INT targeting all women and costing $80 million or less would be highly cost-effective; an AD-INT targeting only blacks and costing $16 million or less would also be highly cost-effective (Table 1).

**Conclusions:** An ovarian cancer intervention that moderately decreases racial disparities in NCCN guideline-adherent care or improves adherence for all would be cost-effective. Further research may determine which modifiable factors contributing to receipt of nonadherent care may be targeted to help reduce disparities.

### Table 1

<table>
<thead>
<tr>
<th>Population targeted</th>
<th>Cost/ patient ($)</th>
<th>Degree of reduction in non-adherence</th>
<th>ICER ($/year of life saved)</th>
<th>Annual incidence in target U.S. population</th>
<th>Upper limit of cost of an annual nationwide adherence intervention that would remain cost-effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>$4000</td>
<td>25%</td>
<td>$50,000/YLS</td>
<td>20,000</td>
<td>$80 million</td>
</tr>
<tr>
<td>Blacks</td>
<td>$8000</td>
<td>25%</td>
<td>$50,000/YLS</td>
<td>2000</td>
<td>$16 million</td>
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</table>

**Objective:** To our knowledge, no studies have evaluated the association of GDM with EC. This hypothesis-generating study suggests that even a transient diabetic state may increase EC risk. If validated, this would represent a potential opportunity for early risk awareness. Further research should clarify whether GDM affects EC risk independently or only through eventual higher rates of type 2 diabetes mellitus and obesity, which could not be adequately evaluated in this database.

doi:10.1016/j.ygyno.2015.01.474

### 469 – Poster Session

**Gestational diabetes may increase risk of endometrial cancer later in life: Results of a population-based study in Washington State, 1987–2012**


**Objectives:** Several studies have shown that women with type 2 diabetes mellitus have an increased risk of developing endometrial cancer (EC). We investigated whether gestational diabetes mellitus (GDM) is also associated with EC in parous women.

**Methods:** We conducted a population-based case–control study of women in Washington State who were at least 16 years of age at the time of delivery with either a birth or fetal death record from 1987–2011. Cases were women with EC and controls were women without EC, based on Washington State hospital diagnostic codes from discharge data from 1993 to 2012 and linked to the birth registry. Cases and controls were frequency matched by delivery year. Demographic and pregnancy information was obtained from the birth registry. Logistic regression was used to estimate maternal age and parity-adjusted odds ratios (OR) for the association of EC with GDM. Maternal weight and body mass index were not available prior to 1992 and 2003, respectively. We, therefore, performed a subanalysis of those delivered after 1992 using logistic regression to estimate age, parity, and obesity-adjusted ORs.

**Results:** We identified 362 EC cases and 7055 controls. Controls were older than cases at time of delivery (mean age, 34 vs. 32 years) and were more likely to be multiparous (73% vs. 68%). GDM was more frequent for cases (6.6%) than controls (4.0%), resulting in a 1.9 times increased odds of EC among women with a history of GDM (95% CI 1.2, 2.9). For women delivering from 1992 to 2011 (212 cases and 4362 controls), GDM was more common for cases than controls (7.6% vs. 5.0%), resulting in a 1.8 times increased odds of EC (95% CI: 1.2, 2.9). For these years, obesity data were only available for 168 (46%) cases and 3424 (79%) controls. Restricting to this small group, the association between EC and GDM could no longer be assessed (OR = 1.6, 95% CI: 0.8, 2.9). The obesity-adjusted OR was 1.3 (95% CI: 0.7, 2.5).

**Conclusions:** To our knowledge, no studies have evaluated the association of GDM with EC. This hypothesis-generating study suggests that even a transient diabetic state may increase EC risk. If validated, this would represent a potential opportunity for early risk awareness. Further research should clarify whether GDM affects EC risk independently or only through eventual higher rates of type 2 diabetes mellitus and obesity, which could not be adequately evaluated in this database.

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### 470 – Poster Session

**Distance to specialist care is associated with survival in patients with gynecologic malignancies**

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**Objectives:** Women who live in rural regions and develop gynecologic malignancy may have limited access to local specialist care and are required to travel substantial distances to see a gynecologic oncologist. Prior reports have suggested that distance from residence to treatment facility is a barrier to care. We sought to investigate the effect of distance to specialist care (DTSC) at a university hospital on outcomes for patients with gynecologic malignancy.

**Methods:** After institutional review board approval, patients with gynecologic malignancy treated at the Edward Comprehensive Cancer Center and Marshall University between 2006 and 2014 were identified using the cancer registry database. Clinical and demographic data were collected using the American College of Surgeons/Commission on Cancer data elements and met national and state quality edits. DTSC for each patient was calculated in miles and minutes and subject to multivariate analysis for associations with clinical data.

**Results:** A total of 810 patients diagnosed with gynecologic malignancy, including cancers of the ovary (n = 127), uterus (n = 489), cervix (n = 88), vulva (n = 52), peritoneum (n = 22), and other (n = 32), were identified during the study period. Using the median DTSC as a threshold, short DTSC was found to be associated with an improved overall survival (P < 0.001). Caucasian patients who had a short DTSC experienced longer survival than those with greater DTSC, although this was not the case for African-American (AA) patients. No difference in stage, grade, histology, age, family history of cancer, medical comorbidities, or insurance type was found between patients with short vs. long DTSC.

**Conclusions:** Geographic proximity to a university hospital is associated with overall survival for Caucasian but not AA patients with gynecologic malignancy. These findings highlight the importance of access to care and racial disparities in outcome from gynecologic cancer. Further studies may help us identify specific areas of geographic disparity and potential outreach programs.

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### 471 – Poster Session

**Racial disparities and the effect of time on ovarian cancer survival among cases identified through the National Cancer Database**

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**Objectives:** Racial disparities in cancer survival may affect outcomes and survival for women with ovarian cancer. The effect of time may contribute to disparities for various reasons. This study was conducted to evaluate racial disparities in ovarian cancer survival and to compare the effect of time on ovarian cancer survival for each racial group.

**Methods:** The Surveillance, Epidemiology, and End Results (SEER) Program was used to identify racial disparities in ovarian cancer survival. Kaplan-Meier survival analysis was used to evaluate the effect of time on ovarian cancer survival for each racial group.

**Results:** The effect of time on ovarian cancer survival was found to be significant for all racial groups. The effect of time was found to be strongest for non-Hispanic white women and weakest for non-Hispanic black women. The effect of time was found to be more pronounced for women diagnosed before 2000.

**Conclusions:** Racial disparities in ovarian cancer survival may affect outcomes and survival for women with ovarian cancer. The effect of time may contribute to disparities for various reasons. Further research is needed to identify the factors contributing to these disparities and to develop strategies to reduce them.
Objectives: Previous research identified poorer survival among non-Hispanic black (NHB) than white (NHW) women diagnosed with invasive ovarian cancer. Treatment advances may have increased survival disparities because blacks are less likely to receive therapies consistent with National Comprehensive Cancer Network guidelines or even basic oncologic care. The purpose of this study was to evaluate racial disparities in survival among women diagnosed with ovarian cancer in the United States and Puerto Rico between 1998 and 2006 and determine whether disparities have changed over time.

Methods: NHW and NHB cases from the National Cancer Database (NCDB) were analyzed to assess 5-year survival. Univariate analysis was used to compare race-stratified demographic and clinical variables with year of diagnosis analyzed in two periods (1998–2002 vs. 2003–2006). Multivariable Cox proportional hazard regression models were fit to estimate the adjusted HR and 95% CI between race and survival. Tests for interaction between race and year of diagnosis were performed in final models. Interaction was also assessed in adjusted stage-specific models.

Results: A total of 99,774 (92.5%) NHW and 8121 (7.5%) NHB were analyzed. NHB had significantly poorer survival (HR crude = 1.44, 95% CI 1.40–1.49; HR adjusted = 1.19, 95% CI 1.15–1.23). Interaction between race and diagnosis year for all women was not significant (P = 0.51), with similar estimates by period (1998–2002 HR = 1.21, 95% CI 1.16–1.26; 2003–2006 HR = 1.16, 95% CI 1.10–1.22). Interaction between race and year was borderline significant with stage IV disease (P = 0.08) but not others (I: P = 0.20; II: P = 0.74; III: P = 0.58), and stage IV NHB survival improved marginally over time (1998–2002 HR = 1.20, 95% CI 1.12–1.27; 2003–2006 HR = 1.09, 95% CI 1.01–1.18).

Conclusions: Results identify persistent black–white survival disparities, with some indication that stage IV disparities may be decreasing. Findings may underestimate disparities because the NCDB reflects ~70% of United States cases annually, generally including higher-tier, Commission on Cancer (CoC)-approved hospitals.

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472 — Poster Session
HPV vaccination rates among US medical students

Objectives: Human papillomavirus (HPV) vaccination rates in the United States have been stagnant, with only 33% of girls between the ages of 12 and 17 years and 6.8% of boys receiving the vaccine in 2012. Multiple barriers to vaccination have been explored. We sought to determine barriers to vaccination among a well-educated group of medically literate individuals.

Methods: After obtaining institutional review board approval, a web-based survey was sent to all medical students at a single medical school in the United States in the fall of 2013. Data obtained in this survey included sex, age, race, and household income during their secondary education years. Respondents were included only if they were born after 1980 if female or 1982 if male. They were asked if they had received all or part of the vaccine series. Those not vaccinated were asked questions to determine reasons that they did not undergo vaccination. Student’s t-test and chi square analyses were used.

Results: Of a possible 1095 respondents, we received 345 surveys (31.5%). The majority of the respondents were female (209 [61.3%]). Twenty responses were eliminated due to being outside age restrictions. Of the remaining cohort, the majority was Caucasian (62.6%) and had a reported household income growing up of $100,000 or less (59.1%). For the entire cohort, 49.3% reported that they had received at least one shot, with the majority (83.5%) receiving all three shots. Race was not a significant risk factor for all patients being vaccinated (P = 0.28), but having a median household income $100,000 was significant for vaccination (P = 0.046). Common reasons for not receiving the vaccine in this study included not being discussed by the provider (50.5%), insurance not covering series
(11.5%), and concern over adverse effects (9.5%). Surprisingly, only 62.4% of unvaccinated medical students would be interested in receiving the vaccine today.

Conclusions: Although a higher percentage of patients in this well-educated cohort received the HPV vaccine than in other United States cohorts, significant barriers to vaccination still exist. Attitudes and accessibility still remain primary stumbling blocks to vaccinating the general public. Future studies should explore ways to overcome these barriers.

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474 — Poster Session
Complementary and alternative medicine use in patients with gynecologic cancers
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Objectives: Complementary and alternative medicine (CAM) use is common worldwide. We evaluated CAM practices among patients with gynecologic (GYN) malignancies presenting to a National Cancer Institute-designated Comprehensive Cancer Center.

Methods: Women with GYN malignancies enrolled in our institutional prospective clinical registry and specimen repository between January 2003 and January 2014 who had completed a questionnaire assessing sociodemographic characteristics, medical histories, quality of life, and use of CAM were considered for analysis.

Results: Among 2508 women with GYN malignancies who consented to the registry, responses to questions on CAM use were provided by 534 (21.3%). The majority of CAM question respondents were white (93.5%) and older than 50 years (75.8%). Overall, 464 women (18.5% of the total registry and 86.9% of CAM question respondents) used at least one CAM therapy during the previous 12 months. The most commonly used CAM categories were: 1) biologically based approaches (e.g., diets, herbs, vitamins, tea) 83.3%; 2) manipulative and body-based therapies (e.g., massage, chiropractic, osteopathy, reflexology) 81.2%, and 3) mind and body interventions (e.g., yoga, spirituality, relaxation, art and music therapy, biofeedback, meditation) 30.1%. In particular, vitamins and minerals (78%), herbal supplements (27.9%), spiritual healing and prayer (15.1%), and deep breathing relaxation exercises (13.1%) were the most commonly used individual CAM therapies. CAM use was greatest in age groups 20–30 years (manipulative and body-based therapies most common) and >65 years (biologically based most common). CAM use was more prevalent among those who were widowed \( (P < 0.005) \), retired \( (P = 0.02) \), and with higher level of education \( (P < 0.01) \). There was no association with race or ethnicity.

Conclusions: CAM use is highly prevalent among women being treated for GYN malignancies. Given the potential interactions of some CAMs with conventional treatment and the possible benefits in controlling symptoms and improving quality of life, providers should discuss CAM with their patients.

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475 — Poster Session
Real world effectiveness of minimally invasive hysterectomy for uterine cancer
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Objectives: Laparoscopic-assisted vaginal hysterectomy (LAVH) has been demonstrated to be safe and efficacious in randomized trials. However, randomized, controlled trials typically include highly selected patients treated at tertiary centers, and results from these trials often are difficult to translate into real-world populations. We compared the baseline characteristics and outcomes of patients undergoing LAVH in the general population to patients treated by laparoscopy in a cooperative group trial.

Methods: Women who underwent LAVH from 2005 to 2006 and who were recorded in the National Surgical Quality Improvement Project (NSQIP) database were compared to women treated in the Gynecology Oncology Group’s LAP2 (GOG-LAP2) protocol. Preoperative clinical characteristics and postoperative outcomes were compared using chi square tests and multivariable regression models.

Results: A total of 1696 uterine cancer patients treated with laparoscopy in GOG-LAP2 were compared with 3805 non-trial uterine cancer patients from NSQIP who underwent LAVH. Among GOG-LAP2 participants, 91.5% underwent lymphadenectomy (LND) compared to 57.5% of non-trial patients \( (P < 0.0001) \). Patients in both groups were similar with respect to age, although trial patients had lower body mass index and were more likely to be white and functionally independent at baseline. Median operative time was longer for trial vs. non-trial patients \( (204 \text{ min [interquartile range (IQR) 157–229] vs. 172 min [IQR 127–229]}) \). Similarly, length of stay was 3 days \( (IQR, 2–4) \) for GOG-LAP2 participants compared to 1 day \( (IQR, 1–2) \) for non-trial subjects. The rates of postoperative complications, including pneumonia, pulmonary embolism, transfusion, reoperation, and readmission, were lower in non-trial subjects. These findings were similar when GOG-LAP2 patients were compared to only non-trial participants who underwent lymphadenectomy.

Conclusions: Despite differences in patient characteristics, laparoscopy for surgical staging of uterine cancer is associated with overall low rates of postoperative complications and short lengths of stay in both clinical trial and non-trial “real-world” patients.

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476 — Poster Session
Distribution of endometrial cancer histology in a southern urban safety net hospital
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Objectives: African American race has been associated with aggressive histologic type and advanced stage at diagnosis of uterine cancer. We sought to determine the distribution of uterine cancer histology in a county hospital serving an underserved population.

Methods: We conducted a retrospective review of all patients diagnosed with endometrial carcinomas and uterine sarcomas identified in the tumor registry between 2004 and 2013. Demographic, clinical, and histologic information were extracted and analyzed using Science Analysis System Software.

Results: There were 315 patients, of whom 81.9% were African American and 47.0% were uninsured at initial presentation. There were 153 type I endometrial carcinomas (52 grade 1, 77 grade 2, 24 grade 3), 82 type II, 43 carcinosarcomas, 30 other sarcomas, and 7 unknown histology. Mean age at diagnosis was 55.1 years in type I, 63.5 years in type II, and 64.1 years in carcinosarcoma \( (P < 0.001) \). Older patients had more advanced stage at diagnosis \( (P = 0.007) \). More type II and carcinosarcoma presented at advanced stage than type I \( (P < 0.001) \). When compared with Surveillance, Epidemiology, and End Results (SEER) national data, African American women in our population had a higher incidence of type II (32.2% vs. 16.8%) and...
carcinosarcoma (17.8% vs. 12.8%) \((P < 0.001)\). The recurrence rate was higher for both histologic type II and carcinosarcoma \((P = 0.012)\), as was advanced stage at diagnosis \((P < 0.001)\). Histologic type II, carcinosarcoma, and advanced presenting stage were associated with poor survival \((censored log rank P < 0.001)\).

**Conclusions:** Our population had higher percentage of type II and carcinosarcoma compared to national data from SEER. Both histologic types and advanced stage were associated with poor survival. The reasons for this significant difference in histologic distribution in our population are not known. Further studies are indicated to delineate whether referral patterns, population genetics, and environmental factors contribute to these findings.

<table>
<thead>
<tr>
<th>Study population</th>
<th>SEER data</th>
<th>(P) value</th>
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<tbody>
<tr>
<td>African American</td>
<td>African American</td>
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<tr>
<td>Cancer type</td>
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<tr>
<td>Type I</td>
<td>112 (47.5)</td>
<td>2,993 (59.7)</td>
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<tr>
<td>Type II</td>
<td>76 (32.2)</td>
<td>820 (16.8)</td>
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<tr>
<td>Carcinosarcoma</td>
<td>41 (17.3)</td>
<td>627 (12.8)</td>
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<tr>
<td>Other</td>
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</table>


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**477 – Poster Session**

**National age standardized rate (ASR) of uterine corpus cancer (CC) correlates with Human Development Index (HDI), analysis of data from 154 countries**

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**Objectives:** To describe the associations between national CC incidence, HDI, and mean body mass index (BMI).

**Methods:** The United Nations states that HDI is “a summary measure of average achievement in key dimensions of human development: a long and healthy life, being knowledgeable and have a decent standard of living. The HDI is the geometric mean of normalized indices for each of the three dimensions.” Although HDI is primarily a socioeconomic parameter, it has been associated with cancer incidence and mortality in certain geographic regions. The ASR for CC in 2012 and mean BMI in women aged $\geq 20$ years in 2009 were obtained for 190 countries from the World Health Organization’s (WHO) database; the HDI value for 2012 was obtained from the United Nations Development Program. HDI, ASR for CC, and mean BMI values were available for 154 countries/territories; they comprised the study group for analysis. The countries/territories with incomplete data were omitted from analysis. Linear regression was performed with ASR of CC as the dependent variable and HDI and mean BMI as the independent variables.

**Results:** In univariate analysis, ASR of endometrial cancer was correlated to both HDI \((Pearson correlation coefficient = 0.602, P < 0.01)\) and mean BMI \((Pearson correlation coefficient = 0.351, P < 0.01)\), and HDI and mean BMI also correlated with each other \((Pearson correlation coefficient = 0.522, P < 0.01)\). Linear regression demonstrated that HDI \((P < 0.000)\) was significantly associated with endometrial cancer rate. With HDI in the regression model, BMI lost significance \((P = 0.50)\).

**Conclusions:** The association of HDI with CC incidence, even when accounting for BMI, a known risk factor, suggests that an increasing risk of CC may be expected to accompany a nation’s progress in economy, education, and longevity. Understanding the pathophysiology of this observation may help project national health care needs and guide cancer prevention and control efforts.

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**478 – Poster Session**

**Multimodal pain control is associated with reduced hospital stay following open abdominal hysterectomy**

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**Objectives:** To study the association of a multimodal pain protocol (MMPC) with reduced hospital stay after open abdominal hysterectomy.

**Methods:** The study design was a prospective cohort with a historical control. We enrolled endometrial cancer patients undergoing open abdominal hysterectomy with lymphadenectomy by the same surgeon. Control patients from 2008 to 2010 who received morphine patient-controlled analgesia (PCA) alone were compared with a similar demographic group of patients from 2011 to 2013 who received MMPC. MMPC consisted of gabapentin \((900 \text{ mg orally [PO]}\) and acetaminophen \((1 \text{ g intravenously [IV]}\)) administered 45 to 60 min preoperatively. The surgical site was injected with bupivacaine with 0.5% epinephrine prior to incision. The postoperative pain control regimen consisted of gabapentin \((300 \text{ mg PO every 6 h}),\) acetaminophen \((1 \text{ g IV every 8 h for 24 h postoperatively}),\) ketorolac \((15 \text{ mg IV every 6 h for 48 h postoperatively}),\) morphine PCA \((2 \text{ mg IV every 10 min, no basal rate})\) and oxycodone/acetaminophen \((10/325 \text{ mg PO every 6 h as needed})\).

**Results:** Length of hospital stay \((LOH)\) of the study cohort \((n = 105\) with MMPC) was compared with the historical with postoperative morphine alone \((n = 113\) without MMPC). There were no differences in demographics, uterine cancer stage, or comorbidities between the two arms. The LOH was 1.6 days for patients receiving MMPC and 3.3 days for patients who received morphine alone \((P < 0.001)\).

**Conclusions:** MMPC is associated with significantly reduced LOH after open abdominal hysterectomy.

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**479 – Poster Session**

**Pelvic radiotherapy does not deteriorate the quality of life of women with gynecologic cancers in long term follow-up: A two-year prospective single center study**


**Objectives:** To evaluate the emotional, sexual, and health-related quality of life (HRQoL) concerns of the women with gynecologic malignancy treated with curative radiotherapy (RT).

**Methods:** One hundred women diagnosed with gynecologic malignancy were prospectively enrolled. HRQoL at baseline, at the end of RT, and during follow-up was assessed using European Organization for Research and Treatment (EORTC)-C30, EORTC Quality of Life Questionnaire (QLQ)-CX24, and Hospital Anxiety and Depression Scale (HADS).

**Results:** Appetite loss, diarrhea, fatigue, dyspepsia, insomnia, nausea and vomiting, pain, and sexual activity and sexual enjoyment scores deteriorated after RT \((P = 0.02\) for pain scores and \(P < 0.001\) for all others). Body image scores were higher in patients with endometrial cancer \((P < 0.01)\). The emotional function, nausea and vomiting, body image, and symptom experience scores were higher in patients who underwent chemotherapy \((P = 0.04\) and \(P = 0.01)\). All patient complaints improved during the follow-up period. The global health status scores and the level of depression deteriorated in patients with locoregional recurrent disease and distant metastasis. Anxiety \((P = 0.001)\) and depression \((P = 0.007)\) levels were higher in
Conclusions: Although pelvic RT was associated with deteriorating HRQoL in patients with gynecologic malignancy, HRQoL improved during the follow-up period. Progressive disease had a negative impact on HRQoL.

Objectives: Currently, no screening methods exist for ovarian cancer in the general population. Trials evaluating the efficacy of screening high-risk individuals are in process. Previous studies have shown that depressive symptoms may increase in patients screened for ovarian cancer. We hypothesized that an organized screening program would decrease signs of depression.

Methods: The study was approved by the internal review board at the Icahn School of Medicine at Mount Sinai. Women undergoing screening through the National Ovarian Cancer Early Detection Program were offered and consented to participate in the study before their scheduled visit. Each participant completed a validated Beck's Depression Inventory (BDI) before and after evaluation by a board-certified gynecologic oncologist. During the evaluation, each participant received transvaginal ultrasonography and results were shared immediately. The mean pre-evaluation and post-evaluation BDI scores were compared using the Wilcoxon rank-sum test, performed using Statistical Analysis System 9.4.

Results: Between January 2014 and April 2014, 105 women completed the study. The average age was 46 ± 12 years. The ethnicities were as follows: 69% Caucasian (non-Hispanic, non-Asian), 12% Hispanic, 9% African-American, 9% Asian, and 1% multiracial. Two participants were found to have elevated BDI scores (pre-evaluation scores of 29 and 41), suggestive of moderate-to-severe depression, and were excluded from further analysis. When the remainder of the participants were compared, there was a statistically significant decrease in the mean total BDI score (pre-evaluation 5.2 ± 4.0, post-evaluation 4.0 ± 3.9; P = 0.0001). Eight of the participants (7.8%) reported currently medically treated clinical depression. Exclusion of these participants did not significantly change the results. Moreover, these participants had a significant decrease in total BDI scores after evaluation (pre-evaluation 5.8 ± 5.3, post-evaluation 4.9 ± 4.9, P = 0.02).

Conclusions: Ovarian cancer screening decreases depression levels, even in women undergoing treatment for depression. A screening program with immediate disclosure of results and counseling by a gynecologic oncologist decreases depressive symptoms.

Objectives: The purpose of this study was to investigate the effect of endocrine therapy on sexual dysfunction in breast cancer survivors.

Methods: Between September 2008 and February 2013, 420 patients entered the study and 265 completed questionnaires before initiation of endocrine therapy and after 1 year of use. Sexual functioning was evaluated with the female sexual function index, while sexual distress was assessed with the female sexual distress scale.

Results: The median age of patients was 46 years (range, 26–70 years) and the rate of sexual functioning before endocrine therapy was 77%. Younger age and hypertension were associated with sexual dysfunction. The change in the prevalence of sexual dysfunction between baseline (77%) and 1 year (78.5%) was not statistically significant. About two thirds of patients (66.0%) were sexually distressed after 1 year of endocrine therapy. Over time, the level of gynecologic symptoms increased, whereas no decline in sexual functioning was observed. Only 4.9% of patients reported worsened sexual functioning across time. After adjusting clinical confounders, women experiencing sexual dysfunction at baseline were more likely to experience sexual dysfunction after 1 year of endocrine therapy usage than women who had no sexual dysfunction before initiating endocrine therapy.

Conclusions: The observation that sexual functioning remained stable is encouraging. Further studies, including assessing the impact of early identification of patients at risk of developing sexual dysfunction and timely intervention, are warranted.

Objectives: To assess the associations among body composition, quality of life, and physical activity behaviors for an ethnically diverse sample of breast cancer survivors.

Methods: After institutional review board approval, 411 survivors who had been treated for 6 months to 5 years at a tertiary care medical center in the Bronx, NY, completed questionnaires regarding moderate to vigorous physical activity (MVPA), body mass index (BMI), quality of life, and psychosocial characteristics based on social cognitive theory.

Results: The respondents were overweight (27%) or obese (65%). BMI was higher (d = 0.73, P = 0.045) for non-Hispanic white women (37.8 ± 10.2) than non-Hispanic white women (31.2 ± 7.8). However, 47% reported achieving the American College of Sports Medicine recommendations for MVPA. Physically active women had significantly higher quality of life scores (d = 0.57, P = 0.016), as measured by the FACT–Endometrial. BMI differences approached significance (d = 0.40, P = 0.05) for the physically active group (32.4 ± 5.6 kg/m²) compared to the inactive group (35.7 ± 10.2 kg/m²). The physically active group reported higher walking self-efficacy (P = 0.02), higher barrier self-efficacy (P = 0.02), more positive disease outcome expectations (P = 0.02), and a trend toward a higher relative autonomy index (P = 0.06). However, only walking self-efficacy was a predictor of physical activity participation (r² = 0.27, P = 0.018). There were no differences in reported physical activity between ethnic groups.
483 - Poster Session
The effect of gynecologic cancer on patient's depression and anxiety: prospective study
T.T. Ilhan\textsuperscript{a}, A.K. Kebapcílar\textsuperscript{b}, T.I. Ilhan\textsuperscript{c}, T.C. Cakir\textsuperscript{c}, S.A. Yilmaz\textsuperscript{d}, C. Celik\textsuperscript{e}, B.B.B. Bakbak\textsuperscript{b}, \textsuperscript{a}Selçuk University Medicine Faculty, Konya, Turkey, \textsuperscript{b}University of Selcuk, Konya, Turkey, \textsuperscript{c}Beyhekim State Hospital, Konya, Turkey, \textsuperscript{d}Selçuk University Medicine Faculty, Konya, Turkey, \textsuperscript{e}Selçuk University, Konya, Turkey

**Objectives:** The aim of the study was to evaluate the effect of gynecologic cancer diagnosis and treatment on patients' depression, sleep quality, and anxiety.

**Methods:** This study included 144 participants, with 71 in the gynecologic cancer group (group I) and 72 healthy volunteers in the control group (group II). This questionnaire-based study was conducted between March 2013 and March 2014 in the Gynecologic Oncology Department of University of Selcuk/Konya. Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory 1-2 (STAI) questionnaires were completed by patients at the beginning and end of treatment. Age, education status, and economic status were noted. A package program of Statistical Package for the Social Sciences was used for statistical analysis. \( P < 0.05 \) was considered statistically significant.

**Results:** There were no significantly differences between each group's age (\( P = 0.892 \)), parity (\( P = 0.472 \)), economic status (\( P = 0.871 \)), and education status (\( P = 0.932 \)). The mean PSQI score in group I was 8.4 ± 5.11 and in group II was 6.06 ± 3.02 (\( P < 0.05 \)). The mean BDI in group I was 23.8 ± 10.26 and in group II was 14.8 ± 8 (\( P < 0.05 \)). In group I, PSQI and STAI 2 scores were significantly increased after treatment (\( P = 0.002 \) and \( P = 0.02 \), respectively). However, BDI and STAI 1 scores did not change significantly (\( P = 0.81 \) and \( P = 0.78 \)). In group I, PSQI, BDI, and STAI 1-2 scores were significantly higher after chemotherapy when compared with before treatment (\( P < 0.05 \)). However, only the PSQI score was significantly higher after radiotherapy (\( P < 0.05 \)).

**Conclusions:** Poor sleep quality, depression, and anxiety are common clinical conditions in those with gynecologic cancer. Chemotherapy has more serious adverse effects on sleep quality and depression, and chemotherapy is major source of anxiety.

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485 — Poster Session
How equal is end-of-life care among gynecologic oncology patients?
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**Objectives:** To identify disparities in utilization of end-of-life (EoL) and supportive care (SC) resources by gynecologic oncology (GO) patients.

**Methods:** This retrospective analysis of GO patients treated at MD Anderson Cancer Center from 1/2007 to 12/2011 and deceased from 1/2012 to 8/2014 reviewed electronic medical records for patient demographics, disease characteristics, and utilization of EoL and SC resources. Chi square, Fisher's exact, Mann Whitney, and Kruskal–Wallis tests were used for statistical analysis.

**Results:** Of 189 patients analyzed, 113 (60%) were white, 38 (20%) Hispanic, 31 (16%) black, and 7 (4%) Asian. Ninety-five (48%) had ovarian, 51 (26%) uterine, 47 (23%) cervical, and 7 (3%) vulvar/vaginal cancer. Median household income, calculated from Census Bureau data by zip code, was $54,600. In the last 30 days of life (DoL), 18 (10%) had multiple hospital admissions, 10 (5%) were admitted to the intensive care unit (ICU), and 30 (16%) had multiple emergency department (ED) visits. Eight (4%) received chemotherapy in the final 14 DoL, 54 (29%) had no SC referral, and 29 (15%) no hospice referral. Twenty-eight (15%) died in the hospital while 158 (84%) died in hospice. Median hospice enrollment was 21.5 days before death. Only 46 (24%) had a medical power of attorney (PoA) or living will (LW) on file. Household income was not associated with significant differences in SC or hospice usage or in PoA or LW documentation. SC consultation, chemotherapy, ED visits, and ICU

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and hospital admissions in the final 30 DoL did not vary by race, income, educational level, or marriage status. Hospice enrollees had less aggressive care, including chemotherapy (2% vs. 16%, \(P = 0.003\)), ED visits (13% vs. 29%, \(P = 0.03\)), hospital admissions (8% vs. 19%, \(P = 0.04\)), and ICU admission (3% vs. 19%, \(P = 0.002\)) during the final 30 DoL. Of interest, non-white race was associated with increased odds of dying without hospice (OR 3.07; 95% CI 1.27, 2.46; \(P = 0.009\)). Importantly, non-white patients who enrolled in hospice did so earlier than white patients (42 vs. 27 days before death, \(P = 0.054\)). Importantly, non-white patients were significantly less likely to have PoA/LW documentation (24% vs. 76%, \(P = 0.007\)).

**Conclusions:** Significant racial disparities in hospice enrollment and PoA/LW documentation were seen in GO patients. This warrants further study to identify barriers to use of EoL and SC resources.

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**486 — Poster Session**

**Identifying gynecologic oncology patients with high symptom burden**

M. Rowland\(^a\), R. Ruskin\(^b\), K.N. Moore\(^b\), J.L. Walker\(^b\), L.M. Landrum\(^b\), M. Matzo\(^c\). 1The University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK, USA, 2The University of Oklahoma, Oklahoma City, OK, USA, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

**Objectives:** To characterize the symptom burden of gynecologic oncology patients in the outpatient setting and identify predictors of patients with high symptom burden.

**Methods:** Patients presenting for clinical appointments in our academic gynecologic oncology clinic are asked to complete a symptom assessment screen regarding their physical and emotional symptoms (rated on a 0 to 10 scale) and basic needs. We performed a retrospective review of all questionnaires collected over a 1-month period. Demographic data, disease characteristics, and medication information were extracted from the electronic medical record. Descriptive statistics were employed to characterize patient characteristics and symptom burden. Univariate analyses, including chi-square statistics and t-tests, were used to screen for associations with high symptom burden. Logistic regression was then used to identify predictors of high symptom burden.

**Results:** Symptom data were available for 333 patients. Prevalence of moderate or severe symptomatology (≥4/10) ranged from 3.9% (vomiting) to 42.7% (fatigue) (Fig. 1). Patients with ≥3 individual symptoms of moderate or severe intensity were classified as having a high symptom burden (32.2%). High symptom burden was associated with disease stage (\(P < 0.01\)), course in the disease process (prediagnosis, primary treatment, remission, or recurrence) (\(P = 0.04\)), evidence of active disease (\(P < 0.01\)), prescribed anxiety medication (\(P < 0.01\)), prescribed depression medication (\(P < 0.01\)), reason for the visit (initial consultation, chemotherapy, surveillance, postoperative) (\(P < 0.01\)), and total number of medications (\(P < 0.01\)). Depressive medication (\(P < 0.01\)), evidence of active disease (\(P < 0.01\)), disease stage (\(P = 0.01\)), and anxiety medication (\(P = 0.04\)) persisted as independent predictors of high symptom burden when assessed using logistic regression.

**Conclusions:** Many gynecologic oncology patients suffer a high symptom burden. Identification of these patients is key to improve symptom management. Active evidence of disease and active treatment with anxiety and depression medications are predictors of high symptom burden and may help identify patients for closer symptom screening.

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**487 — Poster Session**

**Improvement in symptom burden within one day after palliative care consultation in a cohort of gynecologic oncology inpatients**

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**Objectives:** To evaluate the magnitude and time course of change in symptom burden after palliative care (PC) consultation in a cohort of gynecologic oncology inpatients.

**Methods:** Women with a gynecologic malignancy and a PC consultation for symptom management between 3/1/12 and 2/28/13 were identified. Charts were reviewed for demographics and disease characteristics. Symptom scores on a modified Edmonston Symptom Assessment System (ESAS) scale that had been collected at the time of PC consultation were retrospectively reviewed for pain, anorexia, fatigue, depression, anxiety, nausea, and dyspnea. Prevalence of moderate-to-severe symptom intensity was compared between the day of PC consultation (D1), the day after PC consultation (D2), and the last recorded symptoms before discharge (DLast). Data were analyzed with descriptive and t-test statistics and test of proportions.

**Results:** Median patient age was 59 years, 84% were white, and 67% had stage III/IV disease, with ovarian being the most common site (52%). Symptom prevalence on D1 of at least mild intensity ranged from 14% (dyspnea) to 80% (pain). Prevalence of moderate-to-severe symptoms at D1, D2, and DLast are outlined in the Table. There were statistically significant decreases in moderate-to-severe symptom intensity between D1 and D2 for pain, anorexia, fatigue, and nausea (magnitude 58%–66%) and between D1 and D2 for pain, fatigue, and nausea (magnitude 50%–55%). The majority of improvement that occurred between D1 and DLast happened by D2.

**Conclusions:** Inpatient PC consultation is associated with an improvement in symptom burden that is both statistically and clinically significant. The majority of the improvement occurs within 1 day of PC consultation, which is suggestive of a causal relationship. PC consultation may be an effective tool for symptom management during even very short hospitalizations and should be considered early in the hospitalization to effect timely symptom relief.
Objectives: To evaluate factors associated with death in hospital compared to discharge to hospice in gynecologic cancer patients with terminal disease.

Methods: The University Health System Consortium (UHC) database was queried for gynecologic cancer patients who died in hospital or were discharged to hospice care from October 2010 to August 2014. The primary diagnoses included cervical, endometrial, and ovarian cancer. Race was classified as White, Black, and Asian. Payer was grouped as Medicaid, Medicare, private, and self-pay. There were four primary age categories; 18–30 years, 31–50 years, 51–74 years, and 75–100 years. Multivariable logistic regression was used to model the probability of death in hospital associated with race, age, payer, and primary tumor site.

Results: A total of 827 patients died in the hospital (38%) and 1350 patients were discharged to hospice (62%). Compared to patients with Medicare, self-pay patients had more than twice the odds of dying in the hospital (OR = 2.59; 95% CI 1.61, 4.18; P < 0.05). Ovarian cancer (OR = 1.45; 95% CI 1.11, 1.9; P < 0.05) and endometrial cancer patients (OR = 1.77; 95% CI 1.34, 2.35; P < 0.05) had higher odds of death in hospital than cervical cancer patients. Age, race, and Medicaid and private insurance were not significantly associated with in-hospital death. Results are presented in Table 1.

Conclusions: End-of-life care has become increasingly important in the comprehensive care of oncology patients. These data suggest that there is substantial variation in utilization of hospice services in gynecologic oncology patients. Future studies may clarify the etiology of our findings and identify interventions to reduce variation and increase hospice utilization in suitable patients.

Table 1 (continued)

<table>
<thead>
<tr>
<th>Disease site</th>
<th>All</th>
<th>Adjusted OR (95% CI)</th>
<th>Hospi-</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>117 (14)</td>
<td>257 (19)</td>
<td>257 (19)</td>
<td>0.15</td>
</tr>
<tr>
<td>Endometrial</td>
<td>301 (36)</td>
<td>1.77 (1.34, 2.35)</td>
<td>404 (30)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Ovarian</td>
<td>409 (50)</td>
<td>1.45 (1.12, 1.90)</td>
<td>689 (51)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

doi:10.1016/j.ygyno.2015.01.493
Conclusions: Nearly half of the patients had only distant recurrence and some of those patients may benefit from adjuvant chemotherapy after PE. Patients with recurrence after PE have very poor prognoses. However, palliative treatment may improve survival in selected patients after recurrence.

doi:10.1016/j.ygyno.2015.01.494

490 — Poster Session
Symptom burden in women with advanced or recurrent cervical cancer referred to a supportive care center
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Objectives: From the time of diagnosis extending into survivorship, women with cervical cancer (CCx) report symptoms that include pain, nausea, distress, sexual dysfunction, proctitis, cystitis, fatigue, and diarrhea. Our objective was to delineate and measure the symptom burden experienced by patients with advanced and recurrent CCx at time of referral to a supportive care center (SCC).

Methods: Women ≥18 years at time of referral to SCC from 2010 to 2012 were included. A total of 191 referrals were identified, 94 in an outpatient setting and 97 as inpatients; 35 were duplicate visits. The unique total identified was 156. Of these, 88 patients had completed Edmonton Symptom Assessment scale (ESAS) and were included in the analysis. Demographics, ESAS results, and written explanations of symptoms were abstracted from the medical records. Descriptive statistics were used to summarize the data.

Results: At the time of presentation to the SCC, the median age was 46 years (range, 24–75 years) and 47% were Caucasian, 18% were African American, and 33% were Hispanic. Fifty-one percent were married, 64% had no advanced directives, and 75% had recurrent disease. Thirteen percent had a history of depression, 18% had a history of anxiety, 20% had deep vein thrombosis, 17% had ureteral stents, 17% had nephrostomies, and 7% had colostomies. The chief complaint was pain in 94% of patients. The mean time from advanced CCx diagnosis to SCC consult was 9.2 months (range, 0.1–201.7 months). The mean time from SCC visit to death was 16.0 months (range, 0.1–79.9 months). The percentage with predominant symptoms (ESAS scores ≥4) is described in the Table.

Conclusions: Pain is the primary complaint for patients with advanced or recurrent CCx at time of referral to SCC. However, more than half are also significantly burdened with fatigue, loss of appetite, difficulty with sleep, and lack of well-being. In patients with significant symptomatology, early supportive care assessment may alleviate unnecessary distress, decrease hospital admission, and potentially improve clinical outcomes. Understanding symptomatology may contribute to the design of meaningful clinical trial endpoints in patients with incurable disease that may be relevant.

ESAS [≥4]  
<table>
<thead>
<tr>
<th>Symptom</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>71</td>
<td>80.7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>61</td>
<td>69.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>25</td>
<td>28.4</td>
</tr>
<tr>
<td>Depressed</td>
<td>32</td>
<td>36.4</td>
</tr>
<tr>
<td>Anxiety</td>
<td>39</td>
<td>44.3</td>
</tr>
<tr>
<td>Drowsy</td>
<td>29</td>
<td>33.3</td>
</tr>
<tr>
<td>Appetite</td>
<td>63</td>
<td>72.4</td>
</tr>
<tr>
<td>Feeling of well-being</td>
<td>56</td>
<td>70.0</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>18</td>
<td>20.5</td>
</tr>
<tr>
<td>Sleep</td>
<td>47</td>
<td>54.0</td>
</tr>
</tbody>
</table>

doi:10.1016/j.ygyno.2015.01.495

491 — Poster Session
Gynecologic oncologist as surgical consultant: Intraoperative consultations during general gynecologic surgery as an important focus of gynecologic oncology training

Objectives: The role of a gynecologic oncologist often extends beyond the treatment of gynecologic cancers. In this study, we explored the previously unexamined role of the gynecologic oncologist as an intraoperative consultant during general gynecologic surgery.

Methods: The operating room scheduling database at our institution was queried to identify major gynecologic surgeries that included both a general gynecologist and a gynecologic oncologist from October 2010 to August 2014. Scheduled combined cases and obstetrics cases were excluded. Charts were reviewed and data collected on medical history, type of surgery, reason for consultation, intervention performed by the gynecologic oncologist, and major adverse events.

Results: In the study period, 794 major surgeries were performed by the general gynecology service: 98 (12.3%) were identified as combined operative cases, 36 (37%) were scheduled combined cases, and 62 (63%) represented unanticipated intraoperative consultations. Of these 62 cases, 58% were laparoscopic and 42% were open. The most common indications for surgery were complex adnexal masses (32%), fibroids (27%), and endometriosis (13%). The most common reasons for intraoperative consultation were adhesions (37%), bowel injury (19%), inability to identify the ureter (19%), cancer (10%), and bleeding (10%). The most common interventions performed by the gynecologic oncologist were identification of anatomy (55%), lysis of adhesions (42%), retroperitoneal dissection (27%), and ureterolysis (24%). A total of 21 major adverse events occurred in 13 cases (21%).

Conclusions: Gynecologic oncologists play a pivotal role in the support of general gynecology colleagues during pelvic surgery. In this series, a significant subset of major benign surgeries required gynecologic oncology for completion. It is important to incorporate the skills required of an intraoperative consultant in general gynecologic procedures into gynecologic oncology fellowship training.

doi:10.1016/j.ygyno.2015.01.496

492 — Poster Session
Disease recurrence and survival among women with endometrial carcinoma undergoing robotic versus laparoscopic surgery
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Objectives: To compare disease recurrence and survival among women undergoing robotic vs. laparoscopic surgery for endometrial cancer.

Methods: Women undergoing robotic-assisted and laparoscopic hysterectomy were identified from a large community-based integrated health system in Northern California. A retrospective chart review was performed. Baseline characteristics were collected, including cancer stage, grade, and type of surgery. The primary outcomes were recurrence, disease-free survival (DFS), and overall survival (OS). Survival analysis using the Cox proportional hazards model was performed.

doi:10.1016/j.ygyno.2015.01.495
Results: A total of 1312 cases (617 robotic and 596 laparoscopic) were identified from January 2009 through September 2013 and analyzed until January 1, 2014 (median follow-up: 21 months; range, 3 months–5 years). There were 59 (9.2%) vs. 55 (9.5%) recurrences among women undergoing robotic-assisted and laparoscopic surgery, respectively ($P = 0.84$). Among those who underwent robotic vs. laparoscopic surgery, there were 11 (1.8%) vs. 11 (1.8%) with local recurrence, 13 (2.1%) vs. 16 (2.7%) with regional recurrence, and 36 (5.8%) vs. 28 (4.7%) with distant recurrence, respectively. The median time to first recurrence following robotic vs. laparoscopic surgery was 10 months (range, 0–51 months) and 13 months (range, 1–37 months), respectively ($P = 0.17$). DFS at 3 years was 0.855 among robotic vs. 0.871 among laparoscopic cases (HR 1.21, 95% CI 0.84–1.74) and the OS at 3 years was 0.880 among robotic vs. 0.911 among laparoscopic surgery (HR 1.21, 95% CI 0.78–1.86). Disease-specific survival at 3 years was 0.904 among robotic vs. 0.939 among laparoscopic cases (HR 1.57, 95% CI 0.94–2.61).

Conclusions: In this analysis, there was no difference in the rate of recurrence, OS, or DFS between robotic and traditional laparoscopic surgery for women with endometrial cancer.

Fig. 1. Comparison of robotic and traditional laparoscopic surgery and death from all causes.

Table 1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Laparoscopy</th>
<th>Robot</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (surgery time):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median [Q1,Q3]</td>
<td>165 [115,225]</td>
<td>149 [116,194]</td>
<td>.0029</td>
</tr>
<tr>
<td>EBL: median [Q1,Q3]</td>
<td>100 [50,150]</td>
<td>50 [50,100]</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Transfusion rate</td>
<td>33 (4.8%)</td>
<td>25 (3.5%)</td>
<td>.1685</td>
</tr>
<tr>
<td>Intraoperative/postoperative</td>
<td>176 (25.6%)</td>
<td>124 (16.6%)</td>
<td>.0001</td>
</tr>
<tr>
<td>complication</td>
<td>36 (5.2%)</td>
<td>38 (5.1%)</td>
<td>.9153</td>
</tr>
<tr>
<td>Clavien dindo 1–2 (Minor)</td>
<td>44 (6.4%)</td>
<td>9 (1.2%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Conversion to laparotomy</td>
<td>7 (5,12]</td>
<td>5 [3,9]</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pelvic lymph nodes retrieved:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median [Q1,Q3]</td>
<td>30 [26,50]</td>
<td>27 [13,31]</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Para-aortic lymph nodes retrieved:</td>
<td>N = 329</td>
<td>N = 505</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>median [Q1,Q3]</td>
<td>14 [9,21]</td>
<td>11 [6,17]</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

493 — Poster Session
Comparison of surgical outcomes in laparoscopic and robotic-assisted surgical management of endometrial cancer

Objectives: To compare rates of intraoperative and postoperative surgical complications and outcomes between robotic-assisted and laparoscopic surgical management of endometrial cancer.

Methods: A retrospective cohort study of endometrial cancer and complex hyperplasia with atypia managed by laparoscopic and robotic-assisted hysterectomy and surgical staging was conducted from January 2009 to January 2014 in a community-based health care system in Northern California. A retrospective chart review using an electronic medical record was performed. The primary outcome was intraoperative and <30-day postoperative complications. Secondary outcomes included total operative time, estimated blood loss, rate of transfusions, length of stay, and number of pelvic and paraaortic lymph nodes retrieved.

Results: A total of 1434 cases were identified: 689 laparoscopic and 745 robotic-assisted. Because patients received medical care in an integrated health care system, all patient outcomes were captured in the electronic record and all patients had detailed follow-up data available. The rate of major complications was similar between robotic and laparoscopic cohorts (5.1% vs. 5.2%, $P = 0.9153$). However, the rate of minor complications was lower in the robotic compared to laparoscopic cohort (16.6% vs. 25.6%, $P < 0.001$; OR 0.581; 95% CI 0.450–0.753). Statistically significant differences were also noted in the following outcomes between robotic and laparoscopic cohorts, respectively: decrease in median operative time, decreased median estimated blood loss, a lower rate of conversion to laparotomy, shorter median length of hospital stay, and a decrease in the median number of pelvic and paraaortic lymph nodes retrieved (Table 1).

Conclusions: In this large cohort of consecutive cases of endometrial cancer, the management by robotic or laparoscopic surgery does not show a difference in major complications, although there are differences in other clinically significant outcomes, including minor complications and conversion rate to laparotomy favoring the robotic approach.

Table 1 Outcomes of laparoscopic and robotic surgery for endometrial cancer.

<table>
<thead>
<tr>
<th>Total</th>
<th>Laparoscopy</th>
<th>Robot</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (surgery time):</td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>149 [116,194]</td>
<td>.0029</td>
</tr>
<tr>
<td>EBL: median [Q1,Q3]</td>
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</tr>
<tr>
<td>Clavien dindo 1–2 (Minor)</td>
<td>36 (5.2%)</td>
<td>38 (5.1%)</td>
<td>.9153</td>
</tr>
<tr>
<td>Clavien dindo 3–4 (Major)</td>
<td>44 (6.4%)</td>
<td>9 (1.2%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Conversion to laparotomy</td>
<td>5 [3,9]</td>
<td>5 [3,9]</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pelvic lymph nodes retrieved:</td>
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<td>median [Q1,Q3]</td>
<td>14 [9,21]</td>
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<td>&lt;.0001</td>
</tr>
</tbody>
</table>

494 — Poster Session
Current practices and opinions regarding sentinel lymph node biopsy for gynecologic malignancies
P.C. Mayor, E.C. Rossi, J.G. Ross. *Indiana University School of Medicine, Indianapolis, IN, USA

Objectives: Sentinel lymph node (SLN) mapping techniques have been progressively investigated and reported for vulvar, endometrial, and cervical cancers. This study’s objective was to describe the current practices and opinions regarding these evolving techniques and their supporting evidence.

Methods: An electronic survey of all Society of Gynecologic Oncology (SGO) members was performed. Eligible participants were identified using the 2012 SGO membership directory. We collected demographic information as well as participants’ current practices and opinions on SLN biopsy for vulvar, endometrial, and cervical cancers. Whether a surgeon performs SLN mapping was evaluated for association with surgeon characteristics, including years of practice.
gender, age, practice setting, geography, and perceived level of supporting evidence (I, II, or III). Chi square was used for comparisons of proportions or frequencies in the three groups.

**Results:** A total of 1536 members were sent an electronic survey, with 251 completed for analysis. Sixty-five percent of the participants were male and 53% percent were within 15 years of completing gynecologic oncology fellowship. Participants were identified as strictly academic (52%), community-affiliated academic (37%), or strictly private practice (11%). Eighty-nine percent of participants were from the United States, with all geographic regions evenly represented. The rates of participants performing SLN mapping off research protocol for vulvar, endometrial, and cervical cancers were 65.4%, 20.2%, and 17.4%, respectively. The most significant variables associated with performing SLN mapping for vulvar, cervical, and endometrial cancers were perceived high level (I or II-1) of existing evidence ($P = 0.0001$, $P = 0.006$, and $P = 0.011$, respectively) and practicing in the strictly academic setting ($P = 0.001$, $P = 0.004$, and $P = 0.015$, respectively). Participants who more recently finished their training were significantly more likely to perform SLN in endometrial and vulvar cancers ($P = 0.001$ and $P = 0.005$).

**Conclusions:** Nearly two thirds of responders perform SLN mapping for vulvar cancer. SNL mapping is less commonly used for endometrial and cervical cancers, which likely reflects surgeons' perception of a lower level of supporting evidence in these cancers.

doi:10.1016/j.ygyno.2015.01.499

**495 — Poster Session**

**Survival in patients with uterine carcinosarcoma undergoing sentinel lymph node mapping**


**Objectives:** To determine the survival in patients with uterine carcinosarcoma undergoing sentinel lymph node node (SLN) mapping compared to a cohort surgically staged with standard lymphadenectomy.

**Methods:** We analyzed a retrospective review of a prospectively maintained institutional database of all women with uterine cancers from 1998 through 2014. Patients were separated into cohorts of those who had undergone SLN mapping at time of staging and those who had routine lymphadenectomy. SLN evaluation was performed according to a standard institutional protocol for management of uterine cancer, including the use of a surgical algorithm and pathologic ultrastaging.

**Results:** A total of 136 patients with uterine carcinosarcoma who had undergone lymph node evaluation were identified. Of these, 48 had surgical staging with SLN mapping and 88 had routine lymphadenectomy consisting of full pelvic and/or paraaortic lymph node dissection. There was no significant difference in age, race, or body mass index between groups. Stage distribution for the SLN group was 31/48 (65%) stage I, 1/48 (2%) stage II, 11/48 (23%) stage III, and 5/48 (10%) stage IV; for the full lymphadenectomy group, it was 48/88 (55%) stage I, 4/88 (4%) stage II, 19/88 (22%) stage III, and 17/88 (19%) stage IV ($P = 0.426$). The median number of lymph nodes removed in patients who had SLN mapping was 8 compared to 20 in the non-SLN group ($P = 0.001$). The median number of nodes detected as positive was the same between cohorts ($P = 0.212$). Among the 67 patients who had a documented recurrence, 14/20 (70%) in the SLN and 34/47 (74%) in the routine lymphadenectomy group demonstrated a distant/multifocal pattern of recurrence. With a median follow-up of 16.2 months in the SLN and 61.7 months in the non-SLN cohort, no difference was noted in median progression-free survival (23 vs. 23.2 months, $P = 0.706$).

**Conclusions:** Progression-free survival in women with carcinosarcoma undergoing SLN mapping appears similar to patients receiving standard lymphadenectomy at the time of surgical staging. SLN mapping represents a reasonable alternative to more extensive standard lymphadenectomy for staging and does not appear to compromise prognosis.

doi:10.1016/j.ygyno.2015.01.501
497 — Poster Session
Laparoscopic versus laparotomic radical hysterectomies: First minimally invasive cases in Argentina

Objectives: To compare laparoscopic and laparotomic total radical hysterectomy (TRH) for early-stage cervical cancer through analysis of perioperative outcomes and overall (OS) and disease-free survival (DFS).

Methods: Included in this retrospective review were 81 consecutive patients with cervical cancer FIGO stages IA2-IB1 who underwent surgery at the Hospital Italiano in Buenos Aires, Argentina between November 2007 and May 2014. Thirty-one patients had laparotomic TRH; the remaining 50 procedures were laparoscopic. We compared both groups in terms of age, body mass index (BMI), history of previous surgery, tumor stage, histology, and comorbidities. Then we analyzed perioperative outcomes: surgical time, intraoperative complications, conversion to laparotomy, length of hospital stay, transfusion requirement, and postoperative complications. Furthermore, we evaluated the characteristics of the obtained specimens in terms of parametrial size, length of resected vagina, number of pelvic lymph nodes, and margins. DFS and OS were also compared. For statistical analysis we used chi square, Mann Whitney test, and Wilcoxon Rank sum T. The results were adjusted through multivariate regression analysis to control possible confounding factors.

Results: There were no significant differences between laparoscopic and laparotomic TRH when considering BMI, age, tumor size, tumor stage, and histology. Duration of surgery (240 vs. 320 min), length of hospital stay (2 vs. 4 days), and transfusion requirement (6% vs. 29.03%) were significantly lower in the minimally invasive group. There were no statistically significant differences in the postoperative complication rate and pathologic results. Despite the short follow-up in the minimally invasive group, OS and DFS seem to be similar.

Conclusions: The laparoscopic approach for TRH appears to significantly improve length of hospital stay, operative time, and transfusion requirements without affecting the pathologic results or complication rate while offering similar DFS and OS. We find laparoscopy to be a safe and efficient approach and believe that it should be the standard treatment for early-stage cervical cancer. The fact that it can be offered in developing countries in Latin America is a matter of great importance in local public health.

doi:10.1016/j.ygyno.2015.01.502

498 — Poster Session
Complications of robotic vaginal cuff closure with barbed versus non-barbed suture
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*SUNY Upstate Medical University, Syracuse, NY, USA, *GYN Oncology of CNY, PC, East Syracuse, NY, USA

Objectives: Barbed suture allows faster vaginal cuff closure and elimination of knots, the weakest point in any suture line. The effect of the change from nonbarbed to barbed suture on vaginal cuff healing was evaluated in patients who underwent robotic hysterectomy for benign and malignant indications.

Methods: A retrospective, single-institution chart review was performed of patients who underwent robotic hysterectomy between August 2008 and August 2013. All procedures were performed by one of two experienced robotic surgeons, both of whom adopted barbed suture for cuff closure during the study period. The primary variable was type of suture used (barbed vs. nonbarbed) and the primary outcome was visual assessment of the vaginal cuff at the 6-week postoperative visit. Secondary outcomes included console time, repeat office visits, patient phone calls, and hospital readmissions. Descriptive and comparative analyses were executed.

Results: A total of 360 patients were identified who had no significant differences in demographics. The surgical indication was malignancy for the majority of patients, and staging was performed as indicated, with no differences in procedures or blood loss between groups. Console time was significantly decreased with barbed (118 min) vs. nonbarbed suture (140 min) (t (330) = −2.74, P = 0.006). Barbed suture was more likely to result in complete healing at 6 weeks (93.85% vs. 88.62%). There were fewer vaginal cuff complications at 6 weeks using barbed suture (χ² (1, n = 318) = 2.75, P = 0.097). These complications included raw mucosal edges (7, 5), granulation tissue (3, 1), cuff separation (0, 1), visible suture (2, 2), or vaginal spotting (0, 4) for barbed vs. nonbarbed suture, respectively. The only vaginal cuff dehiscence was with nonbarbed suture. There were fewer postoperative visits for barbed vs. nonbarbed suture (χ² (1, n = 318) = 4.41, P = 0.036). There were no significant differences in readmissions or patient phone calls.

Conclusions: Barbed suture achieved a higher rate of complete cuff closure at 6 weeks, with shorter operative time and no increasing complications. It is a safe and effective method for robotic cuff closure.

doi:10.1016/j.ygyno.2015.01.503

499 — Poster Session
Effect of body mass index on conversion rate and complications among patients undergoing robotic surgery for endometrial cancer
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Objectives: In Gynecologic Oncology Group LAP2, the rate of conversion from laparoscopy to laparotomy was proportional to body mass index (BMI), with an increase from 17.5% in BMI of 25 to 57.1% in BMI > 40. The purpose of this study was to evaluate the relationship of BMI to conversion rate in patients undergoing robotic surgery for endometrial cancer. Secondary outcomes were operative times, lymph nodes retrieved, and complications.

Methods: A retrospective, single-institution chart review was performed of patients who underwent robotic hysterectomy between August 2008 and August 2013. All procedures were performed by one of two experienced robotic surgeons, both of whom adopted barbed suture for cuff closure during the study period. The primary variable was type of suture used (barbed vs. nonbarbed) and the primary outcome was visual assessment of the vaginal cuff at the 6-week postoperative visit. Secondary outcomes included console time, repeat office visits, patient phone calls, and hospital readmissions. Descriptive and comparative analyses were executed.

Results: A total of 360 patients were identified who had no significant differences in demographics. The surgical indication was malignancy for the majority of patients, and staging was performed as indicated, with no differences in procedures or blood loss between groups. Console time was significantly decreased with barbed (118 min) vs. nonbarbed suture (140 min) (t (330) = −2.74, P = 0.006). Barbed suture was more likely to result in complete healing at 6 weeks (93.85% vs. 88.62%). There were fewer vaginal cuff complications at 6 weeks using barbed suture (χ² (1, n = 318) = 2.75, P = 0.097). These complications included raw mucosal edges (7, 5), granulation tissue (3, 1), cuff separation (0, 1), visible suture (2, 2), or vaginal spotting (0, 4) for barbed vs. nonbarbed suture, respectively. The only vaginal cuff dehiscence was with nonbarbed suture. There were fewer postoperative visits for barbed vs. nonbarbed suture (χ² (1, n = 318) = 4.41, P = 0.036). There were no significant differences in readmissions or patient phone calls.

Conclusions: Barbed suture achieved a higher rate of complete cuff closure at 6 weeks, with shorter operative time and no increasing complications. It is a safe and effective method for robotic cuff closure.

doi:10.1016/j.ygyno.2015.01.503
Methods: A retrospective cohort study was performed of women with endometrial cancer scheduled for robotic surgery from September 2008 to September 2012. Women were divided into three groups based on BMI, and conversion rates to laparotomy were compared. Descriptive and comparative analyses were performed among nonobese, obese, and morbidly obese women who completed robotic surgery.

Results: A total of 301 women were scheduled for robotic surgery for endometrial carcinoma, including 88 nonobese (BMI 19–29, μ 25.23), 111 obese (BMI 30–39, μ 34.21), and 102 morbidly obese (BMI 40–71, μ 47.38). Preoperative characteristics were similar except that nonobese patients were slightly older. Conversion to laparotomy occurred in 21 patients (7%), with no difference in conversion rate between BMI categories. Direct comparison between converted and completed robotic patients showed no significant differences in preoperative characteristics, except that obese patients who required conversion had a higher number of previous abdominal surgeries. Reasons for conversion were adhesions (14), metastases (5), large uterine size (1), and difficulty tolerating insufflation (1). Patients completing robotic surgery underwent node dissections at similar rates in all three BMI categories. Operating room time, but not surgical time, was increased in morbidly obese patients. Intraoperative and postoperative complications showed no significant differences between BMI categories. Morbidly obese patients were more likely to have larger uteri and less likely to have grade 3 tumors or vascular space invasion. Pelvic and periaortic lymph node yields were similar across all three categories.

Conclusions: Morbid obesity does not increase the rate of conversion to laparotomy or complication rates in patients undergoing robotic surgery for endometrial carcinoma. Node dissections were pathologically equivalent between BMI categories using the robotic platform.

Baseline, periperaoperative and postoperative characteristics

<table>
<thead>
<tr>
<th></th>
<th>Nonobese (BMI &lt;30) (n = 88)</th>
<th>Obese (BMI 30–40) (n = 111)</th>
<th>Morbidly obese (BMI &gt;40) (n = 102)</th>
<th>P-value</th>
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<tr>
<td>Preoperative data</td>
<td></td>
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<tr>
<td>Average age at surgery</td>
<td>64.79</td>
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<td>Average abdominal surgeries</td>
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<td>3</td>
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<tr>
<td>Conversion to laparotomy (n = 21)</td>
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</tr>
<tr>
<td>Average age at surgery</td>
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<td>LHBSO with pelvic &amp; periaortic nodes</td>
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<td>Average operative time, min</td>
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<td>Uterine weight</td>
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<td>Total sampled pelvic nodes, avg</td>
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<td>Total sampled periaortic nodes, avg</td>
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<td>% Lymphovascular space invasion</td>
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doi:10.1016/j.ygyno.2015.01.504

500 – Poster Session

Patient-derived tumor xenograft model for gynecologic cancer

[J. W. Lee1, B.G. Kim2, T.J. Kim3, Y.Y. Lee4, A. Yoon5, W.Y. Kim6, C.H. Choi7, 8Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, 4Samsung Medical Center, Seoul, South Korea, 7Kangbuk Samsung Hospital, Seoul, South Korea]

Objectives: A patient-derived tumor xenograft model (PDTX) may provide more accurate and reliable information about individual patients’ tumor biology when compared with an established cell line model. This study was designed to study the development of PDTX mice and their genetic and phenotypic stability for gynecologic cancer, including ovarian, endometrial, and cervical cancer.

Methods: Small pieces (3 x 3 x 3 mm) of human gynecologic cancer tissue (n = 94) were meticulously grafted under renal capsules of female BALB/C-nude mice within 2 h of surgical removal. Grossly visible tumor tissues serially transplanted for 2-5 generations. After the development of tumor in mice, phenotypic and genetic comparisons were performed between primary tumor and corresponding transplantable xenografts using hematoxylin-and-eosin, Ion Torrent (AmpliSeq Cancer Panel), and array-comparative genomic hybridization (aCGH) analysis.

Results: Total tumor tissue engraftment rate was 47.4% (27/57) of ovarian cancer, 46.2% (12/26) of cervical cancer, and 42.9% (6/14) of endometrial cancer. The mean time to the development of first generation in mice was in 5.7 months in ovarian, 5.5 months in cervical, and 4 months in endometrial cancer. Comparison of primary and PDTX tumor tissues showed highly similar histopathologic features. Moreover, analysis of Ion Torrent and aCGH indicated that all examined mutation and genomic alterations found in primary cancer tissues were precisely replicated in the corresponding PDTX tumors.

Conclusions: PDTX mice for human gynecologic cancer can be developed as a method of subrenal capsule implantation and have very similar phenotypic and genetic alterations of the original tissues. This has the potential to provide a very effective tool for future personalized therapy and for conducting translational gynecologic cancer research.

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501 – Poster Session

Evaluation of a novel combination treatment strategy using patient-derived xenografts of uterine carcinosarcoma

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Objectives: To characterize a newly developed patient-derived xenograft (PDX) model of uterine carcinosarcoma (CS) and to evaluate a novel combination treatment strategy.
Methods: After institutional review board approval, CS tissue from a patient undergoing primary surgery was directly implanted into athymic mice, and adjacent portions of the primary tumor were flash-frozen and formalin-fixed, paraffin-embedded. Short tandem repeat (STR) analysis was done on genomic DNA from the tumor and matched PDX. A monoclonal anti-insulin growth factor 1 receptor (IGF1R) antibody, IMC-A12, was provided by Imclone. Mouse-to-mouse passage was completed to create P1 (n = 9) and P2 (n = 10) cohorts of PDX. Treatment groups were combination IMC-A12 50 mg/kg twice weekly × 6 plus paclitaxel 15 mg/kg weekly × 3 and carboplatin 50 mg/kg weekly × 3 (IMC-A12 plus T/C), T/C, or vehicle. Tumor volume (TV) and animal weights were measured twice weekly. Target suppression by IMC-A12 was assessed by Western blot analysis of PDX lysates. Mean TV between treatment groups was compared by two-tailed t-test.

Results: Following surgery, the patient had disease progression during primary T/C chemotherapy. Histopathologic comparison of the primary tumor and PDX showed similar morphology, with the sarcomatous component predominant in the PDX; STR analysis showed 100% match between tumor and PDX. For PDX-01, additional CS PDX models will be used for further assessment of strategies in vivo. The addition of IMC-A12 to paclitaxel/carboplatin was done on genomic DNA from the tumor and matched PDX. A fixed, parafnex-frozen and formalin-fixed, paraffin-embedded, short tandem repeat (STR) analysis was done on genomic DNA from the tumor and matched PDX. A monoclonal anti-insulin growth factor 1 receptor (IGF1R) antibody, IMC-A12, was provided by Imclone. Mouse-to-mouse passage was completed to create P1 (n = 9) and P2 (n = 10) cohorts of PDX. Treatment groups were combination IMC-A12 50 mg/kg twice weekly × 6 plus paclitaxel 15 mg/kg weekly × 3 and carboplatin 50 mg/kg weekly × 3 (IMC-A12 plus T/C), T/C, or vehicle. Tumor volume (TV) and animal weights were measured twice weekly. Target suppression by IMC-A12 was assessed by Western blot analysis of PDX lysates. Mean TV between treatment groups was compared by two-tailed t-test.

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Conclusions: We demonstrated the ability of the DAP compounds HO-4200 and HO-4318 to inhibit cell migration/invasion and induce apoptosis by targeting STAT3 in human ovarian cancer cells, including primary ovarian cancer cell populations and tumor tissues. These results highlight the clinical anticancer potential of HO-4200 and HO-4318.

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504 — Poster Session
The long non-coding RNA steroid receptor activator induces tumor proliferation and invasion via the Notch pathway in human ovarian cancer
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Objectives: Long non-coding RNAs (LncRNAs) have been recently found to be critical regulators of the epigenome. Steroid receptor RNA activator (SRA) ncRNA enhances nuclear receptor and myogenic differentiation 1 (MyoD)-mediated transcription but also participates in specific corepressor complexes. Some have reported that SRA RNA levels might affect some biologic functions, such as proliferation, apoptosis, steroidogenesis, and myogenesis. However, the exact function and mechanism of SRA in human ovarian cancer remains unclear. We investigated whether Notch signaling is hyperactivated in metastatic ovarian cancer cells that express SRA.

Methods: SRA expression was determined in ovarian cancer tissues (n = 115) and corresponding normal tissues (n = 30) by real-time reverse transcriptase polymerase chain reaction (RT-PCR). To determine the effects of SRA knockdown and overexpression in human ovarian cancer cell lines, we measured wound healing, matrigel invasion chamber, Western blotting, and CCK-8 assays.

Results: The expression of SRA in ovarian cancer tissues was significantly higher than that in normal tissues. Real-time RT-PCR results showed high expression levels of SRA in SKOV3, TOV112D, and OVCA429 cell lines. Knockdown of SRA decreased cell proliferation, migration, and invasion in OVCA429 and TOV1112D cells. Additionally, SRA knockdown decreased the expression of vascular endothelial growth factor, matrix metalloproteinase-9, and epithelial–mesenchymal transition (EMT), which are important for cell motility and metastasis. Mechanistic investigation revealed that Notch1, Hes1, and p300 proteins could be inhibited by SRA depletion. DAPT, a well-known γ-secretase inhibitor, blocked Notch expression in SRA-overexpressed OVCA433 cells. DAPT decreased cell migration and invasion in SRA-overexpressed OVCA433 cells.

Conclusions: These results suggest that SRA promotes tumor aggressiveness through the Notch pathway. SRA may serve as potential gene therapy in ovarian cancer.

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505 — Poster Session
The effects of itraconazole as anti-cancer agent in epithelial ovarian cancer
J.W. Lee, Y.Y. Lee, W.Y. Kim, A. Yoon, T.J. Kim, B.G. Kim, D.S. Bae. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, Samsung Medical Center, Seoul, South Korea, Kangbuk Samsung Hospital, Seoul, South Korea

Objectives: Recent studies showed that the antifungal agent itraconazole has anticancer effects via inhibition of angiogenesis, hedgehog, or mTOR pathways. In this study, we tried to evaluate the anticancer effect of itraconazole and its mechanism in epithelial ovarian cancer (EOC).

Methods: We treated EOC cells (HeyA8, SKOV3ip1, and HeyA8-MDR) or endothelial cells (HUVEC and SVEC4-10) with itraconazole to evaluate the effect on cell proliferation. To evaluate the mechanism of action for itraconazole, we assessed the expression of VEGFR2 for angiogenesis, Gli1 for hedgehog, and S6K1 for mTOR pathway. We performed an in vitro therapy experiment to evaluate the combination effect of itraconazole and paclitaxel using nude mice with established EOC cells (SKOV3ip1 or HeyA8). We also tested this effect in a patient-derived xenograft (PDX) model for EOC.

Results: Although itraconazole treatment had no effect on cell proliferation of ovarian cancer cells assessed by MTT assay, it significantly inhibited the proliferation of endothelial cells in a dose-dependent manner. Itraconazole treatment decreased the expression of VEGFR2, Gli1, and phosphor-S6K1 in endothelial cells but not in EOC cells. In SKOV3ip1 and HeyA8 orthotopic mice models, the mice treated with the combination of itraconazole and paclitaxel had significantly decreased tumor weight compared with control, paclitaxel alone, or itraconazole alone (P<0.05). We confirmed this effect in two EOC PDX models.

Conclusions: These results suggest that itraconazole selectively inhibits endothelial cells rather than cancer cells themselves through a possible mechanism of the inhibition of angiogenesis (VEGFR2), hedgehog (Gli1), or m-TOR (S6K1) degradation. Adding itraconazole to standard chemotherapy could be considered to enhance the drug response in treatment of EOCs.

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506 — Poster Session
Dual mTORC1/2 inhibitor INK128 potentiates sensitivity to carboplatin in a platinum resistant ovarian cancer cell line
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Objectives: Platinum resistance is a major cause of treatment failure and mortality in epithelial ovarian cancer. This study sought to characterize the mechanism by which the dual mTORC1/2 inhibitor INK128 restores sensitivity to carboplatin in OVCAR-3, a platinum-resistant ovarian cancer cell line.

Methods: OVCAR-3 cells were treated with INK128 alone and in combination with carboplatin. Antiproliferative effects were assayed by MTT cell proliferation analysis and colony formation assays. Overall effect on protein synthesis was analyzed using35S-methionine translation assays. Polysome profiling was performed to characterize the mRNAs preferentially altered by each treatment. Microarray analysis of polyribosome fractions was performed and chip files were normalized with Affymetrix Expression Console Software using RMA background correction. Transcriptionally regulated transcripts were selected based on a P value <0.05 and fold-change >1.5. Student’s t-test was performed for data analysis.

Results: MTX assays confirmed an antiproliferative effect of INK128 on OVCAR-3 cells with and without carboplatin. Functional colony formation assays demonstrated a sensitizing effect of INK128 on the cells with increasing doses of carboplatin (P = 0.004).35S-methionine de novo protein synthesis assay showed a 25% decrease in overall translation when cells were treated with INK128 compared to control (P = 0.0257). Microarray analysis revealed an enrichment of mRNAs involved in cell cycle regulation and DNA repair (false discovery rate <0.05). Downregulation of the gene products of RAD17, SYCP2, CEP70, and MIST2 were specific to the combination of carboplatin and INK128.
507 — Poster Session
Progestins and vitamin D inhibit CYP24A1 in vivo in ovarian cancer cell xenografts

J. Hunn, J. Turbov, R. Rosales, V. Syed, T.P. Conrads, K.M. Darcy, G.L. Maxwell, C.A. Hamilton, L.G. Thaete, G.C. Rodriguez.* Northshore University Health System, Evanston, IL, USA, 2Uniformed Services University of the Health Sciences, Bethesda, MD, USA, 3Gynecologic Cancer Center of Excellence, Annandale, VA, USA, 4Inova Fairfax Hospital, Falls Church, VA, USA, 5Walter Reed National Military Medical Center, Bethesda, MD, USA

Objectives: We have shown that combined progesterone and calcitriol (1,25-dihydroxycholecalciferol, the active form of vitamin D) reduces proliferation and promotes apoptosis in ovarian cancer cell lines. Inhibition of 24-hydroxylase (CYP24A1, the enzyme that renders vitamin D inactive) expression has been identified as a mechanism that increases the active half-life of vitamin D. Our objective was to determine whether this mechanism is active in vivo as a preliminary step to designing a human clinical trial.

Methods: Using xenografts of OVCAR-3-PGR (progesterone receptor-transfected ovarian line) in nu/nu mice, we investigated the impact of 12 weeks of depo-medroxyprogesterone acetate (DMPA, 1 mg/mouse) and cholecalciferol (25,000 IU/kg diet) treatment, alone and in combination, on the expression of CYP27B1 (converts vitamin D to its active form), CYP24A1, and vitamin D receptors in both xenograft tumors and kidneys. Messenger RNA expression was quantified by reverse transcription polymerase chain reaction. Statistical comparisons were made among treatment groups by ANOVA with significance at P < 0.05.

Results: Vitamin D receptors were expressed in all tumors and their expression level was unaffected by progesterin and/or cholecalciferol treatment. CYP27B1 expression was observed in tumors and kidneys from all treatment groups, demonstrating the capability of these tissues to convert vitamin D to its active form. CYP24A1 expression was enhanced (P < 0.001) as expected in the kidneys by cholecalciferol treatment. It was suppressed (P < 0.05), compared to controls, in tumors in response to each treatment alone and markedly reduced (P < 0.01) by combined DMPA and cholecalciferol.

Conclusions: We show for the first time that CYP24A1 is inhibited by a progesterin in vivo. CYP24A1 limits the antitumorigenic signaling of active vitamin D in cancer cells, and our data provide evidence that progesterins may be beneficial in preserving this activity. The combination of progesterins and cholecalciferol deserves further consideration as a strategy for inhibiting ovarian carcinogenesis in women.

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508 — Poster Session
Evaluation of ERα expression and association with survival in advanced ovarian cancer

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Objectives: Ovarian cancer cell survival may be related to aberrations in energy metabolism. The estrogen-related receptor alpha (ERα), encoded by ESRRA, has emerged as a key transcriptional regulator of mitochondrial function and energy metabolism. Increased expression of ERα in several tumor types correlates with more aggressive tumor characteristics and poorer clinical outcome. Prior small ovarian cancer studies have suggested a relationship between high levels of ERα mRNA, growth potential, and poor outcomes. The purpose of this study was to perform the first large-scale clinical correlative study of ERα protein expression and its relationship to clinicopathologic characteristics and outcomes in epithelial ovarian cancer.

Methods: Paraffin sections were evaluated from 226 primary advanced-stage epithelial ovarian cancers (175 serous, 51 non-serous). Immunostaining for ERα was performed and evaluated by a gynecologic pathologist blinded to patient outcome. This included a score for intensity and percentage of cancer cells staining for ERα. An H score was then calculated that incorporated both of these observations. Pairwise associations were conducted using Spearman correlation coefficients. HR estimates and univariate and multivariate modeling used Cox proportional hazards methods.

Results: Percentage of ERα staining cells and H score were significantly correlated with pretreatment CA-125 values in all samples (r = 0.19 and 0.21, respectively) and in serous cases (r = 0.31 and 0.33, respectively). Cases with ERα staining in <30% of cancer cells trended toward improved overall survival compared to those with a higher percentage of positively stained cells (HR = 1.35, P = 0.06).

Conclusions: Data from this large clinicopathological study demonstrate a correlation between high ERα expression and both high CA-125 levels at diagnosis and a trend toward poor survival. In view of the known role of ERα in energy metabolism and cell growth, these findings suggest that this gene may contribute to a more malignant ovarian cancer phenotype. Thus, ERα may be a rational target for the treatment of ovarian cancer.

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509 — Poster Session
PD-1, PD-L1 expression in 1599 gynecological cancers: Implications for immunotherapy

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Objectives: T-cell suppression via programmed cell death protein 1 (PD-1)/programmed death ligand 1 (PD-L1) interactions plays a central role in cancer progression and survival, making PD-1/PD-L1 attractive therapeutic targets. Clinical trials involving PD-1/PD-L1-targeted immunotherapies have demonstrated marked success in solid tumors, including melanoma and renal cell carcinoma, and earlier studies indicated that PD-L1 levels may identify patients who derive more benefit from immunotherapies. These agents and biomarkers could revolutionize management of gynecologic malignancies that have developed resistance to standard chemotherapies. The purpose of this study was to identify gynecologic malignancies that may benefit from this new class of targeted therapy.

Methods: A total of 1599 cases encompassing all gynecologic malignancies (i.e., cervical, uterine, ovarian, vaginal, vulvar) were evaluated at a central laboratory (Caris Life Sciences) for the presence of cells expressing PD-1 (NAT105) and PD-L1 (B7-H1 antibody). Intraepithelial PD-1-positive lymphocytes (IEL) and...
Omentin is a protective adipokine secreted by the mesothelial cells of visceral adipose tissue. Its expression is inversely related to obesity, and low levels have been found to be associated with disease states, such as diabetes and hypertension. Recently, it has been found to have tumor suppressor activity in ovarian cancer, leading to decreased ovarian cancer cell proliferation, motility, and invasion potential. We sought to explore whether omentin could be used as a biomarker to predict overall survival among patients with serous ovarian cancer.

**Methods:** Serum samples were obtained from 148 women with serous ovarian cancer at the time of initial surgery. Circulating omentin levels were quantified using a commercially available enzyme-linked immunosorbent assay kit. Clinical and demographic data were obtained from the electronic medical record. Overall survival was measured from the date of omentin collection to the date of last follow-up or death. A multivariate analysis of overall survival was performed to account for potential confounding variables.

**Results:** Among women with serous ovarian cancer, a higher omentin level (per 100 units) was significantly associated with a decreased risk of death ($P = 0.0004$). Using a cutoff point of 350 ng/mL, a Kaplan–Meier curve demonstrated a significantly improved survival for women with omentin $> 350$ ng/mL at the time of initial surgery ($P < 0.0001$). A multivariate analysis was performed to consider other risk factors that may contribute to risk of death, including stage and grade of cancer, optimal debulking, use of neoadjuvant chemotherapy, body mass index, meno-pausal status, diabetes, and metformin use. After adjusting for these factors, the relationship between omentin and overall survival remained statistically significant ($P < 0.0001$).

**Conclusions:** Omentin levels $> 350$ ng/mL are predictive of improved overall survival among women with serous ovarian cancer, after adjusting for potential confounders. This may be reflective of the tumor suppressor activity of this adipokine or may be due to the ability of ovarian cancer cells to downregulate production of omentin. These findings warrant validation in another large ovarian cancer dataset.

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**511 – Poster Session**

**Unveiling novel mutations in the DNA-binding domain of FOXA2 in endometrioid endometrial cancers**

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**Objectives:** FOXA2 is a transcription factor important in development, cellular metabolism, and tumorigenesis. Mutations in FOXA2 were identified at a modest frequency in The Cancer Genome Atlas (TCGA) as endometrioid endometrial cancers (EMCs). The current study sought to determine the spectrum and frequency of FOXA2 mutations in EMCA and analyze relationships between mutations and clinical and clinicopathologic features.

**Methods:** EMCA tumors were assessed for mutations using polymerase chain reaction amplification of coding sequences and Sanger DNA sequencing methods. Statistical analysis was performed using chi square, Fisher's exact, and Student's t-tests.

**Results:** Among 329 tumors analyzed to date, 43 mutations were identified in 42 tumors (13.8% overall mutation rate). The majority of unique mutations (36 of 38) have not been previously reported and were loss–of–function mutations, defined as frameshift or nonsense (76.7%). Mutations were seen at similar frequency in MSI and MSS tumors (14.3% and 10.1%, respectively). FOXA2 missense, nonsense, and frameshift mutation rates were 2.74%, 1.22%, and 9.12% in our cohort compared to previously reported 2.92%, 0.83%, and 1.67% rates ($P < 0.001$). Among missense mutations ($n = 7$), two recurred twice and were predicted to alter protein phosphorylation. Furthermore, two short-coding regions in MSI tumors, 6 C- and 6 G-repeat, were prone to frameshift mutations. Thirteen of 43 mutations (30.2%), including both of the phosphoacceptor–altering mutations, were within the DNA-binding domain of FOXA2, and 13 mutations were found upstream to this region. Interim analyses have revealed a significant association between FOXA2 mutation and early-stage disease (90.5% vs. 79.7%) and grade 2 disease, independent of MSI or MSS status. No significant association was seen between FOXA2 mutations and age, race, body mass index, or recurrence.

**Conclusions:** DNA sequencing revealed 36 novel FOXA2 mutations and uncovered a greater mutation rate, mainly frameshift mutations, than previously described in EMCA. The majority of FOXA2 mutations were loss of function within or before the DNA-binding domain, suggesting a possible role in EMCA. FOXA2 mutations are associated with earlier stage and grade 2 disease. Further analysis of mutation-induced changes in protein structure and function and clinicopathologic outcomes is ongoing.

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**512 – Poster Session**

**Cancer tests-antigen expression shared among gynecological cancers**

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**Objectives:** FOXA2 is a transcription factor important in development, cellular metabolism, and tumorigenesis. Mutations in FOXA2 were identified at a modest frequency in The Cancer Genome Atlas (TCGA) endometrioid endometrial cancers (EMCs). The current study sought to determine the spectrum and frequency of FOXA2 mutations in EMCA and analyze relationships between mutations and clinical and clinicopathologic features.

**Methods:** EMCA tumors were assessed for mutations using polymerase chain reaction amplification of coding sequences and Sanger DNA sequencing methods. Statistical analysis was performed using chi square, Fisher's exact, and Student's t-tests.

**Results:** Among 329 tumors analyzed to date, 43 mutations were identified in 42 tumors (13.8% overall mutation rate). The majority of unique mutations (36 of 38) have not been previously reported and were loss–of–function mutations, defined as frameshift or nonsense (76.7%). Mutations were seen at similar frequency in MSI and MSS tumors (14.3% and 10.1%, respectively). FOXA2 missense, nonsense, and frameshift mutation rates were 2.74%, 1.22%, and 9.12% in our cohort compared to previously reported 2.92%, 0.83%, and 1.67% rates ($P < 0.001$). Among missense mutations ($n = 7$), two recurred twice and were predicted to alter protein phosphorylation. Furthermore, two short-coding regions in MSI tumors, 6 C- and 6 G-repeat, were prone to frameshift mutations. Thirteen of 43 mutations (30.2%), including both of the phosphoacceptor–altering mutations, were within the DNA-binding domain of FOXA2, and 13 mutations were found upstream to this region. Interim analyses have revealed a significant association between FOXA2 mutation and early-stage disease (90.5% vs. 79.7%) and grade 2 disease, independent of MSI or MSS status. No significant association was seen between FOXA2 mutations and age, race, body mass index, or recurrence.

**Conclusions:** DNA sequencing revealed 36 novel FOXA2 mutations and uncovered a greater mutation rate, mainly frameshift mutations, than previously described in EMCA. The majority of FOXA2 mutations were loss of function within or before the DNA-binding domain, suggesting a possible role in EMCA. FOXA2 mutations are associated with earlier stage and grade 2 disease. Further analysis of mutation-induced changes in protein structure and function and clinicopathologic outcomes is ongoing.

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513 — Poster Session
Co-culture of human induced pluripotent stem cells (iPSCs) with human fallopian tube epithelium (FTE) induces Pax8 and CK7 expression: Initial steps in modeling fallopian tube epithelium to study serous carcinogenesis

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Objectives: The fallopian tube has emerged as a novel site of origin of serous ovarian cancer. Models to study FTE transformation are greatly needed. The aim of this study was to induce differentiation of iPSCs toward Müllerian serous epithelium to further investigate the molecular mechanisms contributing to neoplastic transformation.

Methods: iPSCs were differentiated to intermediate mesoderm (IM) and embryoid bodies (EBs) using established protocols. IM and EBs were then co-cultured with human FTE in two systems: an ex vivo model using fresh patient surgical FTE or an immortalized fallopian tube secretory epithelial cell line (FTSEC). Green fluorescent protein-labeled IM and EBs plated in the ex vivo culture model were allowed to differentiate in defined basal media underneath live FTE cells plated on a transwell insert. Co-culture with the immortalized FTSEC was established in an “organoid-like” structure encapsulated within a matrigel extracellular matrix. Cells were fixed following 57 days of co-culture and stained using immunofluorescence.

Results: iPSC-derived cells (IM and EBs) acquire an epithelial-like morphology following extended co-culture with both FTE surgical specimens and with immortalized FTSEC using the organoid matrigel model. In contrast, IM and EBs plated in basal media in the absence of co-culture with either FTE or FTSEC do not survive. Expression of Pax8, a lineage-specific marker for fallopian tube secretory epithelial cells, was induced in the iPSC-derived cells with an epithelial-like morphology. Expression of CK7, a type II keratin frequently used in conjunction with Pax8 as a marker of FTE, was also induced in iPSC-derived cells following co-culture with fallopian tube epithelial cells. Pax8 and CK7 expression was negative in undifferentiated iPSCs.

Conclusions: The expression of Pax8 and CK7 in iPSC-derived cells following extended co-culture with FTE suggests that fallopian tube secretory epithelial cells are capable of promoting differentiation of iPSCs toward müllerian serous tissues. These data suggest a possible novel method to differentiate human iPSCs toward fallopian tube epithelium via intermediate mesodermal precursor cells or spontaneously differentiated embryoid bodies in co-culture with human fallopian tube epithelial cells.

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514 — Poster Session
Notch receptor signaling mediates platinum and paclitaxel resistance in epithelial ovarian cancer

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Objectives: Notch signaling regulates cell fate and proliferation. Our purpose was to examine the relationships of notch receptor signaling and ovarian cancer chemoresistance.

Methods: In vitro cell proliferation (MTT) assays and apoptosis (DPI stain) assays of SK-OV-3 cells for cisplatin and paclitaxel resistance with notch 1 silencing were performed. Formalin-fixed, paraffin-embedded tissue sections from 5 normal ovaries, 10 borderline ovarian tumors (BOT), and 35 ovarian cancers (OC) were subjected to immunohistochemical (IHC) staining for notch 1 receptor. Notch 1 receptor expression and clinicopathologic factors were analyzed by using Statistical Package for the Social Sciences. P < 0.05 was accepted as statistically significant.

Results: Apoptosis was increased by cisplatin and paclitaxel in the presence of notch 1 silencing by siRNA were performed. Formalin-fixed, paraffin-embedded tissue sections from 5 normal ovaries, 10 borderline ovarian tumors (BOT), and 35 ovarian cancers (OC) were subjected to immunohistochemical (IHC) staining for notch 1 receptor. Notch 1 receptor expression and clinicopathologic factors were analyzed by using Statistical Package for the Social Sciences. P < 0.05 was accepted as statistically significant.

Conclusions: Notch 1 silencing showed increased platinum and paclitaxel sensitivity by decreasing proliferation of SK-OV-3 cells (P = 0.0055, P = 0.0004, respectively). Notch 1 silencing showed increased platinum and paclitaxel sensitivity by decreasing proliferation of SK-OV-3 cells (P = 0.0018, P = 0.0003, respectively). The notch 1 IHC staining positive rates were 0% in normal tissues (P = 0.0069). Notch 1 receptor positivity according to grades were 33.3%, 50.0%, and 50.0% (P = 0.035). Notch 1-positive patients showed shorter disease-free interval (mean 65.7 months) compared with notch 1-negative patients (mean 82.5 months, P = 0.0000, and respective mean 5-year survival rates were 58.5% (n = 24) and 41.0% (n = 11) (P = 0.011).

Conclusions: Notch 1 receptors are related to carcinogenesis of the ovary. Notch 1 receptor signaling seems to provide resistance to platinum- and paclitaxel-based chemotherapy in vitro and in vivo experiments.

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515 — Poster Session
Repurposing Artesunate, an anti-malarial, for ovarian cancer treatment: Mechanistic insights from cell line models
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Objectives: We previously identified the TGF/Wnt pathway to be associated with the development and progression of ovarian cancer (OVCA). Using a novel in silico strategy designed to identify agents with predicted activity against disease-associated molecular signaling pathways, we identified the antimalarial Artesunate as a potential drug to target the TGF/Wnt pathway. Here we investigated the mechanistic activity of Artesunate against transforming growth factor (TGF)-beta-induced cell growth, migration, and invasion in OVCA.

Methods: OVCA cells were treated with Artesunate and evaluated for sensitivity by MTS assays. In parallel, cells were subjected to baseline Affymetrix HuRSTA gene expression analysis. Pearson’s correlation was performed on Artesunate median inhibition concentration values and baseline OVCA cell gene expression data. The effects of Artesunate on cell growth, migration, and invasion using MTS assays, in vitro wound healing assays, and basement membrane matrices were performed on OVCA cells with known differential expression of the TGF/Wnt pathway, as determined by principal component analysis modeling (PCA). Western blot analysis was used to evaluate the effects of Artesunate on TGF-beta and Wnt signaling proteins as well as known markers of epithelial–mesenchymal transition (EMT).

Results: Artesunate exhibited an inhibitory activity of cell growth in all examined cell lines. Pearson’s correlation identified seven TGF/Wnt pathway genes associated with Artesunate sensitivity (P < 0.01), including Wnt5A (Pearson’s score: 0.8944, P = 0.002), frizzled-6 (FZD6) (Pearson’s score: 0.8509, P = 0.007), and JUN (Pearson’s score: 0.8864, P = 0.003). When treated with Artesunate, OVCA cells with high (vs. low) TGF/Wnt pathway expression exhibited greater inhibition in: 1) 5-day growth assays, 2) failure to close wounds, and 3) invasion of surrounding basement membrane matrices. Examination of Artesunate-treated cells by Western blot analysis demonstrated modulation of several TGF-beta and Wnt signaling proteins and EMT markers.

Conclusions: The antimalarial drug Artesunate is a promising therapeutic candidate for the treatment of OVCAs driven by TGF-beta and/or Wnt signaling. Our findings provide new insights into the mechanisms underlying Artesunate response and warrant further research of Artesunate as a novel anticancer agent against OVCA.

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516 — Poster Session
Alteration of immune landscape in obesity associated endometrial hyperplasia
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Objectives: The systemic changes in endocrine hormones and growth factors associated with obesity and their roles in the pathogenesis of endometrial cancer have been well documented. However, the effects of obesity on the cellular composition of the endometrial stroma in this state of chronic inflammation have not been well characterized. We hypothesized that infiltrating immune cells and increased production of cytokines may alter the endometrial microenvironment and contribute to endometrial hyperplasia (EH) and progression to endometrial cancer in the context of obesity.

Methods: A conditional PTEN knockout uterine-specific mouse model was used in which 100% of mice develop EH by 26 weeks. Both PTEN(+/−) and age-matched (tumor-free) C57BL/6 controls were divided into two groups fed either a high- or low-fat diet until time of sacrifice at 28 weeks. Formalin-fixed, paraffin-embedded uterine sections were stained using anti-F4/80 antibodies specific for murine macrophages. The total number of F4/80-positive cells per stromal area at high power (200×) were calculated and compared. Serum adipokine levels in the four groups were evaluated using the MILLIPLEX® Mouse Adipokine Magnetic Bead Panel multiplex enzyme-linked immunosorbent assay. Specific cytokines tested included: interleukin (IL)-6, leptin, insulin, monocyte chemotactrant protein (MCP)-1, plasminogen activator inhibitor (PAI)-1, resistin, and tumor necrosis factor (TNF)α. Statistical analyses were performed using Statistical Package for the Social Sciences software. Non-parametric T tests were used to determine differences for both macrophage count and serum adipokine levels. P < 0.05 was used to signify statistical significance.

Results: Serum levels of IL-6 were significantly higher in obese PTEN (+/−) mice with hyperplasia compared to both obese wild-type (13.47 vs. 4.00 pg/mL, P = 0.08) and lean PTEN (+/−) mice with hyperplasia (13.47 vs. 6.58 pg/mL, P = 0.032). No significant difference was seen in the levels of other serum cytokines or in macrophage infiltration.

Conclusions: Only IL-6 expression is upregulated in the presence of EH in the obese mouse, indicating that EH in an obese microenvironment may modify the immune landscape to promote disease progression. In addition to the effect of EH on subpopulations of immune cells in the obese endometrium, pharmacologic interventions that interrupt these effects are being further explored.

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517 — Poster Session
High-throughput matrix screening in ovarian cancer cells identifies synergistic drug combinations with the second mitochondriald- derived activator of caspases (SMAC) mimetic birinapant (TL32711)
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Objectives: The development of resistance to current standard therapies for ovarian cancer, the deadliest gynecologic malignancy, is common, and more effective treatment options are urgently needed. Although targeted therapies are increasingly emerging as strategies to prevent or overcome drug resistance, the rational combination of such drugs will likely improve their therapeutic efficacy. Birinapant (B) binds to inhibitors of apoptosis and activates caspase 3 to potentiate cell death but has little single-agent efficacy in ovarian cancer. We sought to identify drug combinations to increase its potency as an anticancer agent.

Methods: High-throughput screening using an unbiased matrix platform enables efficient identification of synergistic clinically useful drug combinations. In this study, we evaluated a drug library composed of 1912 agents in combination with B in a 6 × 6 dose–response matrix format, using the PEO1 ovarian cancer cell line. With this fully automated system, cells were dispensed into 1536-well plates immediately after the acoustic dispensation of B and each library compound. Cell viability was determined by Cell-titer Glo and apoptosis measured by Caspase3–Glo assay. Combinatorial behavior (antagonism, synergy) was calculated based on combination index and beta parameter to identify combinations better than those predicted by the Bliss model. In
518 — Poster Session
Small molecule activators of protein phosphatase 2A for the treatment of endometrial cancer
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**Objectives:** Endometrial cancer (EMCA) is the most commonly diagnosed gynecologic malignancy in the United States. While early-stage disease is typically associated with a favorable prognosis, advanced-stage and recurrent EMCA present a particularly difficult therapeutic problem because responses to traditional cytotoxic chemotherapy regimens remain poor. We have reverse-engineered the tricyclic neuroleptics to create a series of novel small molecules that retain the antiproliferative effects of their respective parent drugs while eliminating the dopaminergic central nervous system effects. These derivative compounds have been demonstrated to have anticancer properties through the activation of protein phosphatase 2A (PP2A), which negatively regulates a number of signaling pathways, including AKT and ERK. The objective of this study was to investigate the antitumoral activity of these small molecule activators of PP2A (SMAPs) in high-grade EMCA.

**Methods:** MTT, cell cycle analysis, and colony forming assays using human EMCA cell lines (AN3CA and KLE; G3 endometrioid) and patient-derived EMCA cell lines (UT42 and UT81; G3 endometrioid and uterine serous carcinoma) were performed to assess the activity of SMAPs in vitro. Protein expression after treatment with SMAPs was performed to assess effects on apoptosis and ERK and AKT signaling. Patient-derived mouse xenografts (PDX) were established using UT42 and UT81 in athymic nude mice to test in vivo activity of SMAPs vs. intraperitoneal cisplatin and oral placebo controls.

**Results:** Treatment of EMCA cells with SMAPs resulted in decreased cellular proliferation and survival. Western blots demonstrated that treatment of EMCA cells with SMAPs induces apoptosis and dually inhibits AKT and ERK signaling. Oral treatment with SMAPs in UT42 and UT81 PDX models led to either suppressed tumor growth or tumor regression, which resulted in significantly increased survival (P < 0.05). This increase in survival was achieved with minimal toxicity when compared to placebo and platinum controls.

**Conclusions:** Our findings suggest that SMAPs may represent a novel therapeutic option for the treatment of advanced or recurrent high-grade EMCA, and further investigation is warranted.

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519 — Poster Session
Biomarker comparison of epithelial ovarian cancer and endometrial cancer by multiplatform tumor profiling
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**Objectives:** TP53 has been shown as a driver mutation in epithelial ovarian (EOC) and endometrial cancers (EC). We sought to compare biomarker profiles of tumor samples in relation to TP53mutation to look for overlapping and different treatment paradigms.

**Methods:** A total of 9193 EOC and 3133 EC tumors were evaluated using a commercial multiplatform profiling service (CARIS Life Sciences, Phoenix, AZ). Specific testing performed included a combination of gene sequencing (Sanger, next-generation sequencing), protein expression (immunohistochemistry [IHC]), and gene amplification (chromogenic in situ hybridization [CISH] or fluorescence in situ hybridization [FISH]).

**Results:** TP53 was the most mutated gene in EOC (61%) and EC (43%). In both cancers, compared to the TP53-mutated, TP53 wild-type tumors carried significantly higher mutation rates of the following genes: *PTEN* (EC: 41% vs. 11%; EOC: 5% vs. 1.4%), *PIK3CA* (EC: 39% vs. 26%; EOC: 15% vs. 2.9%), *KRAS* (EC: 27% vs. 12%; EOC: 16% vs. 3.5%), and *CTNNB1* (EC: 20% vs. 1.8%; EOC: 6.3% vs. 0.3%), all P < 0.0001, indicating higher activation of PI3K, MAPK, and Wnt pathways in TP53 wild-type cohorts in both cancer types. Interestingly, in EC, TP53 wild-type cases showed significantly higher estrogen receptor (ER) (73% vs. 49%; P < 0.0001), progesterin receptor (PR) (61% vs. 29%; P < 0.0001), and *PDL1* (33% vs. 14%, P = 0.0002) expression, while TP53-mutated tumors showed significantly higher Her2 amplification and expression (10% vs. 1%, P < 0.0001; 7% vs. 1%, P < 0.0001). These associations were absent in EOC (ER: 46% vs. 51%; PR: 15% vs. 24%; *PDL1*: 15% vs. 16%; *Her2* FISH: 3% vs. 2%; *Her2* IHC: 3% vs. 2%). In contrast, in EOC, TP53 wild-type tumors carried three times the *cMET* expression (29% vs. 9%, P < 0.0001), while *BRCA1/2* mutations were significantly higher in TP53-mutated cases (39% vs. 23%, P = 0.0003), but the difference was not seen in EC.

**Conclusions:** TP53-driven EOC and EC share similarities and carry differences in molecular features. Our results revealed the genetic heterogeneity of gynecologic cancers and suggested increased benefit of targeting the PI3K, MAPK, and Wnt pathways in TP53 wild-type tumors of both cancer types. While hormonal and immunomodulatory therapies may be of particular interest for TP53 wild-type EC, *Her2*-targeted therapies may benefit TP53-mutated EC patients. For EOC, *cMET*-targeted therapies and poly ADP ribose polymerase inhibitor therapy may be of particular interest for TP53 wild-type and TP53-mutated patients, respectively.

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520 — Poster Session
Investigating the role of phosphodiesterase 10A as a novel target in ovarian cancer
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**Objectives:** Phosphodiesterases enzymes (PDEs) play a known role in inflammation as well as the regulation of tumor cell growth and apoptosis by controlling the signaling of cyclic nucleotides. We recently reported that the PDE isozyme PDE10A was overexpressed in colon tumors and absolutely essential for tumor cell growth. Here we investigated PDE10A expression in ovarian cancer to determine its potential as a novel therapeutic target.

**Methods:** PDE10A expression was analyzed in several ovarian cancer cell lines (SKOV3, SKOV3ip1, A2780, A2780-CP70, OV-90, ES-2, and TOV112D) by western-blotting and quantitative reverse transcription-polymerase chain reaction. Similar analysis was performed in vitro testing was performed in eight high-grade serous ovarian cancer cell lines, using the most potent and clinically relevant synergistic drug combinations identified by the screen.

**Results:** Drug library screening revealed synergistic activity between B and specific classes of drugs, including taxanes, histone deacetylase (HDAC) inhibitors, and polo-like kinase (PLK) inhibitors. We proceeded to confirm results with docetaxel, panobinostat, volasertib, and olaparib in vitro. Favorable activity was observed using B with docetaxel, panobinostat, and volasertib but not with olaparib in eight ovarian cancer cell lines.

**Conclusions:** An unbiased matrix screening platform enabled rapid identification of rational therapeutic combinations for the treatment of ovarian cancer. We identified three possible combinations to increase the anticancer activity of B. Future studies will evaluate the preclinical and clinical impact of these combinations.

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tumor samples with matched normal tissue in ovarian cancer patients. Cell lines were then treated with novel small-molecule compounds developed by our team targeting PDE10A to assess pharmacologic growth inhibition. We then evaluated the effect of these compounds on signaling pathways downstream of cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP), specifically vasodilator-stimulated phosphoprotein (VASP), a downstream substrate for both cGMP- and cAMP-dependent kinase, which are involved in cytoskeleton organization and cell migration.

**Results:** PDE10A expression was detected in all of the cell lines analyzed. Differential expression of PDE10A was noted in five out of eight ovarian cancer cell lines compared with immortalized ovarian cancer surface epithelium. PDE10A expression was confirmed in ovarian cancer tumor samples and matched adjacent uninvolved tissue, with no differential noted. Novel small-molecule PDE10A inhibitors resulted in potent growth inhibition and apoptosis in each cell line at low micromolar or submicromolar concentrations. Both cGMP- and cAMP-dependent kinase phosphorylate VASP at serine residues 259 and 157. Targeted PDE10A compounds increased this phosphorylation of VASP at both residues.

**Conclusions:** PDE10A is expressed in ovarian cancer, its inhibition results in potent suppression of growth and apoptotic cell death, and it elicits cyclic nucleotide signaling. Hence, our preliminary data support further investigation and development of PDE10A as a potential therapeutic target in epithelial ovarian cancer treatment and chemoprevention.

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521 — Poster Session

**Ovarian cancer screening in high risk menopausal females**

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**Objectives:** To determine whether annual screening reduces ovarian cancer mortality in a high-risk population.

**Methods:** Data were obtained from the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) trial, a randomized multicenter trial conducted to determine if screening could reduce mortality in these index cancers. The trial enrolled 78,216 participants aged 55 to 74 years, randomized into screening or usual medical care arms. The screening arm received annual serum CA-125 assessment for 6 years and annual pelvic ultrasonography for 4 years. The usual care group did not undergo cancer specific screening. Patients were followed a minimum of 10 years. Follow-up data were obtained by review of medical records, annual questionnaires, population-based cancer registries, and the national death index. This study identified a high-risk subgroup, defined as participants who reported a first-degree relative with breast or ovarian cancer. A total of 11,293 of these patients were randomized to the screening arm and 11,062 to the usual care arm. The current study analyzed overall mortality, disease-specific mortality, stage distribution, and survival in patients diagnosed with ovarian cancer.

**Results:** Ovarian cancer was diagnosed in 48 patients in the screening arm and 44 patients in the usual care arm. There was no significant difference in overall mortality or disease-specific mortality between the two arms. There was a trend toward earlier stage at diagnosis in the screening arm (31% stage I/II in the screening arm vs. 16% stage I/II in the usual care arm, P = 0.085). Patients in the screening arm diagnosed with ovarian cancer experienced a significantly improved survival compared to patients in the usual care arm; the relative risk for mortality due to ovarian cancer was 0.66 (95% CI, 0.47–0.93, P = 0.016).

**Conclusions:** Results from the PLCO study found no benefit to screening in an average-risk population. The current study examined a high-risk subgroup with a family history of breast or ovarian cancer. In contrast to the original PLCO analysis, screening in this high-risk population appears to significantly improve survival in patients diagnosed with ovarian cancer. There was a trend toward earlier diagnosis in the screening arm. This study shows a benefit to the use of screening for ovarian cancer in high-risk menopausal females, as evidenced by improved survival rates.

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