

**Abstracts Presented for the 49th Annual Meeting of the Society of Gynecologic Oncology
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Opening Scientific Plenary I

Saturday, March 24, 2018

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1 - Scientific Plenary

GOG 3007, a randomized phase II (RP2) trial of everolimus and letrozole (EL) or hormonal therapy (medroxyprogesterone acetate/tamoxifen, PT) in women with advanced, persistent or recurrent endometrial carcinoma (EC): A GOG Foundation study

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Objective: Preclinical and clinical evidence has documented that blockade of the PI3K/AKT/mTOR pathway may suppress and/or overcome resistance to endocrine therapy in several solid tumors, including endometrial carcinoma (EC). The efficacy of everolimus and letrozole (EL) in women with recurrent EC has been reported. This trial was designed to determine the response, adverse events (AEs), and progression free survival (PFS) of EL or medroxyprogesterone acetate/tamoxifen (PT) in the treatment of metastatic EC.

Method: An open-label, noncomparative RP2 trial was executed. EL (everolimus 10 mg PO, letrozole 2.5 mg PO daily) or PT (tamoxifen 20 mg PO BID); on alternating weeks, medroxyprogesterone acetate 200 mg PO daily with T) was randomized at a ratio of 1:1 within strata. Activity and AEs were assessed. Eligibility included measurable, stage III–IV or recurrent EC, and 1 or fewer systemic regimens. Dose reductions of everolimus were allowed for grade 3–4 AEs. RECIST response imaging was planned after 8 weeks and then every 12 weeks while on therapy. The decision rule for each arm was based on the number of patients with no prior chemotherapy (NPC).

Results: A total of 74 patients were accrued between February 2015 and April 2016 (EL = 37, PT = 37). Most patients were white/non-Hispanic (85%), had a performance status of 0 (73%), had endometrioid histology (66%), and had systemic therapy (60%). Nine patients in the EL arm (1 CR, 8 PR) and 8 patients in the PT arm (2 CR, 6 PR) had objective responses; 1 patient was never treated; 17 patients (EL = 10 vs PT = 7) continue on treatment; 45 (EL = 20, PT = 25) discontinued treatment because of disease progression; and 3 discontinued because of toxicity. Trial outcomes are presented in Table 1. No statistically significant differences in grade 3–4 AEs between the 2 groups were seen.

Conclusion: EL is an active regimen in 24% of patients with recurrent EC. Responses in the NPC stratum suggest that EL is active in patients with chemo-naïve recurrent EC. Further study of its activity in chemo-naïve patients is warranted. While not statistically significant, more patients with PT had thromboembolic events.

Table 1.

Regimen	N	RR-Intent-to-treat	RR-NPC	RR or Stable	PFS mos.	Overall Survival mos.	Grade 3/4 TE
EL	37	24%	53%	78%	6.4	20.0	0%
PT	36	22%	43%	69%	3.8	16.6	8.3%

2 - Scientific Plenary

Novel intrauterine polymer system delivers everolimus at biologically active levels in rats

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Objective: Clinical trials have demonstrated the efficacy of everolimus (an mTOR inhibitor) in combination with hormonal therapy for advanced/recurrent uterine cancer. This combination is now being evaluated in conservative management of early-stage uterine cancers, using levonorgestrel intrauterine device (IUD) combined with oral everolimus. However, oral therapy with everolimus is associated with adverse events such as stomatitis and hyperglycemia. Intrauterine progesterone may be paired with local delivery of anticancer agents to improve the efficacy of conservative management while limiting systemic effects. With this goal in mind, we developed a novel, drug-eluting polymer system to deliver everolimus at sustained doses long term. We sought to evaluate the biologic activity of everolimus delivered via our polymer rod using a rat model and to define the distribution in the reproductive tract.

Method: Sprague-Dawley rats were implanted with an everolimus-eluting or vehicle control polymer rod. To stimulate estrogen and mTOR signaling, rats were treated with subcutaneous estradiol (40 ug/kg) and sacrificed to test everolimus activity after 7, 21, or 70 days. Epithelial cell height, uterine weight, and immunohistochemical staining for proliferation (Ki67) and Phospho-p70S6 Kinase (PS6K) were compared between control and treated rats. Chemical imaging using Matrix-assisted laser desorption/ionization mass spectrometry was used to describe everolimus distribution in the uterus.

Results: Our studies confirm that everolimus was delivered at biologically active doses. Mean uterine weight was lower for rats treated with intrauterine everolimus compared with controls (0.5 g vs 0.6 g, $P < 0.05$). Epithelial cell height was decreased compared to tissue from the control cohort (mean 20.6 μm vs 34.5 μm , $P < 0.001$). At day 21 postimplantation, proliferation (Ki67) and PS6K staining were decreased in everolimus-treated rats compared with control (Ki67, 74.0 vs 129.1, $P < 0.05$; PS6K, 13.4 vs 101.9, $P < 0.05$).

Conclusion: Our novel, everolimus-eluting device demonstrates intrauterine biologic activity in the rat model. Refinement of drug dose and release kinetics will inform the potential for this device to fill an unmet clinical need in patients who fail conservative management of uterine cancers with hormonal therapy alone.

3 - Scientific Plenary

Disparities in the allocation of research funding to gynecologic cancers demonstrated by funding to lethality scores

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Objective: To analyze funding distributions from the National Cancer Institute (NCI) to gynecologic cancers compared to other cancer sites over the period 2007–2014.

Method: Using the NCI's Surveillance, Epidemiology and End Results, Cancer Trends Progress Report and Funding Statistics, we calculated a score for the funding received per years of life lost from 100 incident cases of uterine, ovarian, and cervix cancer standardized for mortality and incidence. These funding-to-lethality scores were analyzed against 10 other cancer sites that are notable, are of similar incidence, or uniquely affect men. Scores were calculated for each year of the 8-year period to compare trends over time. If funding was equitably allocated based on considerations of incidence and mortality, we would expect scores to be similar across cancer sites.

Results: Of the 13 cancers analyzed, uterine cancer ranks next to last in annual NCI funding. Over the 8-year period, the most recent year (2014) saw decreases in funding from peak levels of 18.5% for ovarian cancer and 18.8% for uterine cancer compared to only a 9.9% decrease for breast, 7.1% for testicular, 6.3% for leukemias, and 5.7% for kidney/renal pelvis, and a 67% increase for pancreatic cancer. Prostate cancer ranks first with an 8-year average of \$1.81 million received per years of life lost from 100 incident cases (funding-to-lethality score 1.81) followed closely by breast cancer (score 1.80). Ovarian cancer ranks ninth (score 0.097), cervix cancer tenth (score 0.087), and uterine cancer twelfth out of 13 (score 0.057). Breast and prostate cancers had scores nearly 32 times higher than uterine, 21 times higher than cervix, and 19 times higher than ovarian ($P < 0.00001$ for all comparisons). The average funding-to-lethality scores for all 3 gynecologic cancers were significantly lower than all cancers ranked first through eighth ($P < 0.05$ for all comparisons).

Conclusion: Funding for gynecologic cancers is significantly lower than that for other cancer sites. This disparity is persistent across each of the most recent 8 years for which data are available. Without a correction, gynecologic cancers will continue to be underfunded and risk lagging behind other cancer sites in critical discoveries for cure and life prolongation in this important era of immunotherapy, molecular targeting, and personalized medicine.

4 - Scientific Plenary

Changes in the Affordable Care Act affecting women: Fiscal 2014-2017

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Objective: The Patient Protection and Affordable Care Act (ACA) was intended to lower costs and increase health care accessibility. Since first reported in 2014, changes have occurred in enrollments, in the affordability of the least expensive bronze plans as well as in the most expensive platinum plans, and the cost of care for women.

Method: Health insurance premiums displayed on exchange-based qualifying health plans (QHPs) were examined for cities in several states that were reported on previously. National figures were obtained from government and nongovernment sources. Changes in the cost of clinical services were included in these efforts.

Results: Monthly premiums increased by >40% in urban and >70% in rural areas, with a low increase (<3%) in total deductible and maximum out-of-pocket expenses increases of ~8% for the lowest premium bronze plan. For the most expensive platinum plan, premiums increased 14%–32% in urban areas and 47%–50% in rural areas with a 45% increase in total deductible and 173%–376% increases in out-of-pocket expense. For women with a dependent child, increased out-of-pocket expense ranged from 82% to 217%. Increases in the cost of a vaginal delivery (\$3,404–\$38,451), C-section (\$8,585–\$73,335), laproscopic hysterectomy (\$9,426), and ovarian cancer treatment (>\$250,000) resulted in an 8.6% increase in cost to the individuals on the bronze plan (maximum \$8,990) and 33.9% on the platinum plan (maximum \$6,224). Despite increases in premiums, deductibles, and out-of-pocket expenses, there has been a decrease in uninsured individuals nationwide (42.9%), while QHP enrollment increased by 42.6% and Medicaid/Children's Health Insurance Program (CHIP) by 6.1% since 2014. Kentucky had the greatest increase in Medicaid/CHIP enrollments over pre-ACA enrollment (103%), which was 22% greater than in 2014. Of the 11 states with >50% increases over pre-ACA Medicaid enrollment, 9 were participating in Medicaid expansion, while 2 had a Medicaid Expansion Alternative. These 11 states averaged 38.6% enrollments in exchange QHPs, which is below the national average of 42.6%.

Conclusion: Increased premium costs on QHPs since inception have been accompanied by sizeable decreases in the uninsured and increases in QHP enrollment.

5 - Scientific Plenary

The Affordable Care Act reduced racial and socioeconomic disparities in access to health insurance among women diagnosed with a gynecologic malignancy

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Objective: To examine the impact of the Affordable Care Act (ACA) on insurance rates among women diagnosed with a gynecologic malignancy comparing differences based on race and socioeconomic status.

Method: Women diagnosed with cervical, uterine, or ovarian cancer between 2011 and 2014 were identified using the Surveillance, Epidemiology, and End Results (SEER) database. A difference of differences analysis was performed for each disease site, comparing the change of uninsured rates from 2011–2013 to 2014 between Medicaid expansion (ES) and nonexpansion states (NES). Standard deviations were estimated for each binomial distribution and propagated for each subtraction, enabling calculation of z for the difference of differences, and estimation of a 2-tailed P value.

Results: A total of 52,917 patients age 18 to 64 years were analyzed. Racial minorities and those living in high-poverty zip codes were more likely to be uninsured and living in NES. The rate of uninsured decreased more in ES compared to NES (6% to 3% compared to 11.5% to 10%, $P = 0.017$). There was a trend toward a greater reduction in uninsured among blacks in ES over that in NES ($P = 0.07$), with a significant increase in Medicaid coverage ($P = 0.005$). Among patients living in the highest poverty zip codes, there was a reduction in uninsured rates in ES compared to NES (6% to 2%, compared to 14% to 13%, $P = 0.009$). Among cervical cancer patients, there was a reduction in uninsured rates among those living in high poverty zip codes in ES ($P = 0.001$). There was a significant reduction in uninsured rates among black patients with ovarian cancer (9.2% to 0.5%). There were no significant differences in uninsurance trends among uterine cancer patients during this time period.

Conclusion: Black and poorer patients are more likely to be uninsured and live in a state that has opted not to expand Medicaid. States that have implemented the ACA Medicaid expansion reduced socioeconomic disparities in access to

insurance, with a trend toward reductions in racial disparities with cervical and ovarian primaries. Further research is necessary to assess whether increased insurance access can reduce other racial health care-related disparities and to determine whether outcomes are improved.

6 - Scientific Plenary

Participation in clinical trials may overcome health disparities in the treatment of advanced or recurrent epithelial ovarian cancer

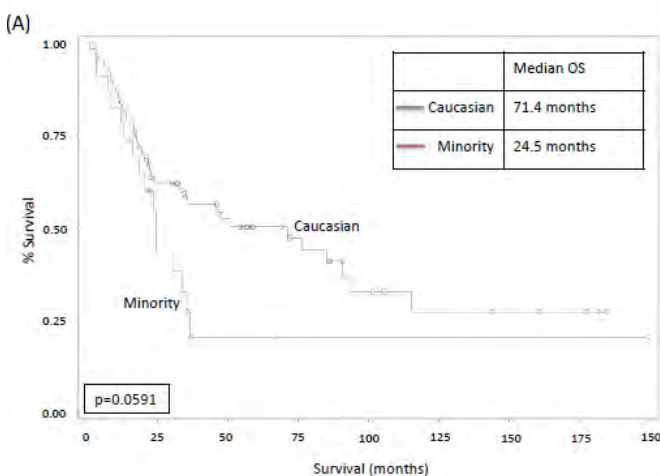
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Objective: To evaluate the effect of clinical trial (CT) participation on overcoming health disparities as related to overall survival (OS) in patients with epithelial ovarian, fallopian tube, and peritoneal cancer (EOC).

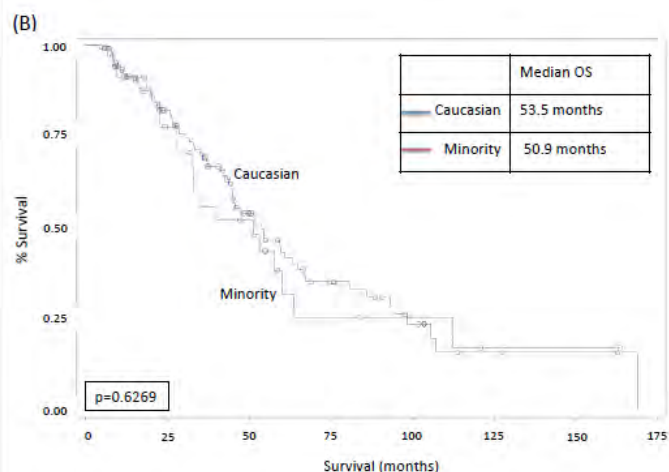
Method: An institutional review board-approved, retrospective study identified patients diagnosed with advanced or recurrent EOC between January 2004 and June 2017, treated at a single institution. Demographics were abstracted from patient charts. Number of CT and OS were calculated. Cox proportional hazard models and log rank tests were used to calculate significance ($P < 0.05$).

Results: We included 236 patients with stage III or IV primary or recurrent EOC with complete follow-up data. Patients were divided into 2 groups based on CT enrollment: (1) CT participants ($n = 145$) and (2) patients never treated on a CT ($n = 91$). Of all patients, 60.3% of minority patients were enrolled on a CT, while 61.8% of white patients participated in a CT. Overall demographics were similar in the 2 groups, but 2 trends were present. First, white patients were more likely to have stage III disease than minority patients (82.6% vs 74.1%, $P = 0.055$). Second, white patients were more likely to live <25 miles from the treatment center than minority patients (60.7% vs 50.0%), who were more likely to live >50 miles away (19.1% vs 29.3%, $P = 0.2261$). When examining the overall effect of race and distance on treatment center on OS, patients who were white and lived >50 miles from treatment center had significantly improved OS (HR = 0.274, 95% CI 0.098–0.768, $P = 0.0286$). A near significant trend improving OS was seen between white versus minority patients who did not enroll in CT ($P = 0.0591$; Figure 1A), and when controlling for age and distance, being white was significantly protective for OS compared to minority (HR = 0.398, 95% CI 0.216–0.732). However, patients who participated in CT had no difference in survival between white and minority ($P = 0.6269$; Figure 1B). When controlling for age and distance, there is no significant protective benefit to OS between white and minority (HR = 0.841, 95% CI 0.505–1.401).

Conclusion: This study demonstrated a significant health disparity exists for race and treatment-center distance for patients with EOC. While white race was significantly protective for OS, participation in clinical trials for minorities overcomes this health disparity. The potential survival benefit due to clinical trial participation for minorities with advanced or recurrent EOC warrants further investigation.



Time (months)	Caucasians alive	Minorities alive
36	58.38%	27.30%
60	50.24%	20.47%
100	32.78%	20.47%



Time (months)	Caucasians alive	Minorities alive
36	69.21%	55.78%
60	43.36%	31.86%
100	23.65%	25.49%

Fig. 1. Overall survival by race. (A) Difference in overall survival between Caucasians and minorities never enrolled on a clinical trial; (B) Difference in overall survival between Caucasians and minorities treated on at least one clinical trial.

Scientific Plenary II: Contemporary Challenges

Saturday, March 24, 2018

Moderators: Jason A. Lachance, MD, *Maine Medical Partners, Scarborough, ME, USA*

Shitanshu Uppal, MD, MBBS, *University of Michigan Health Systems, Ann Arbor, MI, USA*

7 - Scientific Plenary

Tackling the opioid crisis: Implementation of an ultra-restrictive opioid prescription protocol in patients undergoing major gynecologic surgery radically decreased dispensed opioid without reducing pain control

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Objective: Prolonged postoperative opioid use increases the risk of chronic opioid use, abuse, and diversion. Thus, we implemented an ultrarestrictive opioid prescription protocol (UROPP) for postoperative gynecologic oncology patients to minimize these risks while maintaining appropriate analgesia after hospital discharge.

Method: The prospective UROPP was implemented in June 2017 to September 2017 for all patients undergoing gynecologic surgery. Patients undergoing minimally invasive surgery (MIS) were not prescribed opioids unless they required more than 5 doses of an oral or IV opioid while inpatient. Patients meeting this criteria as well as patients who underwent a laparotomy were given a 3-day postdischarge supply. Patients were encouraged to call if pain was not well controlled. Factors associated with increased postoperative pain, amount of prescribed opioids, pre- and postoperative pain scores, inpatient and prior opioid use, and refill requests were tracked in all patients and compared to all surgical patients at our center in the prior 12 months. ANOVA analysis was used for continuous variables and χ^2 or Fisher exact tests for categorical variables.

Results: A total of 99 patients had surgery and were treated with the UROPP, and their data were compared to those for 626 patients from the prior 12 months. Mean age, BMI, number of prior surgeries, surgical complications, surgical approach, and inpatient opioid use were not statistically different between the two cohorts. The mean number of short-acting opioids given at discharge prior to UROPP was 31.7 versus 5.1 in the post-UROPP group ($P < 0.001$). Total opioid pain medications prescribed in the perioperative period were also higher pre-UROPP, 51.4 versus 16.3 tablets post-UROPP ($P < 0.001$). After a laparotomy during pre- and post-UROPP, there was a mean of 43.6 versus 12.3 opioid tablets dispensed at discharge, respectively, and a total of 68.1 versus 18.1 pills in the perioperative period (both, $P < 0.001$), while in the MIS patients 28.2 versus 3.2 tablets were dispensed at discharge, and 46.3 versus 10.9, respectively, during the perioperative period ($P < 0.001$). Only 3% of patients requested refills post-UROPP. There was no change in postoperative visit pain scores.

Conclusion: Implementation of an UROPP decreased the amount of opioids prescribed by 85% to postoperative patients without changes in pain scores, patient satisfaction, or increase in medication refills.

8 - Scientific Plenary

Opioid use in gynecology oncology patients after minimally invasive hysterectomy

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Objective: Opioids are a mainstay of postoperative pain control for gynecologic oncology patients. Yet, there is limited information on the appropriate quantity of pills to prescribe. The purpose of this study is to quantify the opioid requirement for gynecologic oncology patients undergoing minimally invasive hysterectomy.

Method: For this prospective cohort study, gynecologic oncology patients ($n = 140$) planning to undergo laparoscopic or robotic hysterectomy were prospectively recruited at a single institution. Postoperative opioid usage was evaluated via chart review, surveys at 1–2 week and 4–6 week postoperative clinic visits, and pharmacy records. Opioid amounts were converted to morphine milligram equivalents (MME) for standardization.

Results: A total of 126 eligible women ultimately underwent minimally invasive hysterectomy. Of these, 122 women completed the initial postoperative visit; 118 completed the final visit; and 114 completed all assessments. Malignancy was present in 82% of cases, 72% of which were endometrial cancer. The majority of surgeries were performed with straight stick laparoscopy (72%). Mean hospital length of stay was 1.1 days (range 1–4 days). While inpatient, patients received a mean of 3 opioid doses totaling 39.1 MME (SD = 36.9) with a range of 0–14 doses (0–187.5 MME). Twenty-five women (20.5%) used no opioids while inpatient. At the 1–2 week follow-up visit, 45 women (36.9%) reported using no opioids since discharge, and the median usage was 9 pills (63.8 MME) with a range of 0–78 pills (0–390 MME). After the full follow-up, the median usage since discharge from the hospital was 11 pills (82.5 MME) with a range of 0–78 pills (0–525 MME). The median number of opioid pills prescribed was 30 (range 10–50). Inpatient usage predicted outpatient usage at both follow-up visits ($\rho = 0.52$, $P = < 0.0001$; $\rho = 0.21$, $P = 0.02$).

Conclusion: In this cohort of patients, opioids were overprescribed relative to use. While 100% of patients received an opioid prescription, more than 30% used no opioids after discharge from the hospital. Median prescribing outstripped median use by a factor of 3. More restrictive opioid-prescribing practices may be a pathway to reduce opioid misuse, persistent use, and diversion.

9 - Scientific Plenary

Variation of cost and resource utilization associated with the surgical management of women with ovarian cancer

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Objective: To characterize the magnitude of variation in total hospital costs and resource utilization between centers and to evaluate the major factors that drive cost in providing surgical care for women with ovarian cancer.

Method: We performed a retrospective cohort study of women with ovarian cancer undergoing surgery using the Premier Perspective database. The primary outcome was total hospital cost. To assess the relationship between hospital spending and patient outcomes, we identified 4 measures of quality: (1) postoperative complications, (2) reoperation, (3) extended length of stay (LOS) of more than 15 days, and (4) unplanned readmission. We specified a cost model to identify drivers of cost and estimate risk-adjusted hospital spending and used a two-level hierarchical regression model to account for clustering of patients within hospitals and a gamma distribution with log link to account for the skewed distribution of cost.

Results: After applying the exclusion criteria, the final dataset included 15,932 patients treated at 225 hospitals. The median standardized cost was \$10,932 (IQR = \$7,876). Overall, 13.3% of patients were rehospitalized within 90 days; 5.5% were hospitalized for more than 15 days; and 5.7% had a reoperation. The biggest drivers of hospitalization cost were undergoing a laparotomy, number of procedures, reoperation, and complications. We found significant variation in risk-adjusted hospital spending among hospitals. The average risk-adjusted hospital spending for hospitals in the highest spending quartiles is 57% higher than the average hospital spending for hospitals in the lowest spending quartile (\$10,906 versus \$17,149). We found that higher spending by hospitals is associated with adverse patient outcomes. Compared to hospitals in the lowest quartile, hospitals in the highest quartile have higher 90-day rehospitalization rate (11.6% versus 16%), higher reoperation rate (4.8% versus 7.9%), higher extended LOS rate (2.6% versus 9.6%), and higher moderate (28.8% versus 31.6%) and major (11.4% versus 21.2%) complication rates. See Figure 1.

Conclusion: We found a significant degree of variation between hospitals in resource utilization, even after accounting for important patient and hospital characteristics. In addition, we found that there was an association between higher resource utilization and worse quality of care provided.

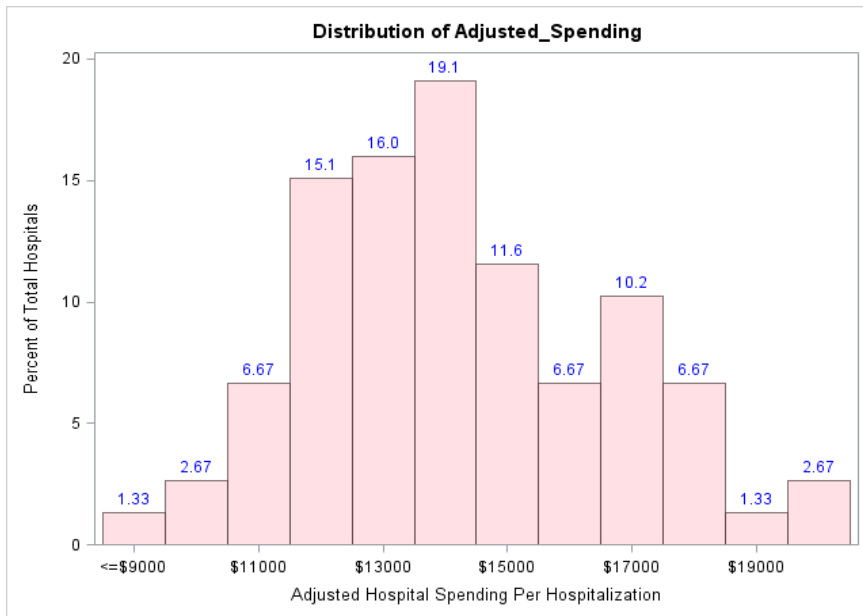


Fig. 1. Distribution of Adjusted Standardized Hospital Spending.

*Standardized hospital spending is adjusted for patient baseline characteristics and number of procedures.

10 - Scientific Plenary

Development of an alternative payment model (APM) for early-stage cervical cancer: Opportunities to reduce cost and improve quality

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Objective: The Medicare Access and Children's Health Insurance Program Reauthorization Act (MACRA) calls for the development of alternative payment models (APMs) for diseases and procedures. The goal of APMs is to structure reimbursements to incorporate total costs of care across providers and facilities, while at the same time improving quality. We piloted development of an APM for primary surgery in early-stage cervical cancer to identify opportunities to reduce cost and improve quality.

Method: The MarketScan database was used to identify women with cervical cancer who underwent radical hysterectomy from 2009 to 2016. Reimbursements from 30 days preoperatively until 60 days postoperatively were captured. Patients were stratified by route of hysterectomy, and reimbursements were categorized into 1 of 8 cost centers: laboratory, radiology, surgical facility, physician's procedural cost, emergency department (ED)/readmissions, skilled nursing/home health, other physician costs, and other. A decision analysis model was developed to estimate the changes in cost that could be achieved by altering each cost center.

Results: A total of 2,978 women were identified. The median cost of an episode of care was \$31,016. The most important modifiable factors driving cost were route of hysterectomy, length of stay, and ED visits/readmissions. The median cost of radical abdominal hysterectomy (\$31,988) was greater than either robotic-assisted (\$30,635) or laparoscopic (\$30,003) hysterectomy. Likewise, costs increased for each additional day of hospitalization at the time of surgery regardless of the route of surgery. Overall, readmissions occurred in 11.2% of patients and had a median cost of \$13,218, while ED visits were required in 15.1% with a median cost of \$1,362. Utilizing these baseline data in which 56% of patients underwent a minimally invasive radical hysterectomy, a model of optimized care in which the rate of minimally invasive surgery was increased by 10% (to 66%), length of stay reduced by 15%, and ED visits/readmission reduced by 20% lowered the average case cost by \$1,035 (3.9%).

Conclusion: The current surgical care of women with cervical cancer in the United States demonstrates several opportunities to reduce cost and improve quality. Modest alterations in the way cervical cancer care is rendered can result in cost savings.

11 - Scientific Plenary

GOG 244, the lymphedema and gynecologic cancer (LEG) study: Incidence and risk factors in newly diagnosed patients

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Objective: To prospectively estimate the incidence of lower extremity lymphedema and investigate potential risk factors in patients undergoing radical surgery for gynecologic malignancy on GOG study 244.

Method: Women undergoing a lymph node dissection (LND) as part of the surgical management for endometrial, cervical, and vulvar cancer were eligible for study enrollment. Leg volume was measured by taking the circumferential measurements at 10 cm intervals starting 10 cm up from the bottom of the heel and continuing to the inguinal crease, and the leg volume is the summation of each truncated cone volume. Reference measurements were obtained from the waist and an arm. Measurements were obtained preoperatively and postoperatively at 6 weeks and at 3, 6, 9, 12, 18, and 24 months. A limb volume change (LVC) >10% was considered consistent with lymphedema of the lower extremity (LLE).

Results: A total of 1,054 women were enrolled on study, and 913 participants were eligible for the data analysis. The study sample included 733 endometrial, 138 cervical, and 42 vulvar cancer patients. The median age and range for study participants by disease cohort was 61 (28–91) years in the endometrial, 44 (25–83) in the cervical cancer, and 58 (35–88) in the vulvar group. LVC >10% was identified in 34% (246), 35% (48), and 43% (18) of the endometrial, cervical, and vulvar patients, respectively. LVC >15% was identified in 19% (140), 25% (35), and 19% (8) of the endometrial, cervical, and vulvar patients, respectively. LVC >20% was identified in 11% (79), 12% (17), and 14% (6) of the endometrial, cervical, and vulvar patients, respectively. The peak incidence of LVC increase was at the 6-week assessment. But patients remained at risk for development of an increase in LVC and LLE throughout the 24-month follow-up. The association between LLE and stage/perioperative variables will be presented.

Conclusion: Women who received an LND as part of the management of their gynecology malignancy were at increased risk for LLE as manifested by an increase in LVC. The risk of a new diagnosis of LLE was present throughout the 24 months of follow-up in this prospective study.

12 - Scientific Plenary

The FILM Trial: A randomized phase III multicenter study assessing near infrared fluorescence in the identification of sentinel lymph nodes (SLN)

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Objective: Interstitial injection of indocyanine green (ICG) for lymphatic mapping and sentinel lymph node biopsy is considered an off-label use because it is currently not FDA-approved. The goal of this registration trial was to assess the effectiveness and safety of near infrared imaging with ICG compared to isosulfan blue dye in detecting sentinel nodes (SLNs) in cervical and uterine cancers.

Method: Patients were randomly assigned to an intraoperative cervical injection with either 4 ml blue dye (1% isosulfan blue) followed by 4 ml ICG (1.25 mg/mL) or ICG followed by blue dye. Laparoscopic surgery utilizing a camera system equipped with near infrared imaging was utilized on all cases. Intraoperatively, SLNs were detected first with white light (blue dye) followed by near infrared imaging (ICG) or vice versa based on 1:1 intraoperative randomization. Standardized data collection sheets were used to describe intraoperative findings. Patients were followed for at least 30 days postoperatively to assess toxicity.

Results: Between December 2015 and May 2017, 180 patients were enrolled (90/arm) with 176 evaluable. A total of 545 SLNs were identified (3.1/patient). Overall, at least 1 SLN was identified in 172 patients (97.7%), and bilateral SLNs were identified in 143 (83.1%). Blue dye identified at least 1 SLN in 131 patients (74.4%) compared to 168 (95.5%) identified by ICG ($P < 0.001$). Blue dye identified bilateral SLNs in 54 women (31.4%) compared to 138 (80.2%) by ICG ($P < 0.001$). Blue dye identified a total of 257 SLNs (1.46/patient) compared to 527 SLNs (2.99/patient) identified by ICG. Randomization group did not affect ability of blue dye or ICG to detect any or bilateral SLNs. Of the 545 SLN identified intraoperatively, 513 (94.1%) were confirmed to be lymph nodes on pathologic processing with no difference between ICG (93.9%) and blue dye (92.6%). Fifteen (8.5%) patients had metastatic disease. All were detected with ICG. There were no adverse events reported from injection of either dye.

Conclusion: In this prospective randomized study, following a cervical injection, ICG proved significantly better than isosulfan blue in identifying any SLNs and bilateral SLNs in women with cervical and uterine cancers. ICG with near infrared visualization should become the standard dye for SLN mapping of uterine malignancy where the technology is available.

13 - Scientific Plenary

Sentinel lymph node (SLN) isolated tumor cells (ITCs) in otherwise stage I/II endometrioid endometrial cancer: To treat or not to treat?

E.J. Backes^a, A.S. Felix^b, J. Grégoire^c, M. Plante^d, S.A. Sullivan^e, E.C. Rossi^e, E.J. Tanner III^f, K.I. Stewart^g, P.T. Soliman^h, D. Cohenⁱ, R.W. Holloway^j, N.R. Abu-Rustum^k and M.M. Leitao Jr.^k ^aThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, ^bThe Ohio State University, Columbus, OH, USA, ^cL'Hotel-Dieu de Quebec, Quebec City, QC, Canada, ^dLaval University, L'Hotel-Dieu de Quebec, Quebec City, QC, Canada, ^eUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, ^fJohns Hopkins Hospital, Baltimore, MD, USA, ^gThe University of Texas, MD Anderson Cancer Center, Houston, TX, USA, ^hThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, ⁱOhio State University, Columbus, OH, USA, ^jFlorida Hospital Cancer Institute, Orlando, FL, USA, ^kMemorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: The objective of this study is to assess associations between treatment and recurrence-free survival (RFS) among EC patients with isolated tumor cells (ITCs) and otherwise stage I–II endometrioid endometrial cancer.

Method: A multiinstitutional study of patients with sentinel lymph node (SLN) ITCs (<200 cells and <0.2 mm) identified by H&E or cytokeratin (CK) immunohistochemistry was performed. Only patients with otherwise stage I–II EC, endometrioid histology, and no evidence of micro- or macrometastases were included. Univariate and multivariable Cox proportional hazard models were used to evaluate associations between treatment, tumor characteristics, and RFS.

Results: A total of 175 patients were identified. Median follow-up time was 31 months. Of all patients, 49% had stage IA, 39% stage IB, and 12% stage II disease (all with ITCs). Fifty-one percent underwent SLN assessment only, and the remainder underwent SLN and lymphadenectomy. A total of 76 (43%) received either no adjuvant therapy or vaginal brachytherapy only (NAT/VBT); 21 (12%) had external beam radiation (EBRT); and 78 (45%) received chemotherapy +/- radiation. Patients who received chemotherapy more often had tumors with deep myoinvasion, LVSI, and higher grade. Nine (5.1%) patients recurred: 5 distant, 3 retroperitoneal, and 1 vaginal. Extravaginal recurrences were similar in patients with or without chemotherapy (5.2% vs 3.8%, $P = 0.68$). After controlling for stage, LVSI, and grade, chemotherapy was not associated with recurrence (HR = 0.63, 95% CI 0.11–3.52, $P = 0.39$). EBRT ($n = 57$) was not associated with RFS (HR = 0.90, 95% CI 0.22–3.61). Type of lymph node dissection (complete vs SLN only) and SLN detection method (H&E vs CK only) were not associated with RFS. In the subset of patients with SLN detected by H&E, chemotherapy did not improve RFS or OS (for RFS, HR = 0.53, 95% CI 0.11–2.62; and for OS, HR = 1.09, 95% CI 0.10–12.07).

Conclusion: Risk of retroperitoneal and/or distant recurrence is low (4.6%) for patients with stage I–II endometrioid EC and ITCs in SLNs regardless of adjuvant treatment or observation. Our preliminary data suggest that adjuvant therapy does not appear to significantly affect RFS. However, longer follow-up time and more patients are needed before more definitive

recommendations regarding adjuvant therapy can be made.

Education Forum I: Immunotherapy 2018: Updates and Toxicities

Saturday, March 24, 2018

Course Director: Christine Walsh, MD, Cedars-Sinai Medical Center, Los Angeles, CA

14 - Education Forum

An in vitro evaluation of neoantigens derived from gene fusion events in ovarian cancer patients

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Objective: Immunotherapy has become an increasingly successful treatment modality in immunogenic tumors. These tumors have a large amount of nonsynonymous mutations, which lead to neoepitope presentation, resulting in robust T cell infiltration. Most of the neoantigens studied to date derive from base pair mutations. We sought to investigate the immunogenicity of neoantigens derived from gene fusions, an understudied research area.

Method: Following institutional review board approval, we obtained banked human high-grade serous ovarian cancer (HGSOC) from the University of Pittsburgh. Tumor-extracted RNA was subjected to RNAseq. FusionCatcher software was used to identify (mutanome) in-frame gene fusion events. Varying length neoantigens were made for each fusion event, all containing the amino acids at the fusion site. HLAmimer was used to determine each patient's haplotype. IEDB and NetMHC were used to perform an in silico analysis of the immunogenicity of each neoantigen for the patient-specific haplotype from which it was derived. Neoantigen-specific T cell responses were assessed via an in vitro model utilizing peripheral blood mononuclear cells (PBMCs). Haplotype-specific PBMCs were stimulated in vitro with their corresponding MHC I and II restricted neoantigens. The response of T cells within the PBMCs was evaluated with digital imaging, IFN gamma ELISA, and flow cytometry.

Results: RNAseq data were available for 9 patients. Eight MHC-I and 5 MHC-II neoantigens were synthesized from gene fusions for 3 of the 9 patients, represented by 6 sets of haplotype-specific PBMCs. Compared to negative controls, neoantigen-treated PBMCs showed increased cell clumping, a marker of T cell activation. An objective response with an IFN gamma ELISA was seen for 6 peptides at 2 different concentrations and 5 peptides at 1 concentration. Selective flow cytometry revealed an expansion of CD4+ and CD8+ T cells and an increase in PBMC activation.

Conclusion: Neoepitopes represent a unique and personalized opportunity in ovarian cancer therapy. We were able to identify that gene fusions are a potential source of neoepitopes that are immunogenic in vitro. An in vivo evaluation in a mouse model of a neoantigen-based dendritic cell vaccine is currently ongoing and will serve as a basis for potential clinical trial in humans.

15 - Education Forum

Adverse events and responses in patients with recurrent ovarian cancer undergoing early-phase immune checkpoint inhibitor clinical trials

E.M. Hinchcliff^a, D. Hong^b, H. Le^b, G. Chisholm^a, R. Iyer^a, A. Naing^b and A.A. Jazaeri. ^aThe University of Texas MD Anderson Cancer Center, Houston, TX, USA, ^bThe University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: To describe the clinical outcomes associated with the use of checkpoint inhibitor immune therapy in recurrent ovarian malignancy.

Method: Women with recurrent ovarian cancer treated with an immune checkpoint inhibitor between January 2012 and August 2017 were included. Clinical, radiographic, and biologic data were collected; RECIST criteria were used to determine disease status, and adverse events (AEs) were graded per trial protocols. Descriptive statistics were performed, and predictors of AE were compared using Wilcoxon rank sum and Fisher exact tests. Predictors of progression-free survival (PFS) were analyzed using Cox regression and Kaplan-Meier methodology.

Results: Forty-four women were included with a median age of 53 years (range 28–73 years) and most commonly high-grade serous pathology (59.1%) and white race (70.5%). The subjects were treated with a median of 4 prior lines of chemotherapy

(range 1–10). The number of cycles of checkpoint inhibitor received ranged from 1 to 27 (median 4). Of the 42 patients with full clinical data available, 3 patients had partial response and 20 had initially stable disease; thus the cohort had a clinical benefit rate of 54.8%. Three patients had pseudoprogression (7.1%). The median duration of response was 4.45 months, while the PFS for the total cohort was 3.32 months following the initiation of checkpoint inhibitor therapy. In multivariate analysis, only high-grade serous pathology independently predicted survival, with decreased PFS (2.9 vs 3.9 months, $P = 0.04$). There were 30 grade 3 or 4 immune-related events in 22 patients (52.4%), and 14 required dose delays (33.3%). Combination therapy rather than monotherapy was a significant predictor of AE (OR = 4.6, CI 1.3–16.3, $P = 0.03$). The most common immune-related AE event was elevation in hepatic or pancreatic enzymes in 11 patients (26.2%). Interestingly, the number of mutations was protective from hepatitis/pancreatitis AE (OR = 0.47, CI 0.2–1.1, $P = 0.03$); each mutation corresponded to a 53% decrease in the probability of hepatic or pancreatic AE.

Conclusion: Checkpoint inhibitor therapy had an overall clinical benefit rate of 54.8%. Grade 3 or 4 hepatic and pancreatic enzyme elevations were the most common AE. Mutation number was inversely correlated to risk of this type of AE but not to total AEs.

Education Forum III: Controversies in Gynecologic Oncology

Saturday, March 24, 2018

Course Directors: Chad Hamilton, MD, *Walter Reed Medical Center, Bethesda, MD* Emma Rossi, MD, *University of North Carolina-Chapel Hill, Chapel Hill, NC*

16 - Education Forum

A cost-effectiveness analysis of three PARP inhibitors for maintenance therapy in platinum-sensitive recurrent ovarian cancer

A.Y. Liu^a, J.G. Cohen^a, C. Walsh^b, C.H. Holschneider^c and A.K. Sinno^a. ^a*University of California, Los Angeles, Los Angeles, CA, USA*, ^b*Cedars-Sinai Medical Center, Los Angeles, CA, USA*, ^c*David Geffen School of Medicine at UCLA, Los Angeles, CA, USA*

Objective: To determine the cost-effectiveness of PARP inhibitors when used for maintenance therapy in platinum-sensitive recurrent epithelial ovarian carcinoma (EOC).

Method: Three decision analysis models were generated to compare the cost of observation versus the cost of PARP inhibitor therapy for patients with platinum-sensitive recurrent EOC with germline *BRCA1/2* mutations (*gBRCA*), evidence of homologous recombination deficiency (HRD), and no germline *BRCA1/2* mutation (non-*gBRCA*). Drug costs were derived from 2016 average wholesale prices. Costs of laboratory tests, imaging, and physician visits were based on 2016 Medicare reimbursement rates. Median progression-free survival was based on published trials within the last year (SOLO2 for olaparib, ENGOT-OV16/NOVA for niraparib, and ARIEL3 for rucaparib). Incremental cost-effectiveness ratios (ICERs) per progression-free life-year saved (PF-LYS) were calculated. A sensitivity analysis was performed to estimate the cost at which each PARP inhibitor would be cost-effective in patients with germline *BRCA1/2* mutations.

Results: Maintenance olaparib in *gBRCA* has an ICER of \$231,567 per PF-LYS. For niraparib, the ICER of \$244,322 per PF-LYS in *gBRCA* is lower than the ICER of \$304,775 in non-*gBRCA*. For rucaparib, the ICER of \$248,992 in *gBRCA* is slightly less than the ICER of \$278,552 in patients with HRD. To put these costs into perspective, the ICER for bevacizumab maintenance therapy is \$531,151 per PF-LYS based on the OCEANS trial. In a sensitivity analysis for the *gBRCA* group, the monthly cost of PARP inhibitors would need to be significantly lower (olaparib: \$5,872, niraparib: \$6,088, and rucaparib: \$5,563) in order to reach an ICER cut-off of \$100,000 per PF-LYS. See Table 1.

While PARP inhibitors demonstrate clinical benefit as maintenance therapy for patients with platinum-sensitive recurrent EOC, they are not cost-effective at their current average wholesale prices based on a traditional ICER cutoff. In order for PARP inhibitors to become cost-effective maintenance therapies, the average wholesale costs would need to decrease by more than 50%.

Table 1.

	gBRCA		non-gBRCA		HRD	
	PFS difference (months)	ICER	PFS difference (months)	ICER	PFS difference (months)	ICER
Olaparib	13.6	\$231,567				
Niraparib	15.5	\$244,322	3.1	\$304,775	9.1	\$255,609
Rucaparib	11.2	\$248,992			8.2	\$278,552
Bevacizumab*			4.0	\$531,151		

*The results for bevacizumab maintenance therapy reflect all EOC patients because the PFS for bevacizumab maintenance therapy has not been stratified based on gBRCA or HRD status.

Sunrise Seminar I: Population Health Strategies

Sunday, March 25, 2018

Course Director: Rachel Clark, MD, *Massachusetts General Hospital, Boston, MA*

17 - Sunrise Seminar

Utilizing the patient-reported outcomes measurement information system (PROMIS) to improve referral to ancillary support services for severely symptomatic patients with gynecologic cancer

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Objective: The Patient-Reported Outcomes Measurement Information System (PROMIS) Network has developed a comprehensive repository of electronic patient-reported outcomes measures (ePROs) of major symptom domains that have been extensively validated in cancer patients. Their use for patients with gynecologic cancer has been understudied. Our objective was to establish feasibility and acceptability of PROMIS ePRO integration in a gynecologic oncology outpatient clinic and assess whether it can help identify severely symptomatic patients and improve referral to supportive services.

Method: English-speaking patients with a confirmed history of gynecologic cancer completed PROMIS ePROs on iPads in the waiting area of an outpatient gynecologic oncology clinic. Using the Assessment Center Scoring ServiceSM, we calculated T-scores in real time for each respondent and grouped respondents using documented severity thresholds. Response data were compared with clinicopathologic characteristics across symptom domains. Severely symptomatic patients were offered referral to ancillary services and asked to complete postexposure surveys assessing acceptability of the ePRO.

Results: A total of 336 patients with uterine (59.2%), ovarian (22.6%), cervical (14.3%), and vaginal (1.2%) or vulvar cancer (2.7%) completed ePROs. Thirty-five percent of the cohort had active disease at the time of their participation, and 19.4% had experienced at least 1 cancer recurrence. A large proportion of patients demonstrated moderate to severe physical dysfunction (59.9%), pain interference (36.1%), fatigue (27.7%), anxiety (8.8%), depression (7.6%), and sexual dysfunction (31.5%). Thirty-nine (11.6%) severely symptomatic patients were identified, resulting in 67 referrals to services such as psychiatry, palliative care, pain management, social work, or Bronx Oncology Living Daily (BOLD), an integrative oncology support program at Albert Einstein College of Medicine (Figure 1). Most survey respondents identified the ePROs as helpful (77.8%) and easy to complete (91.7%).

Conclusion: Outpatient PROMIS ePRO administration is feasible and acceptable to gynecologic oncology patients and can help identify severely symptomatic patients for referral to ancillary support services.

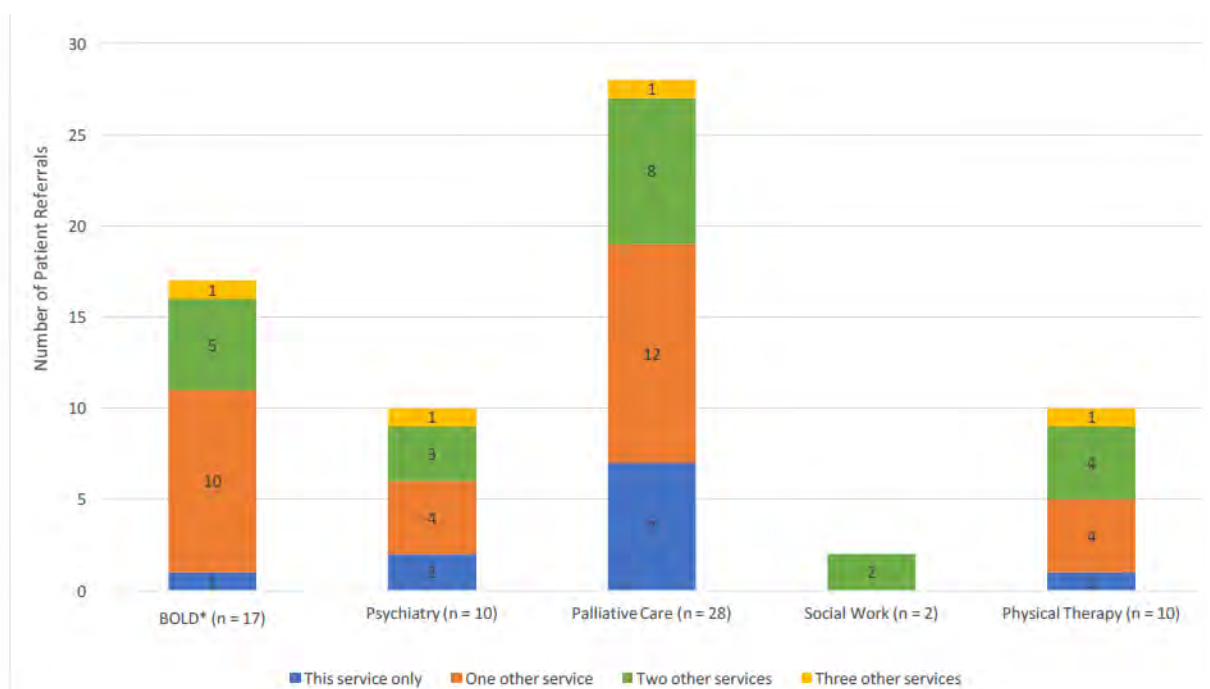


Fig. 1. Ancillary services to which patients were referred through PROMIS ePRO identification of severe cancer symptomology. Patients in blue categories were referred only to the service in the column in which they are included. Patients in orange, green and yellow categories were referred to one, two or three other ancillary services respectively. * Bronx Oncology Living Daily

Scientific Plenary III: PARP-pourri

Sunday, March 25, 2018

Moderators: Lori Cory, MD, *University of Pennsylvania, Philadelphia, PA, USA*

Lejla Delic, MD, *California Pacific & Palo Alto Medical Foundation/Sutter Research Institute, San Francisco, CA, USA*

18 - Scientific Plenary

PARP 7 has a significant role in overall survival of patients with ovarian cancer

L.H. Palavalli Parsons and J.S. Lea. *The University of Texas Southwestern Medical Center, Dallas, TX, USA*

Objective: Poly(ADP-ribose) polymerase (PARP) inhibitors are a recent advancement in ovarian cancer. PARP 7 is shown to approach genome-wide significance in association of ovarian cancer. This study characterizes PARP 7 with ovarian cancer.

Method: Using the The Cancer Genome Atlas (TCGA) database, PARP 7 was analyzed in high-grade ovarian cancer. Then an analog-sensitive PARP 7 protein was made to specifically discover the proteomics of PARP 7 in relationship to ovarian cancer. In order to identify the proteins that PARP 7 interacts with, a mutant PARP 7 (analog) was created to bind with a fluorophore attached to NAD⁺, the substrate of PARP 7. Ten different mutants of PARP 7 were created. These mutants were then placed in a viral expression system to infect insect cells to express PARP 7 protein. The proteins were then purified. The mutant that interacted with analog NAD⁺ most prominently then was used to perform a large-scale reaction with OVCAR 4 (immortalized ovarian cancer cell line) lysate, and specific proteins were identified by mass spectrometry.

Results: The TCGA database showed that there was a significant difference in overall survival (OS) in ovarian cancer patients if there were any genetic alterations within PARP 7. Patients with PARP 7 genetic alterations had a median OS of 44.8 months versus 15.7 months for those with no genetic alterations ($P = 0.0008$). The expression level of PARP 7 was significantly increased if ovarian cancer patients had genetic alterations in PARP 7, rather than no genetic alterations (95% CI 49.65–535.2, $P = 0.02$). Patients who were platinum-resistant and had no alterations versus alterations had OS and PARP 7 expression level of 3.3 months and 620.5 RSEM versus 11.7 months and 825.6 RSEM, respectively. Patients who were platinum-sensitive and had no alterations versus alterations had OS and PARP 7 expression level of 14.7 months and 783.3 RSEM versus 36 months and 981.4 RSEM, respectively. An analog PARP 7 recombinant protein was cloned and purified and through mass spectrometry identified several extracellular matrix proteins as PARP 7's main targets (Figure 1).

Conclusion: PARP 7 has a significant role in ovarian cancer. When PARP 7 has genetic alterations and higher expression levels, patients with ovarian cancer have significantly improved overall survival. Identifying that PARP 7 modifies extracellular matrix protein helps understand the potential biology of PARP 7 significance to ovarian cancer.

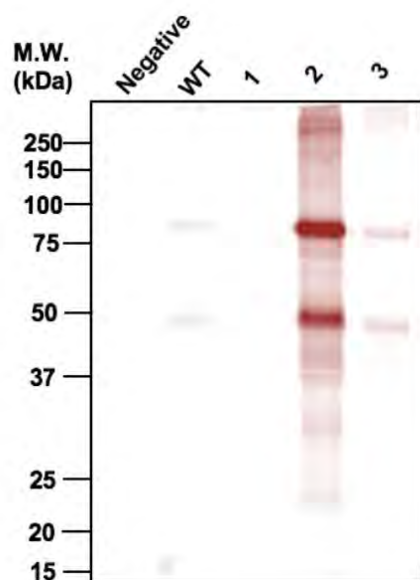


Fig. 1. Three of the most reactive analog sensitive PARP 7 recombinant purified proteins reacting with the analog NAD⁺. Lane 2 shows the best analog PARP 7 reaction. Each individual band in lane 2 identifies all the proteins that PARP 7 interacts with.

19 - Scientific Plenary

Bevacizumab, TKI, or PARPi? A targeted approach using composite value-based endpoints and biomarkers to individualize care for platinum-sensitive recurrent ovarian cancer (PSROC)

J.R. Foote^a, A. Alvarez-Secord^a, M.I. Liang^b, J.A. Ehrisman^a, D.E. Cohn^c, E. Jewell^d and L.J. Havrilesky^a. ^aDuke University Medical Center, Durham, NC, USA, ^bDavid Geffen School of Medicine at UCLA, Los Angeles, CA, USA, ^cThe Ohio State University, James Cancer Hospital, Columbus, OH, USA, ^dMemorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: Therapeutic options for women with PSROC who respond to reinduction platinum have expanded to include several treatment options. Clinical decisions regarding maintenance therapy need to be made prior to initiating chemotherapy. We assessed the clinical benefit of maintenance novel biologic therapies in the management of PSROC using the American Society of Clinical Oncology (ASCO) Net Health Benefit (NHB) and the European Society of Medical Oncology (ESMO) Magnitude of Clinical Benefit Scale (MCBS).

Method: The ASCO revised value framework NHBs and the ESMO-MCBS were constructed for key therapies based on randomized clinical trials involving maintenance therapies in PSROC. *BRCA*-germline/somatic mutations and HRD biomarker status were included. NHB calculations include clinical benefit (OS, PFS, or RR), toxicity, symptom palliation, treatment-free interval, and quality of life (QOL). MCBS grading includes clinical benefit, crossover, toxicity, QOL, and long-term PFS.

Results: ASCO-NHB calculations/ESMO-MCBS grades for VEGF inhibitors were (NHB/MCBS) as follows: maintenance cediranib (ICON6) = 13/2; maintenance pazopanib (AGO-OVAR16) = 16/1; and concurrent + maintenance bevacizumab (OCEANS = 35/2; GOG 213 = 26/2) (Figure 1). NHB and MCBS scores for PARPi were as follows: (1) in the setting of germline- and somatic-*BRCA* mutations: maintenance olaparib (SOLO2) = 47/4, maintenance niraparib (NOVA) = 50/4, and maintenance rucaparib (ARIEL3) = 54/4; (2) homologous-recombination deficiency (HRD)-positive status: maintenance niraparib (NOVA) = 42/4 and maintenance rucaparib (ARIEL3) = 46/4, and (3) wildtype *BRCA*: maintenance niraparib (NOVA) = 36/3, maintenance rucaparib (ARIEL3) = 26/3, and maintenance olaparib (Study 19) = 33/2.

Conclusion: NHB scores and MCBS grades were highest in women with germline- or somatic-*BRCA* mutations or tumor HRD positivity treated with maintenance PARPi. Nonbiomarker-based PARPi had similar ASCO-NHB to bevacizumab, although higher ESMO-MCBS grades due to continued improved PFS at 1 year. The two clinical benefit scoring systems examined are

generally consistent and may help to inform patients about the harm–benefit balance of available maintenance regimens for PSROC.

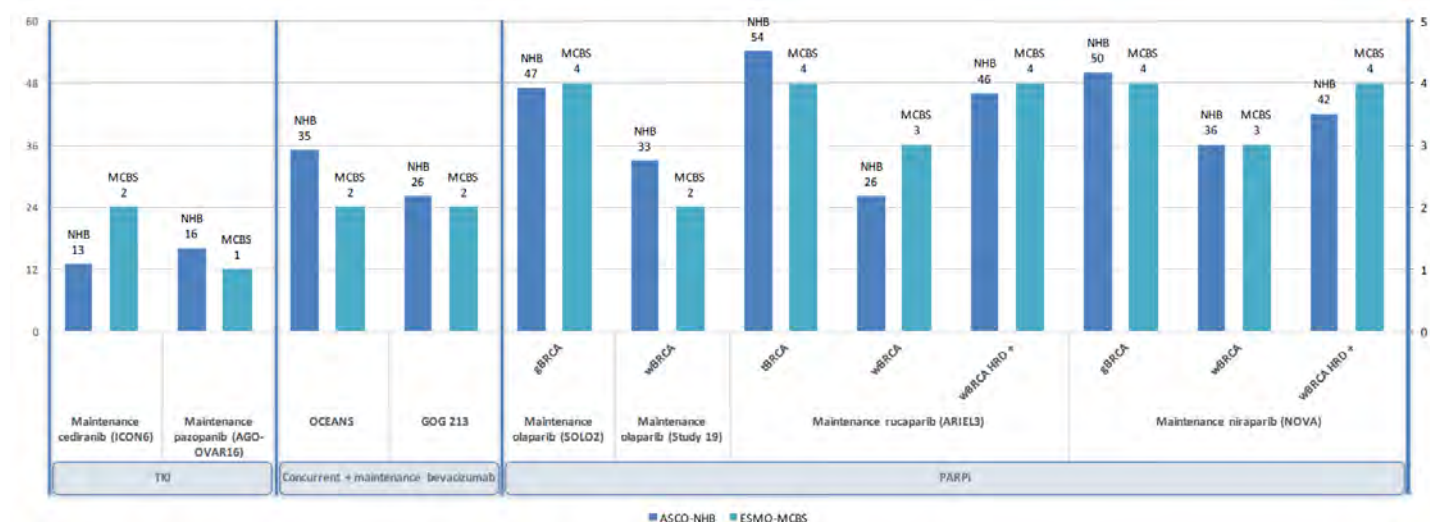


Fig. 1.

20 - Scientific Plenary

Safety and dose modification for patients with low body weight receiving niraparib in the ENGOT-OV16/NOVA phase III trial

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Objective: Niraparib is a poly(ADP-ribose) polymerase (PARP) inhibitor approved for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. This study is a retrospective analysis of patients enrolled in the phase 3 ENGOT-OV16/NOVA trial to determine the impact of body weight on incidence of grade 3/4 treatment-emergent adverse events (TEAEs) and the need for dose reduction.

Method: The ENGOT-OV16/NOVA trial enrolled patients with recurrent ovarian cancer who were in complete or partial response to their last platinum-based therapy. Weight categories were based on quartiles, with the lowest quartile (<58 kg) compared to the highest quartile (≥77 kg). Assessments included demographics, TEAEs, and dose interruptions, reductions, and discontinuations. To further explore a potential relationship between body weight and TEAEs, the correlation between incidence of grade ≥3 thrombocytopenia and baseline body weight was evaluated.

Results: Of the 367 patients randomized to receive niraparib, 87 had baseline body weight <58 kg, and 94 had baseline body weight ≥77 kg. Patients <58 kg had greater incidence than patients ≥77 kg of grade ≥3 TEAEs (83.9% vs 67.0%) and TEAEs leading to dose reduction (79.3% vs 58.5%) or treatment discontinuation (24.1% vs 9.6%). After the first 3 treatment cycles, 13% of patients with a baseline body weight <58 kg remained on a starting dose of 300 mg, compared with 37% of patients ≥77 kg. The incidence of grade ≥3 thrombocytopenia in the first 30 days was 43% in patients <58 kg compared with an incidence of 14% in patients ≥77 kg.

Conclusion: These results suggest that patient body weight should be considered when initiating niraparib. An alternative starting dose of 200 mg niraparib may be considered for frail patients.

21 - Scientific Plenary

Are FDA-approved PARPi cost-effective as maintenance treatment of platinum-sensitive recurrent ovarian cancer?

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Objective: Although the FDA has approved PARP inhibitors (PARPi) for maintenance treatment (MT) of platinum-sensitive recurrent ovarian cancer (PSROC) regardless of genetic mutation, cost-effectiveness remains a concern. We aim to determine whether global use of the PARPi niraparib is cost-effective compared to germline *BRCA* or tumor homologous recombination deficiency (HRD) testing with selective treatment.

Method: A decision analysis compared 4 strategies for MT: (1) observe all; (2) treat all with niraparib to progression; (3) *BRCA* germline mutation testing and selective treatment of carriers; and (4) *BRCA* germline and tumor HRD testing and selective treatment of both *BRCA* carriers and those with HRD + tumors. Costs were estimated in 2016 U.S. dollars and included tumor testing, drug, surveillance, and adverse events. We assumed prior germline *BRCA* testing. Outcomes were derived from the ENGOT-0V16/NOVA trial. Incremental cost-effectiveness ratios (ICERs) were in dollars per progression-free quality-adjusted life-year (PF-QALY). One-way sensitivity analysis tested the cost of niraparib.

Results: MT niraparib was costlier and more effective than observation. Mean costs and median PF-QALY were \$827 and 3.5 months for observation, \$44,221 and 5.8 for germline testing/restrictive treatment, \$105,933 and 8.5 for germline and HRD testing/restrictive treatment, and \$165,703 and 9.4 for treat all. Germline testing/selective treatment had an ICER of \$225,919/PF-QALY compared to observation alone; the other strategies did not approach cost-effectiveness. Necessary reductions in the 100-mg capsule cost of niraparib (\$175) to render each strategy potentially cost-effective compared to observation at a willingness to pay of \$100,000/PF-QALY are as follows: \$77 (germline testing), \$67 (germline and HRD testing), and \$47 (treat all). Assuming 5,570 cases of platinum-sensitive recurrence in the United States, the annual cost to the U.S. health system of treating all compared to a selective treatment strategy is at least \$332 million (Table 1).

Conclusion: Use of the PARPi niraparib as MT for PSROC is not cost-effective. Treatment of patients with *BRCA* germline mutation alone or with HRD + tumors are preferred strategies compared to global treatment. Lowering the per-capsule cost of drug by at least 56% may make selective niraparib MT potentially cost-effective compared to observation.

Table 1. Costs and outcomes related to selected strategies for platinum-sensitive recurrent ovarian cancer.

Strategy	Cost/patient (\$)	PF-QALY Benefit/patient (years)	Incremental cost-effectiveness ratio (\$/PF-QALY)*	Additional annual cost to US health system (\$)
Observation	\$827	0.29	--	--
gBRCA testing/selective treatment	\$44,221	0.48	\$225,919/PF-QALY	\$ 246 million
gBRCA testing + HRD testing/selective treatment	\$105,933	0.71	\$262,463/PF-QALY	\$ 590 million
Treat all	\$165,703	0.74	\$2,377,992/ PF-QALY	\$ 922 million

*All ICERs refer to a comparison to the next less effective strategy in Table.

Scientific Plenary IV: Current Trials, Emerging Targets

Sunday, March 25, 2018

Moderators: David cantu de León, MD, *Instituto Nacional de Cancerología of Mexico, Tlalpan, Mexico*

Victoria L. Bae-Jump, MD, PhD, *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

22 - Scientific Plenary

Randomized phase II trial of carboplatin-paclitaxel compared to carboplatin-paclitaxel-trastuzumab in advanced or recurrent uterine serous carcinomas that overexpress Her2/neu (NCT01367002)

A.D. Santin^a and A.N. Fader^b. ^a*Yale University School of Medicine, New Haven, CT, USA*, ^b*Johns Hopkins School of Medicine, Baltimore, MD, USA*

Objective: Uterine serous carcinoma is a rare, aggressive variant of endometrial cancer. Trastuzumab is a humanized monoclonal antibody that targets Her2/neu, a receptor overexpressed in 30% of uterine serous carcinoma. This multicenter, randomized phase II trial compared carboplatin/paclitaxel with and without trastuzumab in patients with advanced or recurrent uterine serous carcinoma who overexpress Her2/neu.

Method: Eligible patients had primary stage III–IV or recurrent, HER2/neu-positive disease. Participants were randomized to receive carboplatin/paclitaxel (control arm) for 6 cycles with or without intravenous trastuzumab (experimental arm) until progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS), which was assessed for differences between treatment arms via 1-sided log rank tests.

Results: From August 2011 to March 2017, 61 patients were randomized. Forty PFS-related events occurred among 58 evaluable subjects. Among all patients, median PFS was 8.0 months (control) versus 12.6 months (experimental, $P = 0.005$, HR = 0.44, 90% CI 0.26–0.76). Similarly, median PFS was 9.3 (control) versus 17.9 (experimental) months among 41 stage III–IV patients undergoing primary treatment ($P = 0.013$, HR = 0.40, 90% CI 0.20–0.80) and 6.0 (control) versus 9.2 months (experimental), respectively, among 17 patients with recurrent disease ($P = 0.003$, HR = 0.14, 90% CI 0.04–0.53). Toxicity was not different between treatment arms, and no unexpected safety signals emerged.

Conclusion: Addition of trastuzumab to carboplatin-paclitaxel was well-tolerated and increased PFS. This regimen may come to represent the new standard of care for women with advanced or recurrent uterine serous carcinoma who overexpress Her2/neu.

23 - Scientific Plenary

Predictive biomarkers of endometrial cancer response: Results from NRG Oncology/Gynecologic Oncology Group study 86P

D.A. Levine^a, D.S. Dizon^b, J.W. Carlson^c, V.L. Filiaci^d, M.A. Powell^e, A.A. Secord^f, K.S. Tewari^g, D.P. Bender^h, D.M. O'Malleyⁱ, A.R. Stuckey^j, K.N. Moore^k, S.B. Dewdney^l, J. Gao^m, F. Dao^a, R.A. Soslow^m, H.A. Lankes^d and C.A. Aghajanianⁿ. ^a*NYU Langone Health, New York, NY, USA*, ^b*Massachusetts General Hospital Cancer Center, Boston, MA, USA*, ^c*Mercy Clinic - Women's Oncology, Springfield, MO, USA*, ^d*Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA*, ^e*Washington University School of Medicine in St. Louis, St. Louis, MO, USA*, ^f*Duke Cancer Institute, Durham, NC, USA*, ^g*University of California Irvine Medical Center, Orange, CA, USA*, ^h*University of Iowa Hospitals and Clinics, Iowa City, IA, USA*, ⁱ*The Ohio State University, James Cancer Hospital, Columbus, OH, USA*, ^j*Women & Infants Hospital, Brown University, Providence, RI, USA*, ^k*The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA*, ^l*Rush University Medical Center, Chicago, IL, USA*, ^m*Memorial Sloan Kettering Cancer Center, New York, NY, USA*, ⁿ*Weill Cornell Medical College, New York, NY, USA*

Objectives: Endometrial carcinoma has many somatic mutations with potential therapeutic actionability. We correlated somatic mutations with clinical response to novel agents in advanced and recurrent endometrial cancers as part of the NRG/GOG randomized phase II trial 86P.

Methods: Paclitaxel and carboplatin (PC) plus bevacizumab, PC plus temsirolimus, or ixabepilone and carboplatin plus bevacizumab were randomly assigned to 349 patients with chemotherapy naïve advanced stage or recurrent endometrial cancer. Archival normal and tumor tissue were collected from 282 patients for next generation DNA sequencing to a mean depth of 600X. Somatic mutations in genes commonly mutated in endometrial cancer were explored for association with progression free survival (PFS) by treatment arm. Hazard ratios with confidence intervals are reported.

Results: *TSC2* somatic mutations were identified in 14 (5.8%) of 243 patients with sufficient material for sequencing. Among temsirolimus-treated patients, *TSC2* mutations were restricted to endometrioid histology and associated with an improved PFS (HR = 0.11, 95%CI: 0.02 – 0.82), but not among patients who did not receive temsirolimus (HR = 1.34, 95%CI: 0.65 – 2.74). Mutations in *CTNNB1*, which encodes the dual function protein β -catenin, were identified in 64 (26%) patients; 94% were in the canonical exon 3 region. Most patients (95%) with *CTNNB1* mutated tumors had endometrioid histology. Patients with *CTNNB1* mutated tumors treated on either of the bevacizumab arms had longer PFS compared to patients without mutations

that received bevacizumab (HR = 0.73, 95%CI: 0.60 – 0.91, Figure). *CTNNB1* mutation was not associated with PFS in patients who did not receive bevacizumab (HR = 1.06, 95%CI: 0.81 – 1.40).

Conclusions: The data suggest that *TSC2* and *CTNNB1* mutations may be predictive biomarkers associated with response to novel agents in advanced and recurrent endometrial cancer. Loss of function *TSC2* mutations activate mTORC1 signaling which explains the response to the mTOR inhibitor, temsirolimus. *CTNNB1* mutations can lead to activation of VEGF that may explain the improved response in bevacizumab-treated patients. Further prospective validation in enriched populations treated with anti-angiogenesis therapy and/or PI3K/Akt/mTOR pathway blockade is reasonable.

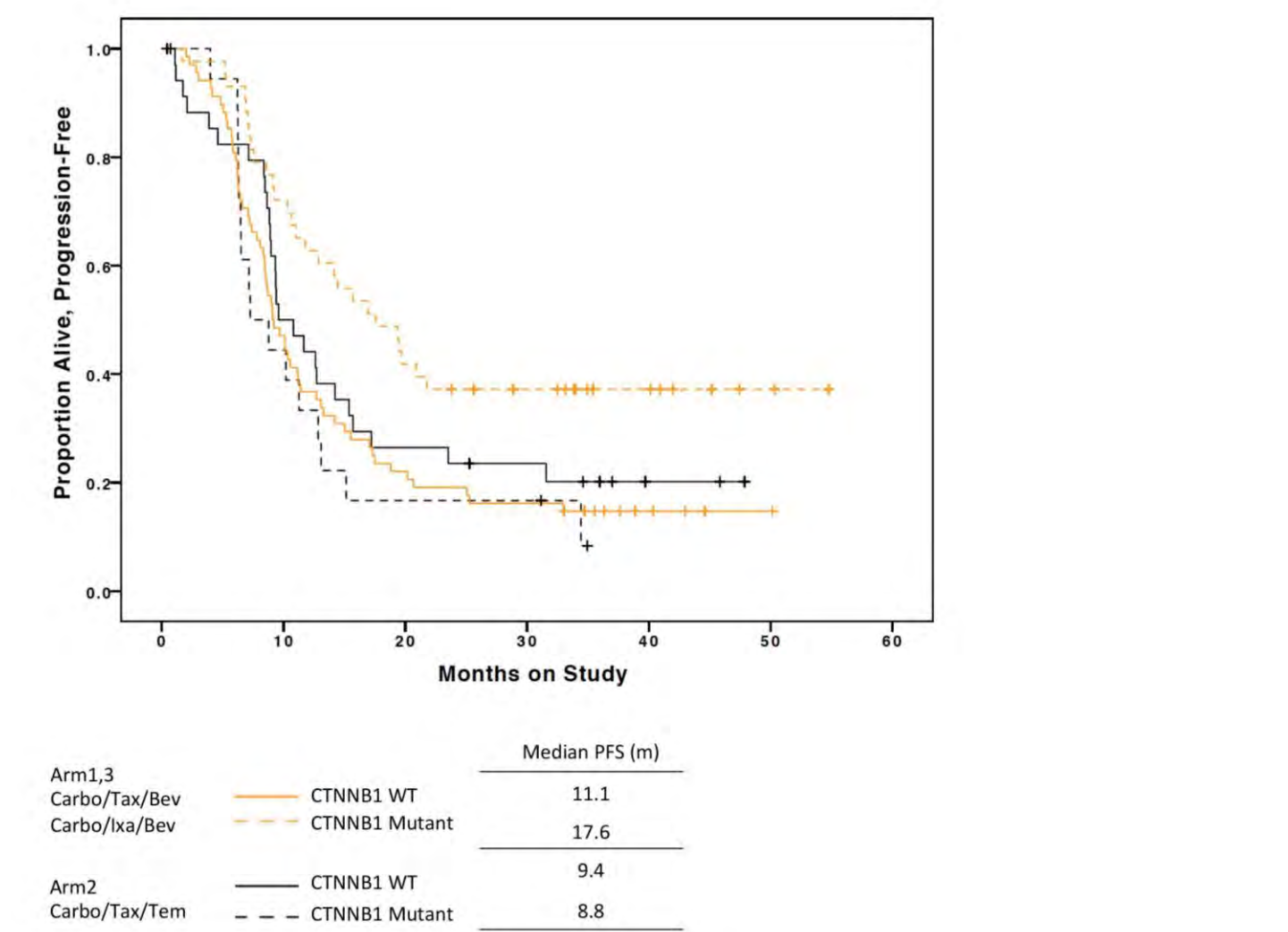


Fig. 1. PFS Kaplan Meier Plot for *CTNNB1* mutations and bevacizumab treatment.

24 - Scientific Plenary

IAP antagonism enhances anti-tumor activity of docetaxel or panobinostat in ovarian cancer cell lines

K.P. Zeligs^a, F. Ning^b, L. Hernandez^c, T. Smyth^d, G. Ward^d and C.M. Annunziata^c. ^aWalter Reed National Military Medical Center, Bethesda, MD, USA, ^bNational Institutes of Health, Bethesda, MD, USA, ^cNational Cancer Institute, Bethesda, MD, USA, ^dAstex Pharmaceuticals, Cambridge, United Kingdom

Objective: The growing clinical challenge of chemotherapy resistance in ovarian cancer has expanded investigation for new treatment modalities. Inhibitors of apoptosis proteins (IAPs) are key regulators of cancer cell viability. Antagonizing IAPs can induce cell death in cancer cell lines, and multiple IAP antagonists have advanced to clinical trials including birinapant, a SMAC-mimetic, selective antagonist of cellular IAP (cIAP), and ASTX660, a nonpeptidomimetic dual antagonist of cIAP1 and X-linked IAP (XIAP). In this study we assessed the ability of birinapant and ASTX660 to increase the anticancer activity of either chemotherapy or a targeted agent in vitro and in vivo.

Method: In vitro single-agent birinapant and ASTX660 proliferation inhibition was characterized in 10 established ovarian cancer cell lines (OVCAR8, CAOV3, SKOV3, OVCAR3, OVCAR4, OVCAR5, PEO1, PEO4, CAOV4, and OV90) using XTT viability assays. A matrix drug screen with birinapant previously identified synergy in combination with taxanes or HDAC inhibitors. Cell viability assays were repeated in 4 ovarian cancer cell lines upon exposure to birinapant or ASTX660 alone and in combination with docetaxel or panobinostat, an HDAC inhibitor. Combination indices were computed using Compusyn. In vivo effects of these agents alone or in combination were assessed using OVCAR8 subcutaneous xenograft mouse model.

Results: Synergism was identified using combinations of either IAP antagonist with docetaxel or panobinostat on in vitro analyses. In vivo, ASTX660 slowed tumor growth in OVCAR8 xenografts, which was significantly enhanced when used in combination with docetaxel (with a 57% reduction in tumor burden) or panobinostat (46%). See Figure 1.

Conclusion: Combination treatment with IAP antagonists has potential to overcome drug resistance and improve outcome of patients with ovarian cancer. The synergism identified both in vitro and in vivo with the experimental agents in combination with docetaxel warrants consideration for phase I clinical trial in patients with chemo-refractory ovarian cancer.

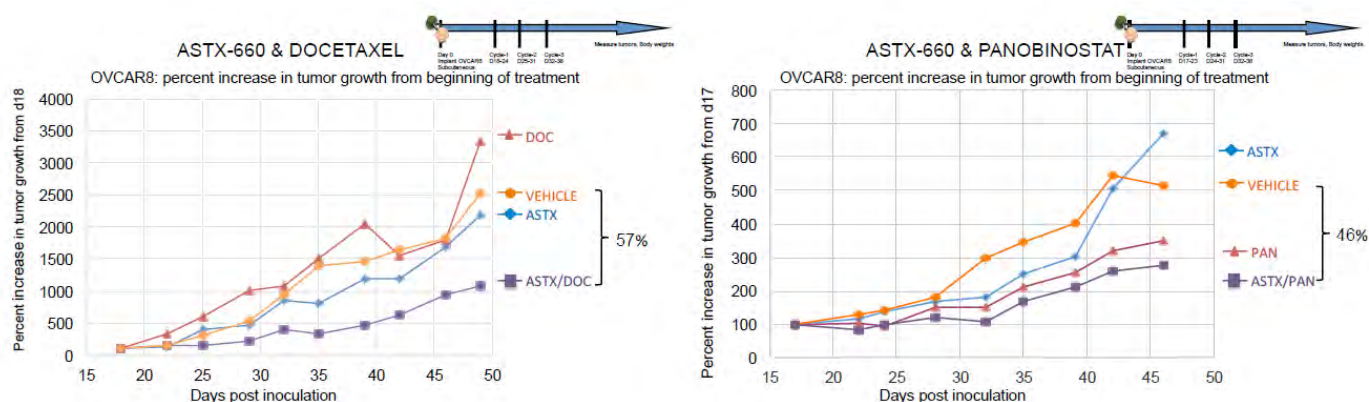


Fig. 1. In vivo results from OVCAR8 subcutaneous xenograft mouse models. Tumor growth was markedly slowed when ASTX660 was used in combination with docetaxel (with a 57% reduction in tumor burden when compared to the control) or panobinostat (46%).

25 - Scientific Plenary

Development of a high-affinity anti-galectin-3 antibody targeting interactions between MUC16/CA-125 and galectin-3 to inhibit oncogenic properties in serous ovarian cancer

M. Stasenko^a, T.D. Rao^a, F. Weis-Garcia^a and D. Spriggs^b. ^aMemorial Sloan Kettering Cancer Center, New York, NY, USA, ^bMemorial Sloan-Kettering Cancer Center, New York, NY, USA

Objective: MUC16/CA-125 is a transmembrane mucin that drives oncogenic behavior. Its extracellular membrane domain interacts with the lectin, galectin-3 (Gal-3), and through this interaction initiates a signal cascade leading to cancer cell invasion and growth. We aim to interrupt this interaction by a high-affinity anti-Gal-3 antibody directed at the carbohydrate recognition domain (CRD) of the Gal-3 carboxyl-terminus.

Method: Murine monoclonal antibodies (MAbs) were generated by creating hybridomas from mice immunized with recombinant human Gal-3 as well as a fusion protein of Gal-3 carboxyl-terminal domain fused to a human-IgG1-Fc backbone. The generated antibodies were confirmed to recognize the human Gal-3 CRD by enzyme-linked immunosorbent assay (ELISA) and surface plasmon resonance (SPR). Functional assays, including Matrigel invasion and laminin binding, were used to confirm MAb activity. Murine models of ovarian cancer were treated with purified MAb to determine MAb effects on tumor growth in vivo. Data were analyzed for statistical significance using paired *t* test.

Results: Initial screening yielded 2 candidate antibodies, of which 1 (14D11.2D2) had superior binding to Gal-3 by ELISA and SPR. The antibody dissociation constant was 14.6 nM by SPR. At a concentration of 150 nM, 14D11.2D2 decreased Gal-3 binding to laminin by 36.6% compared to untreated control. In a Matrigel invasion assay, the MAb significantly inhibited invasion by MUC16 expressing SKOV3 cells and by wildtype MUC16-positive OVCAR3 cells ($P = 0.004$ and $P = 0.003$, respectively). MUC16 expressing A2780 cells showed a statistically insignificant decrease in invasion ($P = 0.15$). The pilot

murine experiment with MUC16 expressing A2780 tumors showed a trend in decreased tumor growth in mice treated with MAb but did not reach statistical significance ($P = 0.32$) (Figure 1).

Conclusion: For the first time in reported literature, we have demonstrated that it is feasible to develop a high-affinity anti-Gal-3 MAb to inhibit MUC16-related cellular invasion and growth. This holds therapeutic potential for MUC16-dependent carcinomas like serous ovarian cancer. Future directions will include verifying our preliminary results with other cell lines in murine models and developing a humanized antibody for further study.

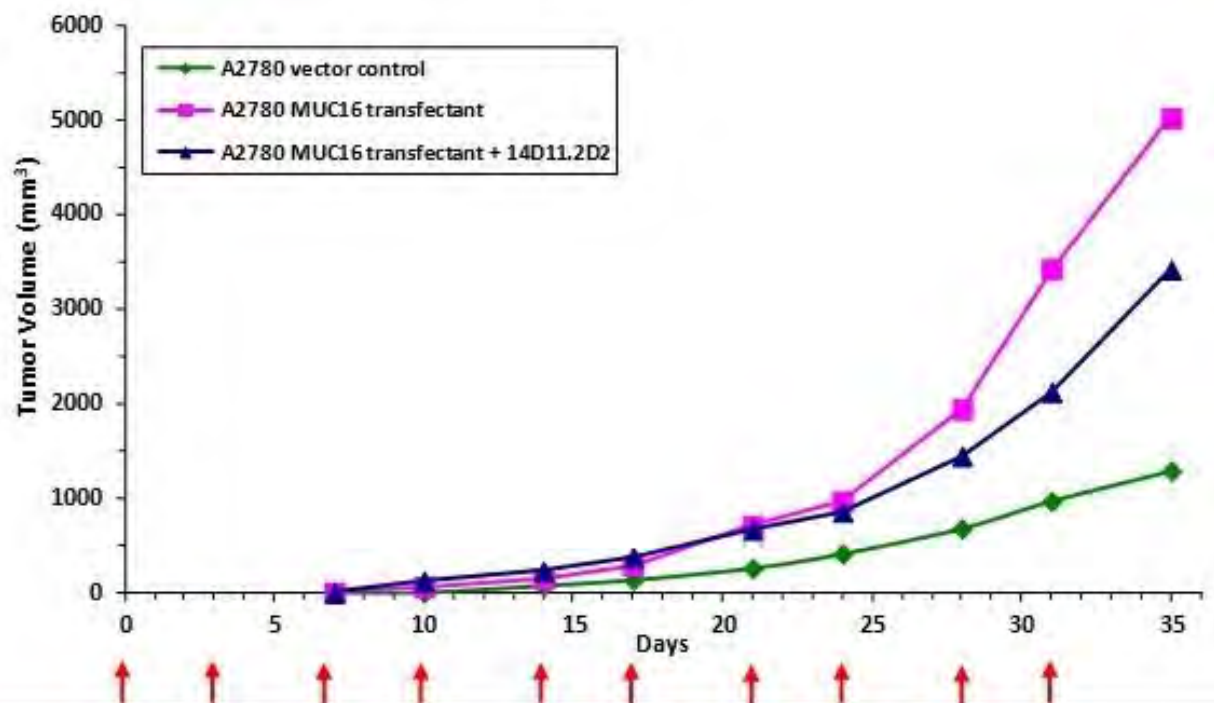


Fig. 1. A2780 transfectant tumor growth in athymic female nude mice. Treatment with 14D11.2D2 MAb led to decreased tumor growth in vivo. MUC16 expression by A2780 cells enhances tumor growth. Although not statistically significant, A2780 MUC16 expressing cell lines showed a decrease in aggressiveness when exposed to the MAb ($P = 0.32$ by paired t-test). Upward arrows denote timing of immunization with the MAb.

26 - Scientific Plenary

Targeting the TIE2 pathway with a novel small molecule vascular endothelial protein tyrosine phosphatase (VE-PTP) inhibitor in high-grade serous ovarian cancer

L.P. Cobb^a, A. Rickard^b, J. Herbert^b, G. Hanna^b, G. Palmer^b, S. Siamakpour-Reihani^b, Z. Huang^b, K. Peters^c, C. Kontos^b, A. Berchuck^d and A.A. Secord^e. ^aDuke University School of Medicine, Durham, NC, USA, ^bDuke University, Durham, NC, USA, ^cAerpio Therapeutics, Cincinnati, OH, USA, ^dDuke University Medical Center, Durham, NC, USA, ^eDuke Cancer Institute, Durham, NC, USA

Objective: We sought to build upon our prior research demonstrating that low TIE2 levels are associated with worse survival in women with high-grade serous ovarian cancer (HGSC) and investigate the effect of a novel activating TIE2 agent, AKB-9785, in a mouse model of HGSC. AKB-9785 represents a new therapeutic class that inhibits vascular endothelial protein tyrosine phosphatase (VE-PTP) and promotes vascular maturation, normalizes existing tumor vasculature, and delays tumor growth and metastases in breast cancer mouse models.

Method: CAOV2 ovarian cancer cells were injected into the flanks of female nude mice using 1×10^6 cells per mouse. Mice were randomized into 4 groups: control ($n = 7$), AKB-9785 alone (50 mg/kg subcutaneously twice daily, $n = 5$), paclitaxel alone (20 mg/kg intraperitoneally twice weekly, $n = 4$), and AKB-9785 + paclitaxel ($n = 4$). Tumor volumes were measured 3 times weekly and normalized to initial volume for comparison. One-way ANOVA analysis was used to analyze the difference in mean tumor volume across groups and individual post-hoc t tests were used to analyze the differences between groups. Survival data were assessed using a Kaplan-Meier survival estimate.

Results: Using one-way ANOVA analysis, in this study there was a significant difference in tumor volume among the groups ($P = 0.0008$). Single-agent paclitaxel did not demonstrate significant antitumor activity compared to the control group. However,

antitumor activity was demonstrated both with single-agent AKB-9785 ($P = 0.03$) and combination AKB-9785/paclitaxel ($P = 0.009$) compared to the control group. Animals treated with combination AKB-9785/paclitaxel also had longer survival compared to controls ($P = 0.002$). Median survival days for the groups were as follows: control = 58 days, AKB-9785 = 60 days, paclitaxel = 56 days, and AKB-9785/paclitaxel = undefined with more than 50% of subjects surviving until end of study. See Figure 1.

Conclusion: In this pilot study, we were able to demonstrate enhanced paclitaxel antitumor activity with the addition of AKB-9785 in a mouse model of taxane resistance. In view of the therapeutic potential for antiangiogenic agents and the negative implications of taxane resistance in ovarian cancer, this novel therapy is worthy of further investigation in larger scale studies.

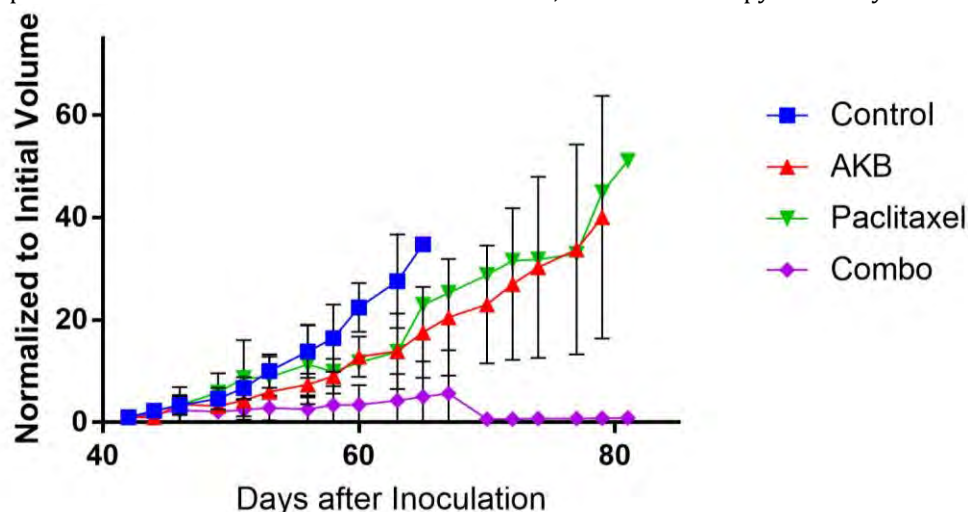


Fig. 1. Tumor Volumes (normalized).

Education Forum IV: Palliative Care

Sunday, March 25, 2018

Course Directors: Paula Lee, MD, *Duke Medical Center, Durham, NC*

Lisa Landrum, MD, *University of Oklahoma, Stephenson Cancer Center, Oklahoma City, OK*

27 - Education Forum

Trends in place of death among gynecologic cancer patients in the United States

K. Hicks-Courant^a, A. Melamed^b and J.A.A. Rauh-Hain^b. ^aTufts Medical Center, Boston, MA, USA, ^bMassachusetts General Hospital, Boston, MA, USA

Objective: Dying at home is associated with improved experiences for patients, families, and caregivers. Although most patients with advanced cancer prefer to die at home, it is not clear whether we are increasingly achieving this goal. This study examined changes over time in place of death among all women in the United States who died of gynecologic malignancies. It also compared trends in place of death between women who died of gynecologic malignancies and women who died from the other leading causes of female cancer deaths.

Method: Using national death certificate data from the Mortality Multiple Cause-of-Death Public Use Data Files, women who died from gynecologic, breast, lung, and colorectal cancers were identified according to ICD-10 cause of death from 2003 to 2015. Regression analyses with ordinary least-squares linear probability modeling were used to test for differences in location of death over time and for differences in trends by cancer type, while controlling for age, race, ethnicity, marital status, and education status.

Results: From 2003 to 2015, 2,144,477 women died from gynecologic (370,761), lung (909,045), breast (533,626), or colorectal (331,045) malignancies. In adjusted analyses, the rate of death at home/hospice among gynecologic cancer patients (49.2%) was significantly greater than those of lung (48.9%, $P = 0.001$), breast (46.8%, $P < 0.001$), and colorectal (48.7%, $P < 0.001$) cancer patients. In adjusted analyses, the trend in the percentage of deaths at home/hospice increased at a rate of 1.54 percentage points per year for gynecologic cancer patients, compared to 1.45 ($P = 0.001$), 1.42 ($P < 0.001$), and 1.49 ($P = 0.136$) percentage points per year for lung, breast, and colorectal cancer patients, respectively. See Figure 1.

Conclusion: Female cancer patients have been dying at home or in hospice at substantially increasing rates over the last 13 years on record. Gynecologic cancer patients are dying at home/hospice at marginally higher rates than female lung, breast, and colorectal cancer patients. Furthermore, the proportion of deaths at home/hospice is increasing over time at a slightly higher rate for gynecologic cancer patients compared to lung and breast cancer patients. Further research examining practice differences in end-of-life care among oncologic subspecialties is needed to better understand these differences.

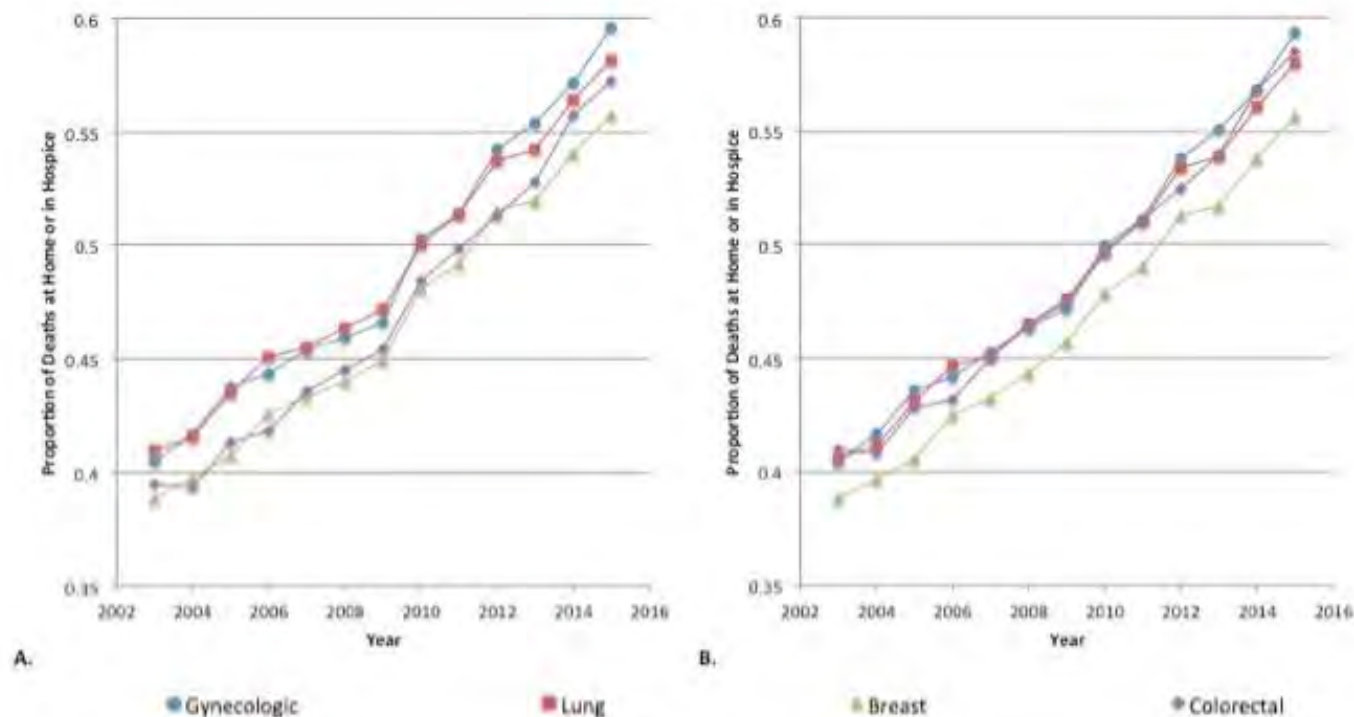


Fig. 1. Trends in the proportion of deaths at home or in hospice by cancer type. A. Unadjusted rates. B. Rates adjusted for age, race, Hispanic ethnicity, marital status, and education status.

Sunrise Seminar V: Health Care Economics

Monday, March 26, 2018

Course Director: Laura Havrilesky, MD, *Duke University Medical Center, Durham, NC*

28 - Sunrise Seminar

Indicated presurgical testing is a priority to achieve high-quality, cost-effective oncologic health care delivery

G.J. Gardner, H. Weiss, A. Klotz, S. Ogden, D. Boccamazzo, J. Hagerty-Paglia, N.R. Abu-Rustum, K. Sepkowitz, G. Fischer and J. Drebin. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objective: Excessive presurgical testing results in nonspecific findings requiring additional investigative testing, additional patient visits, increased radiation exposure, staff workload, and patient anxiety. Standardized guidelines for presurgical clearance are available in the general surgical and anesthesia literature. At a comprehensive cancer center, we sought to develop and implement testing guidelines specific to oncology patients and evaluate them for feasibility, safety, and cost.

Method: A multidisciplinary team was assembled to review the available literature and establish institutional algorithms specific to oncology patients. Implementation of the testing algorithms was activated January 2016 across 5 oncologic surgical teams: gynecology (GYN), urology (URO), head and neck (HN), breast (BRE), and plastics (PLA). Data collection from the preintervention period (PRE), January 2014 to April 2015, and postintervention period (POST), January 2016 to December 2016, was completed and abstracted for total number of presurgical tests performed, perioperative outcomes, and cost. Rates of postoperative cardiopulmonary events and bleeding PRE versus POST were compared using standard statistical tests. Cost analysis was performed for the actual direct cost savings achieved.

Results: A total of 5,754 surgical cases were completed with the testing algorithm including 636 GYN, 672 URO, 427 HN, 3,141 BRE, and 878 PLA cases. Compared to PRE, postalgorithm implementation reduced testing by 39.8% (PRE 9,812/9,832, 99.8%, vs POST 3,450/5,754, 60.0%) for CBCs; by 25.2% (PRE 9,438/9,832, 96.0%, vs POST 4,052/5,754, 70.4%) for EKG; 30.6% (PRE 9,256/9,832, 94.1%, vs POST 3,651/5,754, 63.5%) for basic metabolic panels (BMP); and by 58.5% (PRE 6,775/9,832, 68.9%, vs POST 601/5,754, 10.4%) for chest x-rays. There was no increase in postoperative cardiopulmonary events ($P = 0.44$) or bleeding ($P = 0.24$). Incremental direct cost savings achieved was \$246/case, or \$1.4 million/year.

Conclusion: Indicated presurgical testing reduces overttesting among oncology patients and maintains high-quality perioperative care and cost-effective healthcare delivery. Future work includes development of real-time service-level reporting tools to monitor ongoing compliance and outcomes, refinement for preoperative medical consultations, and expansion to additional surgical teams.

Focused Plenary I: Preclinical and Translational Medicine

Monday, March 26, 2018

Moderators: Michael J. Birrer, MD, PhD, *University of Alabama at Birmingham, Birmingham, AL, USA*

Sophia George, PhD, *University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA*

29 - Focused Plenary

Simvastatin has anti-tumorigenic effects in endometrial cancer via reversal of obesity-driven upregulation of lipid biosynthesis

L. West^a, L.H. Clark^a, S.R. Pierce^a, Y. Yin^a, Z. Fang^a, D. Lee^b, C. Zhou^a and V.L. Bae-Jump^a. ^a*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*, ^b*Omic Insight, LCC, Durham, NC, USA*

Objective: Obesity is associated with worse outcomes in endometrial cancer (EC). Comorbid conditions such as diabetes and hyperlipidemia often exist in the EC patient population. HMG-CoA inhibitors (statins) are known to reduce lipid levels and are commonly used to manage and prevent coronary artery disease. Epidemiologic evidence suggest that statins may decrease cancer risk and improve cancer outcomes, including EC. Thus, we sought to investigate the antitumorigenic potential of simvastatin in a genetically engineered mouse model of endometrioid EC (LKB1^{fl/fl}p53^{fl/fl} mouse model).

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

Results: HFD-fed mice (obese) were larger in body weight than those fed a LFD (lean) (30 g vs 25 g, $P < 0.0001$). This trend was consistent with obese and lean mice treated with simvastatin (28 g vs 24 g, $P = 0.02$). Simvastatin decreased tumor weight/size by 46% in the obese mice and 30% in the lean mice ($P < 0.05$). Metabolomic profiling revealed significant differences between obese and lean mice treated with simvastatin or placebo ($P < 0.05$). Lipid biosynthesis and peroxidation were dramatically upregulated in ECs from obese compared to those from lean mice. Treatment with simvastatin reversed the obesity-driven upregulation of lipid biosynthesis in the endometrial tumors, resulting in lipid degradation and oxidation.

Conclusion: Simvastatin inhibited tumor growth in an endometrioid EC mouse model, and its antitumorigenic effects aligned with obesity status via impacting lipid biosynthetic pathways. Given this, statins may be worthy of drug repurposing as an antitumorigenic agent in obesity-driven EC, and a phase 0 study of atorvastatin in EC is already underway.

30 - Focused Plenary

Overcoming platinum resistance in ovarian cancer by targeting pregnancy-associated plasma protein-a

D. Torres, X. Hou, L.K. Bale, E.P. Heinzen, M.J. Maurer, Q. Zhang, C.A. Conover and S.J. Weroha. *Mayo Clinic, Rochester, MN, USA*

Objective: Pregnancy-associated plasma protein-A (PAPP-A) promotes insulin-like growth factor (IGF) pathway activity, which directly correlates to ovarian cancer (OC) tumorigenesis. Because inhibition of PAPP-A with a novel monoclonal antibody to PAPP-A (mAb-PA) had preliminary activity in an OC patient-derived xenograft (PDX) model, we hypothesize that adding mAb-PA to carboplatin/paclitaxel (CP) would partially overcome platinum resistance in a panel of OC PDX.

Method: PAPP-A expression in 20 platinum-resistant PDX models was determined by ELISA and classified as high (top 50%) or low. Five high and 3 low PAPP-A tumors were revived IP in female SCID/beige mice for *in vivo* efficacy studies with saline, CP/mAb-PA, or CP/IgG2a. Weekly blinded ultrasounds documented tumor size for the primary endpoint: day 28 tumor area relative to baseline. A secondary endpoint was progression-free survival (PFS) in a subset of mice allowed to remain on study with maintenance therapy. Statistical analyses included linear mixed effects modeling and Kaplan Meier curves. Response to therapy was correlated with changes in levels of IGFBP-4 proteolysis (ELISA), IGFBP-5 gene expression (qPCR), and ratio of phosphorylated/total AKT and ERK (Western blot).

Results: The addition of mAb-PA to CP in PAPP-A high PDX models ($n = 5$) resulted in tumor regression below baseline in 2 models. Another 2 models did not regress but exhibited a trend toward tumor growth inhibition relative to CP alone ($P < 0.05$ and $P = 0.12$). None of the PAPP-A low PDX models ($n = 3$) regressed below baseline. The PDX model with the greatest magnitude of tumor regression from baseline after treatment with CP/mAb-PA was maintained on single agent mAb-PA or IgG2a; no PFS benefit was observed with maintenance mAb-PA. The therapeutic benefit observed from the addition of mAb-PA to CP did not correlate with putative biomarkers of IGF pathway down regulation. See Figure 1.

Conclusion: The addition of mAb-PA to CP induced platinum sensitivity or trended toward improved platinum response in 4 of 5 PAPP-A high OC PDX models. The *in vivo* efficacy described herein using clinically relevant OC PDX models provides preclinical data supporting further clinical development of this novel therapeutic strategy.

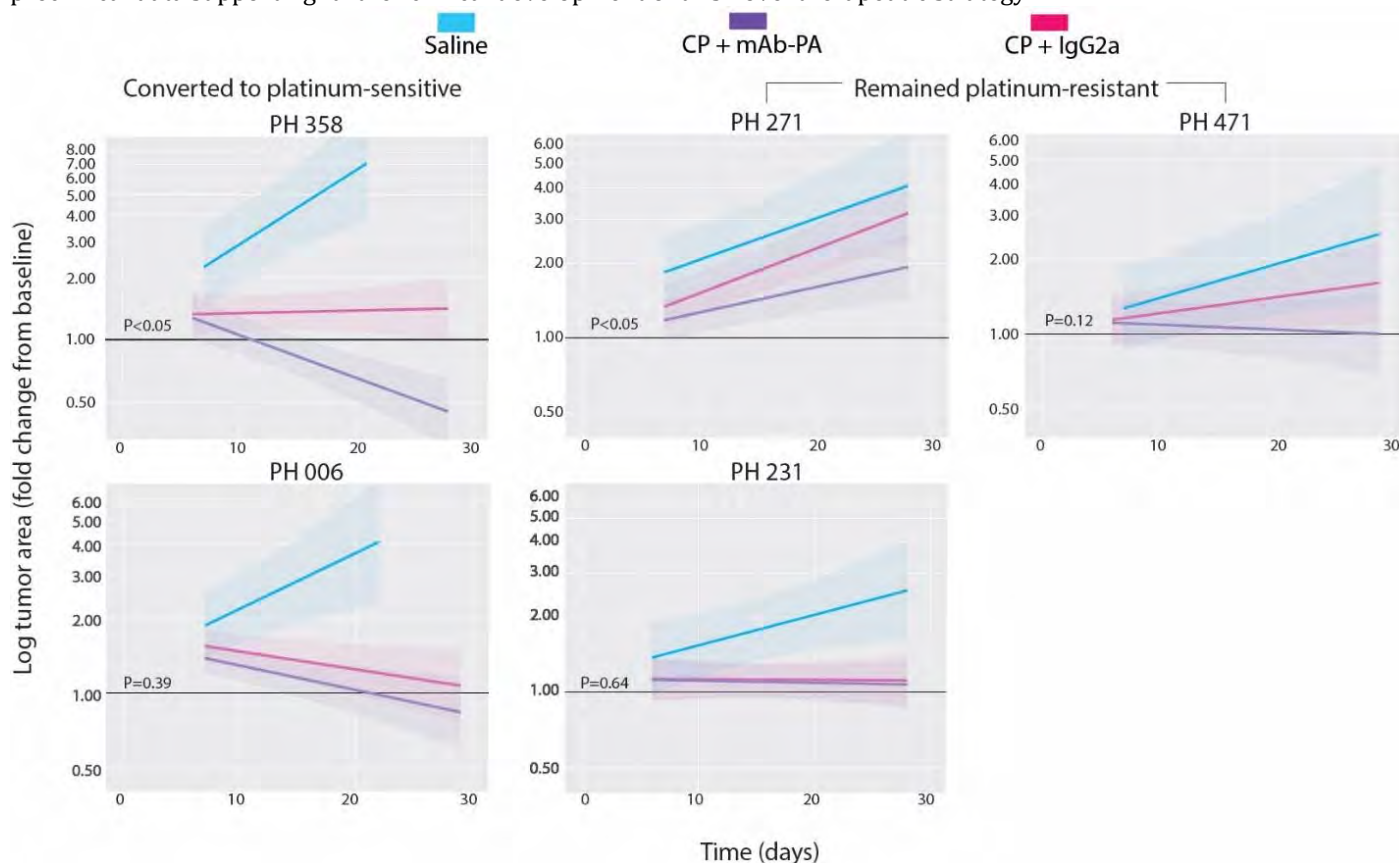


Fig. 1. High PAPP-A Models.

31 - Focused Plenary

Expression of dopamine receptor D2 in endometrial tumors and the impact of DRD2 blockade on cancer proliferation
 S.R. Pierce^a, M. Asher^a, Z. Fang^a, L. West^a, Y. Yin^a, V. Prabhu^b, C. Xu^a, C. Zhou^a and V.L. Bae-Jump^a. ^aUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, ^bOncocentics, Philadelphia, PA, USA

Objective: The imipridone ONC201 (Oncocentics), a dopamine receptor D2 (DRD2) antagonist, is already being explored in clinical trials for endometrial cancer (EC). To better understand the role of DRD2 in EC, we (1) evaluated DRD2 protein and gene expression in ECs, and (2) investigated the antitumorigenic effects of ONC201 in human EC cell lines.

Method: Women who underwent surgical staging for EC at our institution were identified, and a tissue microarray using triplicate cores was constructed from their formalin-fixed, paraffin-embedded hysterectomy specimens. DRD2 protein expression was assessed by immunohistochemistry (IHC). Using The Cancer Genome Atlas (TCGA) database, DRD2 gene expression was compared between the 4 EC subtypes: POLE, MSI, CNL and CNH. Endometrioid (ECC-1, KLE) and serous EC cell lines (Ark1, SPEC-2) were treated with varying concentrations of ONC201. Cell proliferation was assessed by MTT assay. Apoptosis was determined by Annexin V assay. ROS production was measured by DCFH-DA assay. Apoptosis and cellular stress related protein expression were evaluated by Western immunoblotting.

Results: Of the 118 ECs evaluated, increasing DRD2 protein expression was significantly associated with grade ($P = <0.0001$), serous histology ($P = <0.0001$), and stage ($P = <0.0001$), as well as worse OS ($P = 0.02$) and PFS ($P = 0.049$). DRD2 gene expression was higher in CNH ECs when compared to all other subtypes ($P = 0.005$). ONC201 inhibited cell proliferation in a dose-dependent manner in all cell lines after 72 hours of treatment ($IC_{50} = 5\text{--}250\text{ }\mu\text{M}$). ONC201 increased annexin V expression in all cell lines ($P < 0.05$), but appeared to be more potent in serous (35%–38%) versus endometrioid cells (13%–23%). In addition, ONC201 decreased expression of the antiapoptotic proteins Mcl-1, Bcl-2, and Bcl-XL. Last, ONC201 induced ROS production and increased expression of Bip, PERK, and PDI in all cell lines.

Conclusions: DRD2 was more highly expressed in aggressive EC types (CNH, serous histology) and was associated with grade, stage, and worse OS and PFS. DRD2 antagonism with ONC201 potentially inhibited cell proliferation in EC cell lines through induction of apoptosis and increased cellular stress. ONC201 may be a novel targeted agent for EC, particularly in more aggressive EC types for which effective treatments are limited.

32 - Focused Plenary

Stromal cell expression of the receptor tyrosine kinase DDR2 promotes ovarian cancer metastasis

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Objective: To understand the role of stromal discoid domain receptor 2 (DDR2) expression in ovarian cancer metastasis.

Method: Immunohistochemistry was performed using high-grade serous ovarian cancer tumors through the Washington University Gynecologic Oncology Tissue bank. Stromal and tumor cell expression of DDR2 was scored for intensity and frequency. To determine the effect of metastasis with DDR2-deficient stromal cells, global DDR2 knockout (KO) mice (DDR2-deficient) were compared to DDR2 wildtype (WT) mice (DDR2-expressing) when a DDR2-expressing murine tumor cell line (ID8Trp53-/-BRCA2-/-) was injected intraperitoneally. Intraperitoneal spread was quantified using bioluminescence imaging (BLI) and tumor weight. In addition, cell-based mesothelial cell clearance assays utilizing human omentum-cultured mesothelial cells expressing DDR2 were compared to mesothelial cells not expressing DDR2.

Results: IHC tissue specimens were divided into two survival groups: survival of <3 years and >5 years. Patients who lived <3 years had significantly higher DDR2 expression in the stroma when compared to patients living >5 years (mean DDR2 IHC score 76% vs 48%, $P < 0.0001$). Similar findings were observed for DDR2 expression in the tumor cells, with mean IHC score 80% vs 64%, $P < 0.0001$ in patients who lived <3 years vs >5 years. For the metastasis mouse model, DDR2 KO mice (DDR2 deficient in stromal cells) had less intraperitoneal spread of ovarian cancer cells than DDR2 WT by BLI (mean 5.8×10^8 vs 2.2×10^9 total photon flux, $P = 0.01$). Furthermore, we confirmed these findings with DDR2 WT mice having more tumor implants >1 mm (mean 6 vs 2 nodules, $P = 0.006$). In addition, human ovarian cancer cells plated above mesothelial cells that were DDR2-deficient had less tumor cell clearance than those tumor cells plated above mesothelial cells that expressed DDR2 ($P = 0.01$).

Conclusion: The stromal contribution of DDR2 promotes tumor cell clearance of mesothelial cells and metastatic spread. This suggests that stromal expression of DDR2 may be a potential target to guide future therapy, particularly in the maintenance setting.

Focused Plenary II: Reducing Cost and Pain

Monday, March 26, 2018

Moderators: Sean C. Dowdy, MD, *Mayo Clinic, Rochester, MN, USA*

Jose Alejandro Rauh-Hain, MD, *Massachusetts General Hospital, Boston, MA, USA*

33 - Focused Plenary

Can the ASCO alternative payment model achieve cost savings in ovarian cancer care?

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Objective: Efforts to curb the rising the costs of health care include the development of alternative payment models (APM), which provide physician practices with additional payments to reduce avoidable spending through improved care coordination. However, the ability of these payment models to reduce real-world costs requires further evaluation. The objective of this study is to evaluate and compare the American Society of Clinical Oncology's Patient Centered Oncology Payment (PCOP) model to the existing fee-for-service (FFS) payment methodology to empirically evaluate the impact of APMs on cost savings.

Method: Using linked SEER-Medicare data, we identified a cohort of women with stage III–IV epithelial ovarian cancer diagnosed between 2000 and 2012 who received primary debulking surgery (PDS) and adjuvant (ACT) or neoadjuvant chemotherapy (NACT). Total direct medical costs were calculated from Medicare claims files. Treatment and surveillance months were defined based on chemotherapy claims. We constructed a model to compare FFS versus PCOP, which would provide approximately \$2,600 per ovarian cancer patient in additional physician practice payments, to estimate cost savings across a range of plausible values for emergency room visits, hospitalizations, and imaging.

Results: A total of 4,643 women met the study criteria: 3,777 underwent PDS followed by ACT and 866 received NACT. The mean cost of chemotherapy and surveillance was \$71,763 in the PDS cohort compared to \$90,058 in the NACT cohort. In both cohorts, the majority of costs were related to chemotherapy or hospitalization. Patients in each cohort had similar numbers of hospitalizations (PDS, 62%; NACT, 60%). PCOP would be cost-saving compared to the status quo payment schedule, with an absolute drop of 8% in hospitalizations, to rates of 54% and 52% in PDS and NACT, respectively. Because of their lower associated costs, varying the probability of emergency room visits or imaging alone did not have an impact on overall costs.

Conclusion: APMs have the potential to reduce costs and improve care compared to current models of FFS reimbursement. Our study suggests that investment in care coordination to achieve a modest reduction in hospitalizations during the active treatment period can accomplish overall cost savings while appropriately reimbursing gynecologic oncology practices.

34 - Focused Plenary

Evaluation of financial toxicity in women with gynecologic malignancies: A cross-sectional study

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Objective: Studies have demonstrated that financial toxicity, or the financial hardship associated with cancer, adversely affects quality of life, medical adherence, and outcomes. This study identifies the degree and impact of financial toxicity experienced by patients with gynecologic malignancy.

Method: This is a cross-sectional study of patients with gynecologic malignancy. Patients undergoing chemotherapy or who had previously received chemotherapy were eligible. Enrolled participants completed a 41-item survey adapted from the Federal Reserve Board's Survey of Household Economics and Decision-making and published studies, including a Comprehensive Score for Financial Toxicity (COST) measure designed to assess patient-reported financial toxicity in patients with advanced cancer (score range 0–44). Financial toxicity was defined as a COST score of >22. Data analysis was performed with STATA.

Results: Of the 60 women enrolled, the mean age of respondents was 61 years (range 30–84 years); 20% ($n = 12$) were black, 56% ($n = 34$) white, 21% ($n = 13$) Hispanic, and 1% ($n = 1$) Asian. Half were actively receiving chemotherapy. In total, 31% ($n = 19$) reported a decrease in income since receiving a diagnosis of cancer, with 8% ($n = 5$) earning less than half of prior income; 16% ($n = 10$) were in debt because of treatment. Forty-six percent ($n = 28$) experienced an insurance denial for recommended treatment; 36% ($n = 22$) skipped medical care because of financial concerns; and 28% ($n = 17$) were unable to cover the cost of care. Forty-one percent ($n = 25$) had a COST score >22, consistent with distress due to financial toxicity; 44% ($n = 11$) of this subset reported financially motivated medical nonadherence, such as skipping of appointments or medications. No patients with COST scores ≤22 reported financially motivated nonadherence. Blacks were more likely than whites to

experience financial toxicity (odds ratio = 14, 95% CI 6.35–21.90). In a linear regression, younger age of diagnosis was associated with higher COST scores ($P = 0.01$).

Conclusion: Many patients with gynecologic malignancies experience significant financial toxicity, likely worsened by treatment costs and decreased earning potential. Patients experiencing financial toxicity are at high risk of medical nonadherence because of financial constraints.

35 - Focused Plenary

Use of lay navigation in gynecologic oncology patients: A model to reduce costs

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Objectives: To determine the influence of lay navigation on health care spending and resource utilization in gynecologic oncology patients.

Methods: This observational study was performed using 2012-2015 Medicare administrative claims data on health care utilization and costs for navigated and non-navigated patients. Outcomes were evaluated for up to 8 quarters after enrollment and included Medicare spending per beneficiary, emergency room (ER) visits, and hospitalizations. Generalized linear models was used to evaluate health care utilization and cost, adjusting for differences across navigated and non-navigated groups. Differential effects over time were tested with a group*time interaction.

Results: A total of 1,052 patients were included; 390 (37%) navigated and 662 (63%) non-navigated. Mean age was 74 years with 82% of patients being white. Most patients were Stage I (39%), had endometrial cancer (51%) and evaluated during initial phase of care (79%). Groups were similar in regards to age, race, comorbidity score, and ZIP-code SES factors (low education, poverty, and median income). Compared to non-navigated, the navigated group had significant increase in “high-acuity” cancers (stage IV and/or ovarian), 32 vs 44% ($P = 0.0001$). Mean Medicare costs per quarter per patient declined from \$7,737 to \$4,533 (41% savings) in non-navigated compared to \$11,737 to \$5,093 (57% savings) in navigated patients (Figure 1). In adjusted analyses, navigated patients showed a statistically significant steeper decline in Medicare spending over time compared to non-navigated patients (\$644, $P < 0.0001$). Thus, estimated Medicare savings for this entire cohort if navigated would be \$677,067 per quarter, and \$2.71 million per year. ER visits and hospitalizations decreased by 47% and 80%, respectively, per quarter in navigated patients (Figure 1). Adjusted analyses demonstrated $P = 0.2$ for hospitalizations, and $P = 0.71$ for ER visits.

Conclusions: Despite having significant increase of high-acuity patients, health care costs to Medicare significantly declined for navigated gynecologic oncology patients compared to non-navigated patients. Further studies on the source of such cost reductions is warranted to understand how lay navigation programs are most effective. Lay navigated programs should be expanded as health systems transition to value-based health care.

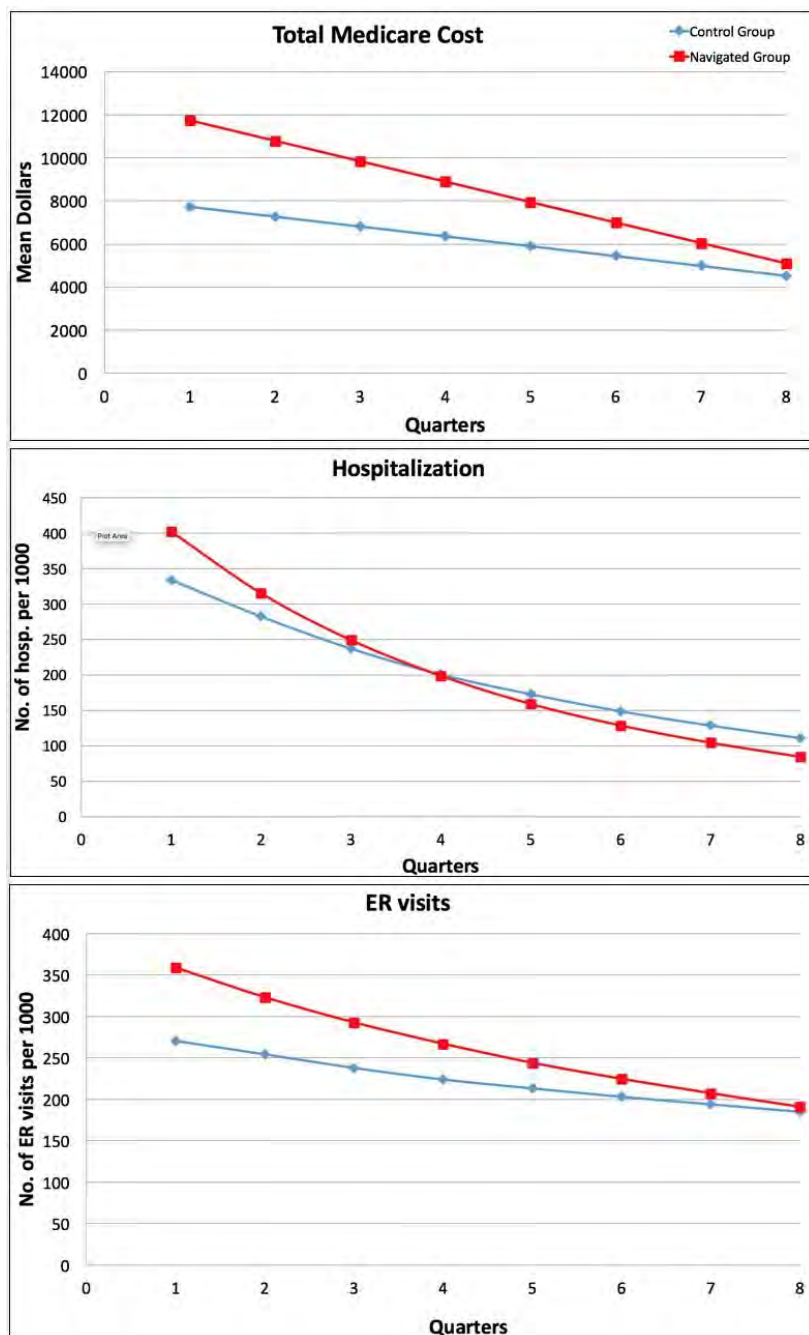


Fig. 1.

36 - Focused Plenary

A comparison of liposomal bupivacaine to bupivacaine HCl in transversus abdominis planus block for abdominal gynecologic surgery: A randomized controlled trial

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Objective: The purpose of the study was to evaluate the use of liposomal bupivacaine in comparison to bupivacaine hydrochloride in a transversus abdominis plane (TAP) block for patients undergoing major gynecologic abdominal surgery. The primary outcomes included length of stay and total opioid use postoperatively.

Method: This study was a prospective single blinded randomized controlled trial. Statistical analysis prior to the start of the study showed the need for $n = 128$, 64 in each group, to achieve statistical significance of decrease in length of stay (LOS) of 0.5 days. After institutional review board approval, subjects were enrolled starting August 2016; as of this presentation a total of 120 subjects were enrolled. Inclusion criteria included gynecologic oncology patients undergoing exploratory laparotomy, and those who signed consents for a TAP block preoperatively. Exclusion criteria included patients under the age of 18, pregnant women, those undergoing minimally invasive surgery, or those with medical contraindications to receiving either bupivacaine or liposomal bupivacaine. All TAP blocks were performed by trained anesthesiologists.

Results: Three of 120 patients were excluded from the study because of lack of intervention. There were 51 patients in the control arm who received bupivacaine HCl, and 66 in the intervention arm who received liposomal bupivacaine. Analysis of this cohort thus far indicated that the median LOS was 3.08 days (IQR = 2.17–5.98) in the control group versus 2.93 days (IQR = 2.04–4.05) for those who received liposomal bupivacaine with their TAP block. Median total opioid use was 56.25 morphine milligram equivalents (MME) (IQR = 18.75–135.00) for the control group, compared to 37.50 MME (IQR = 9.38–75.47) for the intervention group.

Conclusion: Liposomal bupivacaine used in TAP blocks in gynecologic oncology surgeries did not demonstrate a significant decrease in length of stay. However, it reduced opioid use by one-third. This study offers a potential way to decrease postoperative narcotic use and fits well into the Enhanced Recovery After Surgery goals in the field of gynecologic oncology. Understanding that opioid use postoperatively is associated with increased risk of abuse and addiction, our intervention presents an opportunity to improve outcomes and prevent abuse. We plan to complete enrollment shortly and present final statistical analysis for the entire cohort at the meeting.

37 - Focused Plenary

Impact of enhanced recovery after surgery (ERAS) protocol on postoperative pain control in chronic narcotic users
H.J. Smith, T.K.L. Boitano, T. Rushton, M.C. Johnston, C.A. Leath III and J.M. Straughn Jr. *University of Alabama at Birmingham, Birmingham, AL, USA*

Objective: One of the major tenets of enhanced recovery after surgery (ERAS) is limiting opioid use; however, this may be difficult in patients who take narcotics at baseline. We evaluated postoperative pain control with ERAS in gynecologic oncology patients with a history of chronic narcotic use.

Method: This retrospective cohort study included gynecologic oncology patients undergoing elective laparotomy from October 2016 to June 2017 who were managed on an ERAS protocol and a control group from the year prior to ERAS implementation. Patients taking daily opioids prior to surgery were classified as chronic narcotic users and compared to nonnarcotic users. The primary outcome was mean pain score over postoperative stay. Secondary outcomes included amount of narcotics prescribed at discharge in oral morphine equivalents (OME), need for additional narcotic prescription within 30 days, length of stay (LOS), and readmission rates. Statistical analysis was performed using SPSS Statistics v. 24.

Results: A total of 376 patients were identified; 197 in the control cohort and 179 in the ERAS cohort. Rates of chronic narcotic use were similar between cohorts (20.3% vs 19.0%, $P = 0.75$). In the ERAS cohort, chronic narcotic users had a higher mean pain score than nonnarcotic users (2.8 vs 1.8, $P = 0.01$) and required significantly more opioids at discharge (1,940 vs 533 mg OME, $P = 0.002$). They were also more likely to require additional narcotic prescriptions within 30 days of discharge (29.4% vs 7.6%, $P < 0.001$). LOS and readmission rates were similar in chronic narcotic users versus nonnarcotic users. There was no difference in postoperative pain score in chronic narcotic users in the ERAS cohort compared to the control cohort (2.8 vs 3.1, $P = 0.52$), and no reduction in the amount of opioids prescribed at discharge (3,909 vs 3,276 mg OME, $P = 0.61$). In nonnarcotic users, both postoperative pain scores (1.8 vs 2.5, $P < 0.001$) and the amount of opioids prescribed at discharge (1,940 vs 2,610 mg OME, $P < 0.001$) were significantly reduced with ERAS.

Conclusion: Implementation of ERAS improves pain control and decreases the amount of opioids prescribed at discharge in narcotic-naïve gynecologic oncology patients. ERAS does not significantly improve postoperative pain control or decrease opioid use in chronic narcotic users.

Focused Plenary III: New Insights into Rare Tumors

Monday, March 26, 2018

Moderators: Yvonne Lin-Liu, MD, *Genentech, San Francisco, CA*

Nakarin Sirisabya, MD, *Chulalongkorn University, Bangkok, Thailand*

38 – Focused Plenary

KMT2D/MLL2 loss of function is a novel driver of disease recurrence in adult-type granulosa cell tumors of the ovary

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Objective: Ovarian adult type granulosa cell tumors (aGCTs) have an unpredictable recurrence pattern, and thus the identification of tumors at high risk for recurrence remains a significant unsolved clinical problem. A *FOXL2* C402G hotspot mutation is present in 92%–97% of aGCTs but is not predictive of clinical outcomes. In order to identify biomarkers of disease recurrence, we characterized the genomic landscape of primary and recurrent aGCTs.

Method: Whole exome sequencing (WES) was performed on fresh frozen tissue from 24 aGCTs, including 9 primary and 15 recurrent tumors. Matched normal tissue was sequenced for 20 of 24 tumors (83%). All tumors were reviewed by a gynecologic pathologist prior to sequencing. Somatic variants were identified, and the MuSiC2 tool was used to detect significantly mutated genes, employing the Benjamini-Hochberg method to control the false discovery rate. A two-sided Fisher exact test was used for statistical comparisons.

Results: The mean tumor sequencing coverage was 225X, and the mean tumor cell purity was 68%. The *FOXL2* C402G mutation was found in 23 of 24 tumors (96%). In addition to *FOXL2*, the tumor suppressor gene *KMT2D/MLL2* was significantly mutated in aGCTs ($P = 7 \times 10^{-6}$, genome-wide false discovery rate <0.1). All *KMT2D/MLL2* mutations were confirmed using Sanger sequencing. All exonic *KMT2D/MLL2* mutations identified in this cohort result in reading frame truncation, consistent with a driver role for this gene in aGCT. *KMT2D/MLL2* loss of function is significantly more frequent in recurrent aGCTs (7/15, 47%) compared to primary aGCTs (0/9, 0%, $P = 0.022$). Notably, a *KMT2D/MLL2* frameshift mutation was also detected in the KGN cell line, which was derived from a recurrent aGCT. In contrast to aGCT, *KMT2D/MLL2* mutation was rare in the Cancer Genome Atlas high-grade serous ovarian carcinoma cohort (2/316 tumors, 0.6%).

Conclusions *KMT2D/MLL2* is a known tumor suppressor gene frequently inactivated in multiple tumor types. *KMT2D/MLL2* loss of function is a novel driver event in aGCTs, and mutation of this gene represents the first biomarker specifically associated with disease recurrence. Work is ongoing to determine the prevalence of *KMT2D/MLL2* inactivation among primary aGCTs in a large independent cohort, since detection of this mutation at the time of diagnosis may identify tumors with a high propensity for recurrence.

39 - Focused Plenary

Integrated genomic analyses distinguish leiomyosarcomas arising at distinct anatomic origins

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Objective: Uterine leiomyosarcoma (U-LMS) is the most common mesenchymal malignancy arising in the genital tract of reproductive-age women. Recent and ongoing analyses by The Cancer Genome Atlas (TCGA) consortium create unique opportunities to understand the molecular basis of this disease.

Method: State-of-the-art array platforms were used to comprehensively profile high-quality specimens of soft tissue sarcomas ($n = 206$) for alterations in DNA copy number, DNA methylation, and telomere length. Next-generation sequencing was used to profile patterns of DNA mutations and mRNA and miRNA expression. RPPA was used to evaluate patterns of protein expression and phosphorylation.

Results: Unsupervised hierarchical clustering revealed that leiomyosarcomas (LMS), regardless of origin, share multiple features. These include robust expression of gene products linked to myogenic differentiation (MYLK, MYH11, ACTG), high levels of specific noncoding RNAs (miR-143/145) and low levels of inflammatory response genes. Integration of genetic and RPPA analyses revealed lower inferred activity in apoptosis pathways ($P = 1.03^{-9}$), higher expression of steroid hormone receptors (ER/PR, $P = 1.5^{-8}$), and greater inferred activity in PI3K/AKT regulated signaling pathways ($P = 1.02^{-9}$). Despite these shared features, U-LMS ($n = 27$) and soft-tissue leiomyosarcomas (ST-LMS, $n = 53$) had significantly different patterns of DNA methylation and mRNA expression. Specifically, U-LMS were characterized by significantly greater activity and expression of DNA damage response pathways ($P = 0.005$) and hypomethylation of ESR1 target genes. In contrast, ST-LMS were found to have more robust expression of HIF1 α signaling pathways ($P = 6^{-05}$). Additional differentially expressed

patterns of gene and noncoding RNAs will also be presented as well as pathways potentially regulated by progesterone receptor activity relevant to this disease. Clinically, disease-specific survival was significantly shorter for U-LMS than for ST-LMS.

Conclusions: Despite histologic similarity, U-LMS and ST-LMS are molecularly distinct malignancies that likely warrant distinct therapeutic approaches. Future work should focus on clinically leveraging the unique sensitivities of these malignancies to improve their clinical outcomes.

40 - Focused Plenary

Single-course methotrexate and single-course combined methotrexate-dactinomycin: A phase III randomized controlled clinical trial in treatment of low-risk gestational trophoblastic neoplasm

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Objective: To evaluate the most reasonable regimen for the primary treatment of low-risk gestational trophoblastic neoplasia (GTN), with the aims of short duration, minimal toxicity, and rapid return to fertility.

Method: The randomized trial conducted by 6 centers in China was offered to patients with a risk score between 0 and 6. Patients were enrolled in 3 groups according to chemotherapy regimen: multiple-course methotrexate (MTX, 0.4 mg/kg/d*5d, intramuscular, every 2 weeks), single-course MTX (0.4 mg/kg/d*5d, intramuscular), and single-course MTX plus dactinomycin (MTX, 100 mg/m² + 200 mg/m², d1, intravenous; ACTD, 600 ug/m², d1 and d2, intravenous). The cases failed primarily by single-course would have additional courses of the same regimen. The primary objective was to compare the proportion of patients meeting the criteria for a complete response (CR). The main secondary objectives were rate of drug resistance and toxicities.

Results: From December 2012 to December 2015, a total of 291 low-risk GTN cases were enrolled, and 272 were deemed eligible. Of 81 patients, 55 (67.9%) treated with multiple-course MTX achieved initial CR. Single-course MTX had CR as initial treatment by 36.08% (35/97). For the rest who failed, 21 cases reached CR by additional multiple-course MTX. Ultimately 42.27% were diagnosed as drug resistance to MTX, which was similar to the multiple-course MTX group ($P = 0.317$). There was also no difference of medium chemotherapy number between 2 groups [3 (2, 8) vs 3 (1, 7), $P = 0.432$]. Single-course MTX+ACTD achieved 46.81% (44/94) CR rate as initial treatment, which was statistically comparable to single-course MTX ($P = 0.132$). All 3 regimens were less effective if the WHO risk score was 5 or 6 (21.4%, 25%, and 55.56% for single-course MTX, single-course MTX+ACTD, and multiple-course MTX, respectively, $P = 0.331$). In the multiple-course MTX group, 11 cases suffered from severe but not fatal side effects. All other cases were well tolerated. Multivariate analysis showed that hCG level before treatment had a significant relationship with the primary CR by single-course MTX and MTX+ACTD.

Conclusion: Treatment with single-course MTX or MTX+ACTD for patients whose pretreatment HCG level was lower and did not want to have long duration of chemotherapy would be a reasonable choice.

41 - Focused Plenary

The impact of uterine re-curettage on the number of chemotherapy courses in treatment of post molar gestational trophoblastic neoplasia: A randomized controlled study

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Objective: To assess the impact of uterine recurettage on the number of chemotherapy courses in patients with postmolar gestational trophoblastic neoplasia (GTN).

Method: Consecutive patients with postmolar GTN and serum B-hCG levels less than or equal to 5.000 IU/L were randomized between recurettage or not, prior to start of methotrexate (MTX) treatment. This was a stratified (<1,500 IU/L and 1,500–5.000 IU/L, bleeding or nonbleeding), 1:1 randomization study. Eligible participants were 18 years or older, with a WHO low or intermediate risk score. Exclusion criteria were previous uterine perforation and life-threatening bleeding. Patients gave

written informed consent. All received standard MTX treatment; the study group did undergo a uterine resection prior to the first dose. Statistical analyses were done with SPSS, version 22, including uni- and multivariate regression analyses. The study was approved by the Ethical Committee of Faculty of Medicine (Number R/48) and was registered in the Dutch Trial Registry (NTR3390). CONSORT is used for reporting results.

Results: Between October 2011 and December 2015, 89 patients were enrolled. Three were excluded; 2 refused treatment, and 1 did not meet the inclusion criteria. Finally, in the intention-to-treat analyses, 43 patients were included in each arm. Groups were comparable with regard to age, parity, hCG level, WHO score, vaginal bleeding, weight, and BMI. In the resection groups complications did not occur. Groups were comparable for the number of courses needed for normalization, 4.2 courses \pm 2.2 SD in the standard group versus 3.9 courses \pm 2.3 SD in the resection group. In 5 patients in the standard group and 4 in the resection group, second-line treatment was needed to reach normalization of hCG. During the first year of follow-up a relapse occurred in 2 patients in the standard arm and in 1 patient in the resection arm.

Conclusions: Resection does not have an impact on the number of chemotherapy courses in patients with postmolar GTN. Only hCG level relates to the number of courses. This conclusion remains robust in uni- and multivariate regression analyses.

42 - Focused Plenary

Molecular profiling of ovarian germ cell tumors

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Objective: Ovarian germ cell tumors (OGCTs) are rare, and driver molecular alterations are unknown. The aim of this retrospective study was to identify genetic alterations in OGCT.

Method: Patients with OGCT were recruited by their primary provider or through a direct-to-patients outreach campaign, "Make an Impact," to have their tumor samples evaluated by the Memorial Sloan Kettering–Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT). MSK-IMPACT is a hybridization-based targeted next-generation sequencing assay that identifies somatic genomic alterations in 410 key cancer genes. Patient data were abstracted from medical records.

Results: We identified 26 patients with OGCT whose tumor samples ($n = 33$) were sequenced by MSK-IMPACT. Seventeen (65%) of 26 patients were diagnosed with stage III–IV disease; 12/26 (46%) were stratified to the poor-risk group using the modified IGCCCG risk system. Fourteen (54%) of 26 patients had tumors of mixed histology; 7/26 had yolk sac tumors (27%); 3/26 had dysgerminomas (11%); and 2/26 had immature teratomas (7%). Disease recurrence or progression following completion of primary treatment was seen in 12/26 (46%). Of those who recurred, 6/12 (50%) received high-dose chemotherapy with stem cell support as salvage therapy. After a median follow-up of 16.5 months (range 5–97 months), 15/26 are without evidence of disease (58%). The most commonly altered genes were *KIT* (7, 21%), *PIK3CA* (5, 15%), and *KRAS* (4, 12%) (Figure 1). All were putative driver mutations identified as oncogenic-based on OncoKB database. All tumors were wildtype for TP53. In 8 tumors (24%), no mutations were identified. Eight (24%) of 33 tumor samples had an isochromosome 12p. Allele specific copy number analysis noted that 3/33 samples (9%) had whole genome duplication, followed by large copy number losses (copy neutral loss of heterozygosity, CN-LOH).

Conclusion: OGCTs are exceedingly rare. This is the first study to evaluate their somatic genomic alterations. We identified mutations in driver genes and CN-LOH as the most common genomic alterations in OGCT. Several potentially actionable mutations, including in *PIK3CA* and *KIT*, were noted. Future work will include expanding our sample cohort and whole genome sequencing, particularly in patients with recurrent or progressive disease.

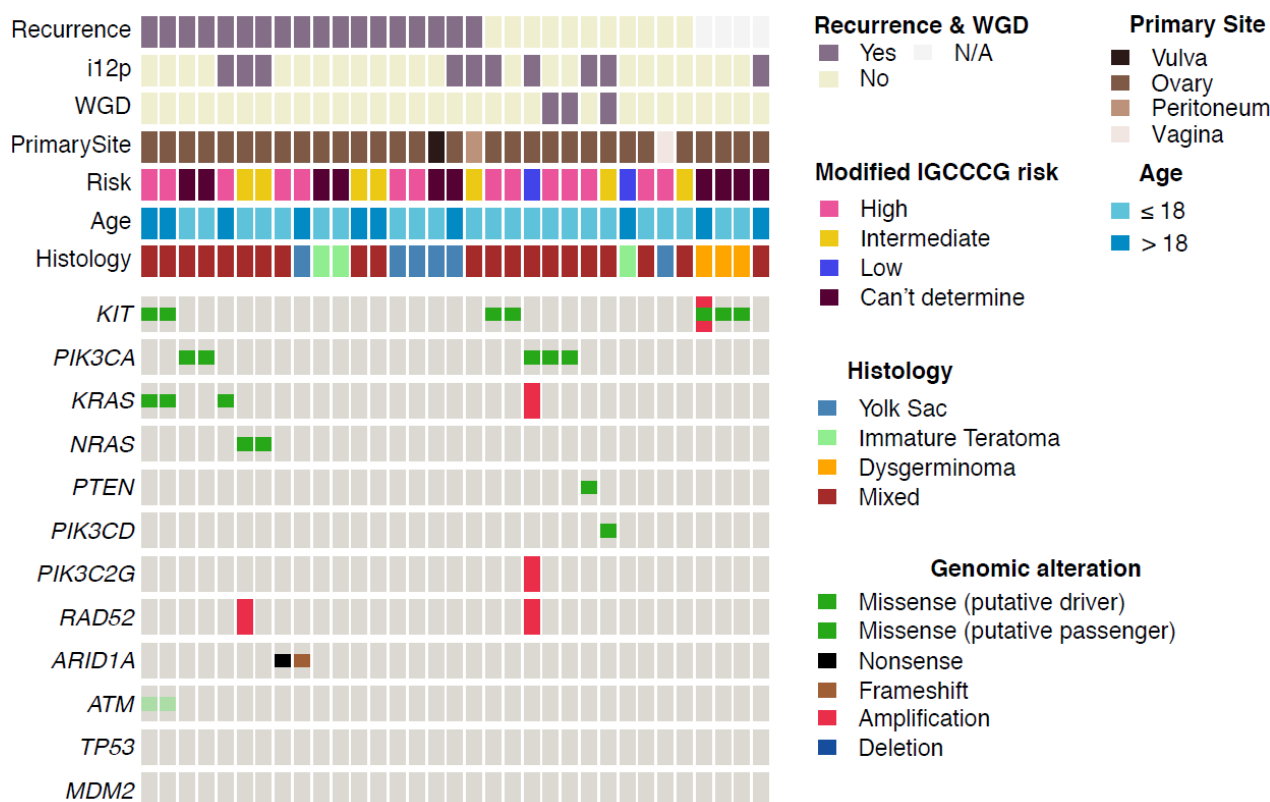


Fig. 1.

Scientific Plenary V: The Farr Nezhat Surgical Innovation Session: Surgical Decision Making in Advanced Ovarian Cancer

Monday, March 26, 2018

Moderators: Vanna Zanagnolo, MD, *European Institute of Oncology, Milan, Italy*

Ahmed N. AL-Niaimi, MD, *University of Wisconsin School of Medicine and Public Health, Madison, WI, USA*

43 - Scientific Plenary

Moving beyond "complete surgical resection" and "optimal": Is low-volume residual disease another option?

B.L. Manning-Geist^{a,b}, K. Hicks-Courant^c, A.A. Gockley^d, R.M. Clark^d, M.G. del Carmen^e, J.O. Schorge^b, N.S. Horowitz^f, R.S. Berkowitz^f, M.G. Muto^g and M.J. Worley Jr.^h ^aBrigham and Women's Hospital/Harvard Medical School, Boston, MA, USA, ^bMassachusetts General Hospital, Boston, MA, USA, ^cTufts Medical Center, Boston, MA, USA, ^dHarvard Medical School, Boston, MA, USA, ^eMassachusetts General Hospital/Harvard University, Boston, MA, USA, ^fBrigham and Women's Hospital, Boston, MA, USA, ^gDana-Farber Cancer Institute, Boston, MA, USA, ^hBrigham and Women's Hospital/Harvard University, Boston, MA, USA

Objective: To examine the effect of residual disease classification and residual disease volume on survival among patients with advanced-stage epithelial ovarian/fallopian tube/primary peritoneal carcinoma after primary debulking surgery (PDS) or neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS).

Method: Medical records of patients with FIGO stage IIIC and IV epithelial ovarian/fallopian tube/primary peritoneal carcinoma, undergoing PDS or NACT-IDS, between January 2010 and July 2015 were reviewed. Patient demographics, operative characteristics, residual disease, anatomic site of residual disease, and outcome data were collected. Among patients with <1 cm of residual disease, the number of anatomic sites (single location vs multiple locations) with residual disease was utilized as a surrogate for volume of residual disease. The effect of residual disease on survival was evaluated.

Results: Of 510 patients, 240 (47.1%) underwent PDS and 270 (52.9%) underwent NACT-IDS. Among patients undergoing PDS, 94 (39.2%) had complete surgical resection (R0), 41 (17.1%) had <1 cm of residual disease confined to a single location (<1 cm-SL); 67 (27.9%) had <1 cm of residual disease in multiple locations (<1 cm-ML); and 38 (15.8%) were suboptimally (SO) debulked. Among patients undergoing NACT-IDS, 173 (64.1%) were R0; 34 (12.6%) were <1 cm-SL; 47 (17.4%) were <1

cm-ML; and 16 (5.9%) were SO debulked. Among patients with <1 cm residual disease, most were <1 cm-ML, and this did not differ when comparing those who underwent PDS to NACT-IDS (62% vs 58%). Among <1 cm-SL patients, the most common site of residual disease was the diaphragm, and this did not differ when comparing PDS to NACT-IDS (31.7% vs 41.2%). Among patients undergoing PDS, median OS for R0, <1 cm-SL, <1 cm-ML, and SO debulked were as follows: not yet reached, 61, 42, and 44 months, respectively ($P = 0.001$). Among patients undergoing NACT-IDS, median OS for R0, <1 cm-SL, <1 cm-ML, and SO debulked was 53, 33, 22, and 28 months, respectively ($P < 0.001$). See Figure 1.

Conclusion: After cytoreductive surgery, R0 and <1 cm-SL patients have the best prognosis, and this effect is the greatest after PDS. In contrast, despite being considered “optimally debulked,” <1 cm-ML patients have a survival similar to those who are SO debulked.

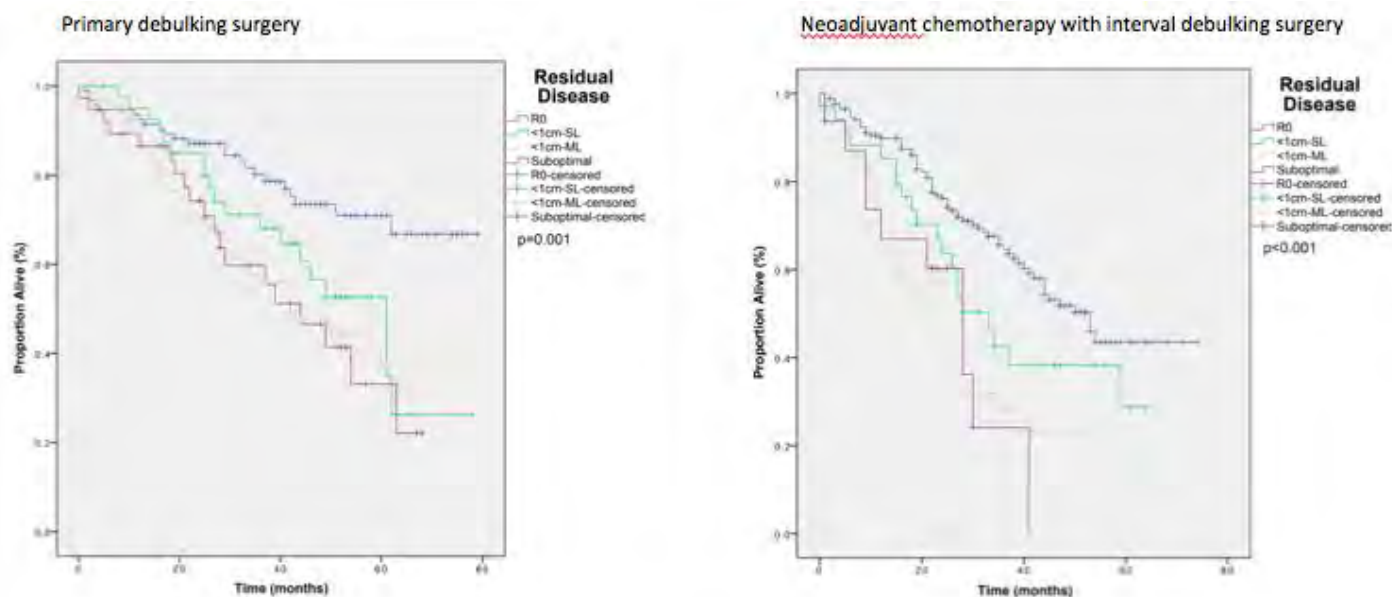


Fig. 1. Influence of residual disease on overall survival by treatment approach.

Education Forum X: Improving Your Well-being Through Coaching: Connect, Engage, Thrive! Monday, March 26, 2018

Course Directors: David Kushner, MD, *University of Wisconsin, Madison, WI*
Leslie Bradford, MD, *Maine Medical Center, Cumberland, MA*

44 - Education Forum

Career demands of gynecologic oncology have a substantial impact on family planning

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Objective: To assess the fertility and infertility experiences among gynecologic oncologists in the United States.

Method: This study was a cross-sectional multiple choice online survey of practicing gynecologic oncologists and fellows-in-training who are members of the Society of Gynecologic Oncology. The survey collected demographic and practice information, fertility and infertility experience, use of assisted reproductive techniques for infertility treatment or fertility preservation, and barriers to desired family size. Responses were collected anonymously, and descriptive analyses were performed.

Results: A total of 211 of 1,243 (17%) members responded to the survey. The majority of respondents were female (70%), were Caucasian (77%), had been practicing less than 10 years (55.5%), and were partnered (93.4%). The median number of children among respondents was 2 (range 0–5); 46.7% ($n = 98$) reported that career influenced the number of children they had or plan to have; 32.2% ($n = 46$) were 35+ years of age at the birth of their first child; and a majority (66%, $n = 138$) reported they would have had children sooner if they had a different job. Of the respondents, 53.3% of those who have not yet conceived ($n = 24$) and 41.6% of those who have conceived ($n = 67$) expressed current or past concerns about their fertility. Among those concerned, 60.4% ($n = 55$) sought infertility counseling and/or treatment, and 48.4% ($n = 44$) considered

fertility preservation via oocyte/embryo cryopreservation. Among respondents who underwent infertility treatment, 44.8% ($n = 33$) reported their colleagues/program administration were unaware of their fertility struggles; 13.6% ($n = 9$) felt stigmatized for having an issue with infertility; and 39.4% ($n = 26$) stated their fertility concerns affected their work life.

Conclusion: These findings suggest that demands of a career in gynecologic oncology have a substantial impact on family planning and often result in childbearing delays and infertility concerns. Support for our colleagues struggling with infertility and/or undergoing fertility preservation or infertility treatment should be addressed by programs such as the Society of Gynecologic Oncology Wellness Initiative.

45 - Education Forum

The career effects of parenting on female and male gynecologic oncologists

L.B. Beffa^a, A.R. Stuckey^b, E.K. Hill^c, A.K. Brown^d, M.E. Gordinier^e, C. Raker^b, M. Clark^f and K.M. Robison^a. ^a*Women & Infants Hospital, Brown University, Providence, RI, USA*, ^b*Women & Infants Hospital, Brown University, Providence, RI, USA*, ^c*University of Iowa, Iowa City, IA, USA*, ^d*Hartford Hospital, Hartford, CT, USA*, ^e*Norton Healthcare, Louisville, KY, USA*, ^f*University of Massachusetts Medical Center, Worcester, MA, USA*

Objective: To compare the effects of parenting on the career of female and male gynecologic oncologists.

Method: A cross-sectional survey was conducted of female and male gynecologic oncology physician members of the Society of Gynecologic Oncology (SGO). The survey was administered electronically (DatStat Illume) in 2015. The survey was sent via email to all society members with 2 reminder emails regardless of completion status. There were 75 fixed-response questions in 4 domains: demographics, mentoring issues, work-life balance, and caregiving responsibilities. Data were analyzed using Stata 10 with χ^2 and Fisher exact tests.

Results: Two hundred sixty-eight SGO members completed the survey (22% response rate), with 172 (64%) female and 96 (36%) male participants. Twenty-five percent were 35 years of age or younger; 41% were between the ages of 36 and 45; 20% were between the ages of 46 and 55; and 13% were older than 55. One hundred ninety-four (72%) respondents had at least 1 child. Forty-five (39%) female participants reported that career plans affected the decision to become a parent somewhat or very much compared to 19 (23%) male participants ($P = 0.01$). Twenty-one percent of female gynecologic oncologists responded that residency or fellowship was the best time to become a parent compared to 33% of male gynecologic oncologists ($P = 0.02$). Eighty-six percent of women felt their career affected the timing of becoming a parent somewhat or very much compared to 45% of men ($P < 0.001$). In addition, 79% of women thought that having children decreased their academic productivity compared to 57% of male respondents ($P < 0.001$). In contrast, there was no difference between men (16%) and women (24%) on perceived negative impact of having children on clinical productivity ($P = 0.28$).

Conclusion: Female gynecologic oncologists perceive that the best time to become a parent is outside of training more frequently than their male counterparts. They are also more likely than males to endorse that having children has a negative impact on academic performance. Increased support for combining childbirth and parenting with training and academic careers may help alleviate these differences.

Scientific Plenary VI: Immuno-Oncology

Tuesday, March 27, 2018

Moderators: Amir A. Jazaeri, MD, *University of Virginia, Charlottesville, VA, USA*

Monica B. Jones, MD, *Anne Arundel Medical Center, Annapolis, MD*

46 - Scientific Plenary

Pembrolizumab in advanced recurrent endometrial cancer: A cost-effectiveness analysis

D.A. Barrington, S.E. Dilley, H.J. Smith and J.M. Straughn Jr. *University of Alabama at Birmingham, Birmingham, AL, USA*

Objective: To determine the cost-effectiveness of pembrolizumab, a PD-L1 antibody, in recurrent endometrial cancer that has failed first-line chemotherapy in women with (MSI-H) and without (MSI-L) microsatellite instability.

Method: We created a model to evaluate the cost-effectiveness of pembrolizumab compared to pegylated liposomal doxorubicin (PLD) or bevacizumab (BEV) for the treatment of women with recurrent endometrial cancer who have failed carboplatin and paclitaxel. Microsatellite instability-high (MSI-H) and microsatellite instability-low (MSI-L) tumors were

evaluated. We included 4,400 patients in the model; 800 (18.2%) patients were assumed to have MSI-H tumors. Drug costs were calculated using 2016–2017 wholesale acquisition costs, and cost of grade III–IV toxicities was estimated from clinical experience. The per-cycle costs of pembrolizumab, BEV, and PLD were \$9,026, \$7,585, and \$2,509, respectively. The probability of grade III–IV toxicity and median number of cycles were estimated from the literature. Effectiveness was calculated as 2-year overall survival (OS), which was estimated to be 20% for PLD, 40% for BEV, 50% for pembrolizumab (MSI-L), and 64% for pembrolizumab (MSI-H). We calculated incremental cost-effectiveness ratios (ICERs) to determine the cost per 2-year survivor. Univariate sensitivity analyses were performed. The willingness to pay threshold was \$100,000 per year of OS.

Results: The costs of therapy with PLD and BEV were \$33.2 million (M) and \$167.9 M, respectively. The cost of pembrolizumab therapy was \$318.3 M for MSI-L patients compared to \$57.9 M for MSI-H patients. For MSI-L patients, BEV was cost-effective relative to PLD with an ICER of \$153,028, while pembrolizumab was not cost-effective relative to BEV with an ICER of \$341,830. For MSI-H patients, pembrolizumab was cost-effective compared to PLD with an ICER of \$147,249, while BEV was dominated. Sensitivity analysis revealed that for MSI-L patients, 1 cycle of pembrolizumab would need to cost \$7,253 or less to be cost-effective.

Conclusion: For patients with MSI-H recurrent endometrial cancers who have failed first-line chemotherapy, pembrolizumab is cost-effective relative to other single-agent drugs. To be cost-effective in MSI-L patients, the cost of pembrolizumab should decrease by \$1,773 per cycle.

47 - Scientific Plenary

Predictors of early treatment discontinuation in ovarian cancer patients on checkpoint blockade immunotherapy

J.L. Boland^a, M. Martin^a, N. Zecca^a, A. Iasonos^a, Q. Zhou^a, C.A. Aghajanian^{a,b}, P. Sabbatini^{a,b}, K.A. Cadoo^{a,b} and D. Zamarin^{a,b}.

^aMemorial Sloan Kettering Cancer Center, New York, NY, USA, ^bWeill Cornell Medical College, New York, NY, USA

Objective: We sought to determine whether pretreatment clinical biomarkers could predict early treatment discontinuation of ovarian cancer patients on checkpoint blockade immunotherapy agents.

Method: A retrospective analysis was performed on all patients diagnosed with epithelial ovarian, primary peritoneal, and fallopian tube cancer who were treated with checkpoint blockade immunotherapy at Memorial Sloan-Kettering Cancer Center from January 1, 2006, to May 20, 2017. Pretreatment clinical properties were recorded from the electronic medical record. Pretreatment computed tomography scans were reviewed to assess for extent and sites of disease. Bulky disease was defined as having any lesion greater than or equal to 5 centimeters. Univariate logistic regression and a multivariate logistic model were built based on relevant clinical variables.

Results: Of 115 identified patients, 12 were excluded for discontinuation early because of toxicity to yield a cohort of $n = 103$; 59.2% of patients ($n = 61$) were discontinued early because of radiographic or symptomatic disease progression, with a median time on therapy of 10 weeks. On univariate analysis, pretreatment bulky disease ($P = 0.038$, OR = 2.927), liver parenchymal metastases ($P = 0.009$, OR = 4.174), and bone metastases ($P = 0.045$, OR = 4.896) were predictive of early discontinuation, as shown in Table 1. On multivariate logistic analyses, the presence of liver parenchymal metastases was predictive of early discontinuation ($P = 0.024$, OR = 3.547). Symptomatic clinical progression was the reason for early discontinuation in 25 (41%) patients.

Conclusion: Retrospective analysis shows that ovarian cancer patients with bulky disease, liver parenchymal metastases, and bone metastases were more likely to discontinue early on checkpoint blockade immunotherapy. Given the potential for delayed responses to immunotherapy agents, patients who are at risk for early discontinuation due to clinical progression may not be suitable candidates for immunotherapy clinical trials. These findings could help guide the selection of appropriate patients who would be more likely to stay on trial beyond 12 weeks, in order to allow for the assessment of potential delayed benefit from these drugs.

Table 1. Univariate assessment of predictors of early discontinuation on immunotherapy.

Clinical Properties	Univariate OR ¹	95% CI Lower Bound	95% CI Upper Bound	P value
Age at Diagnosis				
>=63 years vs. <63 years	0.793	0.333	1.889	0.601

Body Mass Index (BMI) [kg/m ²]				
25-30 vs. <25	1.048	0.394	2.791	0.868
>30 vs. <25	0.806	0.317	2.050	
Number of Prior Lines of Therapy				
3 vs. 0-2	0.600	0.180	2.001	0.500
>4 vs. 0-2	1.121	0.430	2.924	
Disease Status at Study Entry				
Bulky vs. non-bulky	2.927	1.059	8.086	0.038
Carcinomatosis at Study Entry				
Present vs. Not present	1.590	0.670	3.771	0.293
Ascites at Study Entry				
Present vs. Not present	1.630	0.600	4.428	0.338
Albumin [g/dL]				
>=4 vs. <4	0.482	0.201	1.158	0.103
Absolute Lymphocyte Count (ALC) [K/mcL]				
>=1.2 vs. <1.2	1.040	0.472	2.293	0.922
Neutrophil-to-Lymphocyte Ratio (NLR)				
>=4 vs. <4	1.050	0.457	2.410	0.909
Platelet-to-Lymphocyte Ratio (PLR)				
>=300 vs. <300	1.304	0.513	3.311	0.577
Disease Sites				
Liver parenchyma vs. no liver parenchyma metastases	4.174	1.432	12.171	0.009
Lung/pleura vs. no lung/pleura metastases	1.527	0.681	3.424	0.304
Bone vs. no bone metastases	4.896	1.035	23.159	0.045

1 – Odd-ratios are modeled for early treatment discontinuation

48 - Scientific Plenary

Phase II study of pembrolizumab (pembro) combined with pegylated liposomal doxorubicin (PLD) for recurrent platinum-resistant ovarian, fallopian tube or peritoneal cancer

U.A. Matulonis^a, W. Barry^a, R.T. Penson^b, P.A. Konstantinopoulos^a, W. Luo^a, M.A. Hoffman^c, N.S. Horowitz^d, S. Farooq^a, D.S. Dizon^e, E. Stover^a, A.A. Wright^{a,f}, S.M. Campos^g, C. Krasner^h and J.F. Liu^a. ^aDana-Farber Cancer Institute, Boston, MA, USA, ^bMassachusetts General Hospital/Harvard University, Boston, MA, USA, ^cLong Island Jewish Medical Center, New Hyde Park, NY, USA, ^dBrigham and Women's Hospital, Boston, MA, USA, ^eLifespan Cancer Institute, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, USA, ^fHarvard Medical School, Boston, MA, USA, ^gDana Farber Cancer Center, Boston, MA, USA, ^hMassachusetts General Hospital, Boston, MA, USA

Objective: Combined chemotherapy and immune checkpoint blockade may be a rational strategy for the treatment of recurrent ovarian cancer; PD-L1 is over-expressed in ovarian cancer; women with tumor-infiltrating lymphocytes have improved survival, and there is evidence of preclinical synergy when these 2 types of agents are combined. The objectives of this study were to test the safety and efficacy of combined pegylated liposomal doxorubicin (PLD) and pembrolizumab (pembro) in platinum-resistant recurrent ovarian cancer.

Method: A safety lead-in of 6 patients initially tested the combination of PLD 40 mg/m² IV every 4 weeks and pembro 200 mg IV every 3 weeks, 1 cycle = 28 days, and patients were assessed radiographically every 2 cycles. Once the lead-in was deemed safe, the study commenced the phase II portion. The primary objective was to assess the clinical benefit (CR + PR + SD > 24 weeks) of the combination. Other objectives included toxicity assessment, response rate (RR), progression-free survival, and translational objectives. Key eligibility included RECIST 1.1 measureable platinum-resistant cancer, receipt of ≤2 cytotoxic regimens for recurrent cancer, no active autoimmune conditions, and normal organ function.

Results: A total of 26 patients with recurrent platinum-resistant ovarian cancer were enrolled and received at least a dose of 1 study drug. Of all patients, 85% had either high-grade serous or Mullerian cancer; median age was 60 years. Ten patients received 1 prior regimen, 8 received 2 prior regimens, and 8 received 3 prior regimens. Three patients were unevaluable (1 had anaphylaxis to PLD and was removed, and 2 had PD prior to first restaging). Of the 23 evaluable patients, 3 had PR (11.5%, 2 confirmed and 1 unconfirmed), 1 SD >24 weeks, 8 SD <24 weeks and still on treatment, 6 SD <24 weeks and off study, and 5 with PD as best response. Mature clinical benefit results are pending. No grade 4 or 5 toxicities have occurred thus far. Grade 3 toxicities included 19% rash, 8% ALT increase, 4% each of AST increase, anemia, diarrhea, fever, and mucositis; there was 8% grade 2 pneumonitis.

Conclusion: PLD and pembro can be combined safely at their MTD doses to treat platinum-resistant ovarian cancer with RR = 11.5%. The rate of pneumonitis is higher than for other tumor sites/regimens and a potential safety concern for this indication and regimen. Mature and updated clinical benefit (primary endpoint) results will be presented at the meeting.

49 - Scientific Plenary

Phase II, two-stage study of avelumab in patients with microsatellite stable (MSS), microsatellite instable (MSI) and polymerase epsilon (POLE) mutated recurrent or persistent endometrial cancer

P.A. Konstantinopoulos^a, J.F. Liu^a, W. Barry^a, C. Krasner^b, M.K. Buss^c, M.J. Birrer^{d,e}, S. Farooq^a, S.M. Campos^f, E. Stover^a, S. Schumer^a, A.A. Wright^g, D.S. Dizon^h, W. Luo^a, R.T. Penson^d, S.A. Cannistra^c, G.F. Flemingⁱ and U.A. Matulonis^a. ^aDana-Farber Cancer Institute, Boston, MA, USA, ^bMassachusetts General Hospital, Boston, MA, USA, ^cBeth Israel Deaconess Medical Center, Boston, MA, USA, ^dMassachusetts General Hospital/Harvard University, Boston, MA, USA, ^eUniversity of Alabama at Birmingham, Birmingham, AL, USA, ^fDana Farber Cancer Center, Boston, MA, USA, ^gHarvard Medical School, Boston, MA, USA, ^hLifespan Cancer Institute, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, USA, ⁱUniversity of Chicago Medical Center, Chicago, IL, USA

Objective: This is a nonrandomized, 2-stage, phase 2 study to evaluate the activity of avelumab, a fully human IgG1 antibody directed against PD-L1, in two cohorts of EC: (1) a MSI/POLE cohort including ECs with immunohistochemical (IHC) loss of expression of at least 1 of the mismatch repair (MMR) proteins and/or documented mutation in the exonuclease domain of POLE and (2) an MSS cohort including ECs with normal IHC expression of all MMR proteins.

Method: Eligible patients have measurable disease, no upper limit of prior therapies, and any EC histology. Coprimary objectives are objective response (OR) (CR+PR) rate and rate of progression-free survival at 6 months (PFS6). Eligible patients receive avelumab 10 mg/kg IV every 2 weeks until disease progression or unacceptable toxicity. In the first stage of the study, 16 patients would be enrolled in each cohort; if there are ≥2 ORs or ≥2 PFS6 responses, accrual will continue to the second stage in which an additional 19 patients would be enrolled in each cohort. Overall, if there are ≥4 ORs or ≥8 PFS6 responses, avelumab would be considered worthy of further study in the corresponding cohort.

Results: As of September 2017, 16 patients were enrolled in the MSS cohort; 1 patient had a confirmed partial response (PR), which is ongoing. One patient had irRECIST PFS6 but not RECIST PFS6; the remaining 14 patients developed progressive disease (PD) without PFS6 or ORs so a second stage was not warranted for the MSS cohort. In the MSI/POLE cohort, 15 patients have been enrolled; of these, 8 have undergone at least 1 on-treatment scan. One patient never received avelumab because she did not fulfill treatment criteria, while 2 patients did not complete 1 cycle of therapy (i.e., 2 doses of avelumab). Thus far, 3 patients in the MSI/POLE cohort had PR (2 confirmed PRs), which are ongoing, thereby meeting criteria for accrual to stage 2 for this cohort; 4 patients had stable disease (SD) and 1 patient PD as best response. No patient in either cohort discontinued avelumab for toxicity. Treatment-related grade ≥3 events in both cohorts included grade 3 (G3) anemia (1 patient), G3 diarrhea (1 patient), and G3 infection (1 patient). Updated efficacy and safety data will be reported at the meeting.

Conclusion: In a heavily pretreated EC population, avelumab monotherapy met the prespecified study criteria to proceed to the second stage in the MSI/POLE cohort but not in the MSS cohort. No new safety signals of avelumab have been identified.

50 - Scientific Plenary

Gene set enrichment clustering and the tumor microenvironment in primary high-grade serous ovarian cancer (HGSOC)

P. Cybulska^a, A. Jimenez-Sanchez^b, K. LaVigne^a, T. Walther^a, H.A. Vargas^a, O. Zivanovic^a, B. Weigelt^a, E. Sala^a, M. Miller^b and A. Snyder^c. ^aMemorial Sloan Kettering Cancer Center, New York, NY, USA, ^bUniversity of Cambridge, Cambridge, United Kingdom, ^cAdaptive Biotechnologies, Seattle, WA, USA

Objective: Several studies have highlighted intra- and intersite genomic heterogeneity in high-grade serous ovarian cancer (HGSOC), but it is unknown whether this is attended by similar heterogeneity of the infiltrating tumor-immune microenvironment (TME) and gene expression patterns. We hypothesized that primary HGOSC would demonstrate inter- and intrasite TME heterogeneity.

Method: Immunofluorescence (IF) staining and microarray-based gene expression analysis (Affymetrix Clariom D) were performed on 1–3 sites from 2–3 tumor deposits, including the primary tumor of debulking specimens from 8 patients with treatment-naïve HGSOC. Images were acquired on a Panoramic Flash 250, and regions of interest (ROI) containing tumor manually outlined after review by the study pathologist. Cell subpopulations within ROI were counted using FIJI/ImageJ. Pathway analysis of transcriptomic data was performed using single-sample Gene Set Enrichment Analysis (ssGSEA).

Results: Overall transcriptome analysis showed largely patient-specific, rather than site-specific, transcriptome-driven structure: although each patient displayed intersite heterogeneity in gene expression, in most cases, all sites within a patient were more similar to each other than to any site from another patient. For example, all sites from one patient (case 6) displayed enrichment for genes associated with oncogenesis, while in another patient (case 17), stromal enrichment predominated (Figure 1). However, there were notable exceptions, for example, cases 1 and 4, in which some sites showed oncogenic pathway activation and others showed immune predominance. Inter- and intrasite TME variability was confirmed with IF; tumors from each patient displayed a minimum 19-fold difference between sampled areas in expression of CD4, CD8, and FOXP3-positive T cell infiltrates.

Conclusion: Multisite analysis of primary HGSOC demonstrates marked intra- and intersite variability in the TME. Pathway activation was predominantly patient-specific, with important exceptions. No consistent loss or gain of infiltrates was observed with progression from the ovaries to the omentum or other sites of disease spread. This inter- and inpatient heterogeneity of the TME may explain the limited success of checkpoint blockade observed in patients with advanced HGOSC.

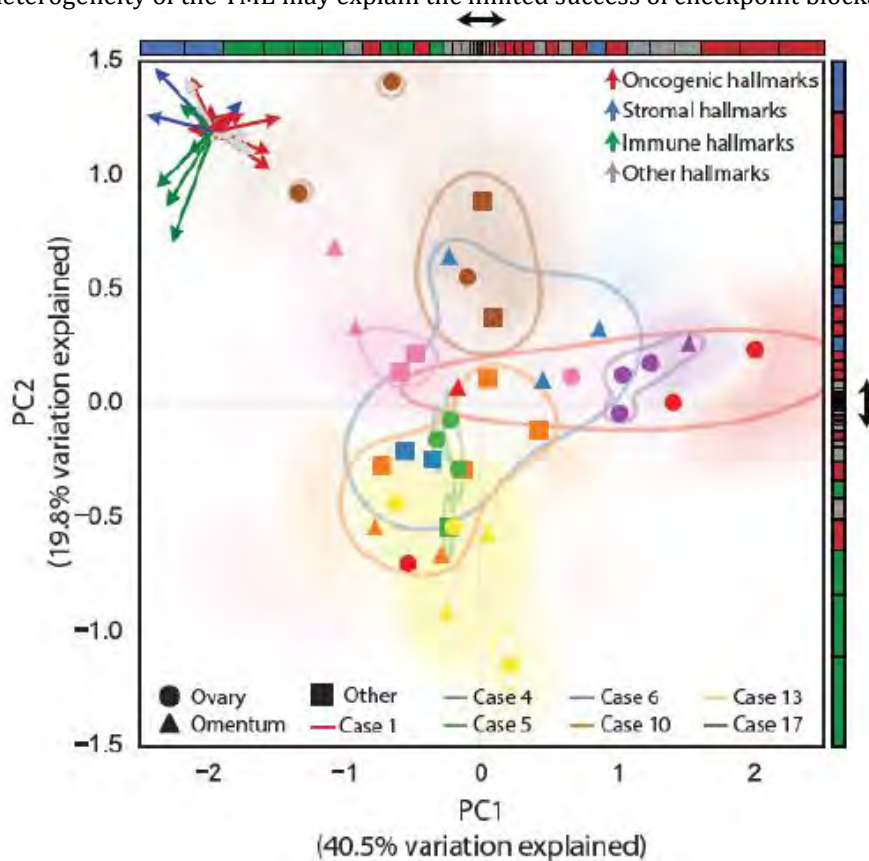


Fig. 1. Principal component analysis of gene set enrichment values. Gene set enrichment values were calculated using ssGSEA. MSigDB hallmark gene sets and ESTIMATE immune and stromal sets were used for the analysis. Top and right stacked bars show the linear combinations of the features (gene sets) that generate the principal components 1 and 2. The length of the rectangle is proportional to the relative of that feature to either direction of the component. Feature projection on the 2 principal component space is shown on the top left (Euclidean vectors*).

* This shows the contribution (length) and direction for each of the gene sets in the PCA plot.

Scientific Plenary VII: Improving Patient Experience and Outcomes

Tuesday, March 27, 2018

Moderators: Kian Behbakht, MD, *University of Colorado Denver, Aurora, CO, USA*

Gregg Nelson, MD, *Tom Baker Cancer Centre, Calgary, Canada*

51 – Scientific Plenary

GOG 244, The lymphedema and gynecologic cancer (LEG) study: The association between the gynecologic cancer lymphedema questionnaire (GCLQ) and lower extremity lymphedema

J.Carter^a, H.Huang^b, J.A.Armer^c, J.W.Carlson^d, S.Lockwood^e, S.Nolte^f, B.R.Stewart^c, L.Wenzel^g, J.Kauderer^b, A.Hutson^b, J.L.Walker^h, A.C.Fleuryⁱ, J.T.Soper^j, C.A.Mathews^k, O.Zivanovic^l, W.E.Richards^l, D.S.Alberts^m and R.R.Barakat^a. ^a*Memorial Sloan Kettering Cancer Center, New York, NY, USA*, ^b*Gynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA*, ^c*University of Missouri, Columbia, MO, USA*, ^d*Mercy Clinic - Women's Oncology, Springfield, MO, USA*, ^e*SGNO, Fort Worth, TX, USA*, ^f*Abington Memorial Hospital, Abington, PA, USA*, ^g*University of California, Irvine, Irvine, CA, USA*, ^h*The University of Oklahoma, Oklahoma City, OK, USA*, ⁱ*Women's Cancer Center of Nevada, Las Vegas, NV, USA*, ^j*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*, ^k*Women & Infants Hospital, Brown University, Providence, RI, USA*, ^l*Lewis Cancer & Research Pavilion at St. Joseph's Candler, Savannah, GA, USA*, ^m*The University of Arizona Cancer Center, Tucson, AZ, USA*

Objective: To explore whether patient self-reported symptoms, as measured by the Gynecologic Cancer Lymphedema Questionnaire (GCLQ), are associated with a diagnosis of lower extremity lymphedema (LLE) and limb volume change (LVC) in patients who have undergone surgery, including lymphadenectomy, for endometrial, cervical, or vulvar cancer on GOG study 244.

Method: The GCLQ has 20 questions (symptoms) that can be grouped into 7 symptom clusters: aching, heaviness, infection-related, numbness, physical functioning, swelling (general), and swelling (limb). A symptom cluster score was calculated by summing items within each cluster, and GCLQ total score was the summation of 7 symptom cluster scores. LLE was defined as patients reporting an LLE diagnosis on the GCLQ post surgery. Leg volume was measured by taking circumferential measurements at 10-cm intervals starting 10 cm above the bottom of the heel and continuing to the inguinal crease; leg volume was the summation of the truncated cone volumes. A linear mixed model was fitted for the change in symptom cluster scores and GCLQ total score and adjusted for disease sites and assessment time.

Results: Among 1,000 eligible patients, including 800 endometrial, 158 cervical, and 42 vulvar cancer patients, 931 were evaluable for GCLQ data and 895 evaluable for the association between GCLQ score and LVC by limb measurement. Thirteen percent of the evaluable patients reported a diagnosis of LLE; this included 17% (24/142) of cervical, 11% (83/750) of endometrial, and 38% (15/39) of vulvar cancer patients. Significantly more patients reported ≥ 4 increase in GCLQ total score in those diagnosed versus those not diagnosed with an LLE ($P < 0.001$). Changes from baseline were significantly larger on all GCLQ symptom cluster scores in patients with LLE when compared to those without LLE. LVC of 10% or greater (vs $< 10\%$) was significantly associated with symptoms of swelling in general ($P < 0.001$), heaviness ($P = 0.005$), infection-related symptom ($P = 0.002$), and physical functioning ($P = 0.004$).

Conclusion: Patient self-reported symptoms measured on the GCLQ were able to discern between those with and without an LLE diagnosis and LVC. The GCLQ can be readily used to identify LLE symptoms, thereby enabling evidence-based triage for early intervention in patients at risk for the development of LLE.

52 - Scientific Plenary

Patient-reported symptom burden and functional recovery before and after enhanced recovery after surgery (ERAS) implementation: A comparison between open and minimally invasive surgery

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Objective: Enhanced Recovery After Surgery (ERAS) protocols are associated with improved clinical outcomes in women undergoing open gynecologic surgery. The benefits of ERAS in patients undergoing minimally invasive surgery (MIS) is not well understood. We compared patient-reported outcomes (PROs) and self-reported functional recovery longitudinally between patients who underwent gynecologic surgery (open vs MIS) before and after implementation of ERAS.

Method: Perioperative symptom burden and functional recovery was measured using the MD Anderson Symptom Inventory-Ovarian Cancer (MDASI-OC), a 27-item validated tool. All patients completed a preoperative baseline. For open surgical patients, PROs were collected daily while hospitalized and at least weekly for 8 weeks. For MIS patients, PROs were given daily for 7 days, then weekly for 6 weeks. LOWESS curves were created through locally weighted polynomial regression. Linear mixed-effect modeling was performed. Kaplan-Meier curves were used to estimate median time to return to mild/no symptom burden. Adjustment for multiple comparisons for the log rank test was done.

Results: In total, 555 patients were included (open control $n = 65$, open ERAS $n = 267$, MIS control $n = 147$, MIS ERAS $n = 76$). The top 5 highly rated symptoms after surgery were fatigue, pain, abdominal pain, disturbed sleep, and drowsiness. Longitudinally, participation in ERAS improved fatigue, pain, sleep, and walking in women undergoing open surgery (Figure 1a-d). Among MIS patients, only disturbed sleep was significantly improved through ERAS (Figure 1c). For open surgical patients, ERAS significantly decreased return to mild/no fatigue (9 days vs 30 days, $P = 0.008$), but there was no difference in the MIS groups (3 days for both ERAS and control, $P = 0.4$). Similarly, participation in ERAS decreased time to mild/no pain (11 vs 16 days, $P = 0.03$), for patients undergoing open surgery compared to 4 days for both MIS groups, $P = 0.84$. Interference with walking was decreased in ERAS open patients versus control (5 vs 13 days, $P = 0.001$), compared to ERAS MIS versus control (2 vs 3 days, $P = 0.99$).

Conclusion: ERAS programs significantly improved patient-reported symptom burden and functional recovery in women undergoing open gynecologic surgery. While participation in ERAS narrows the gap between PROs in open and MIS surgery, MIS is preferable whenever possible given the consistent improvements in symptom burden and functional recovery.

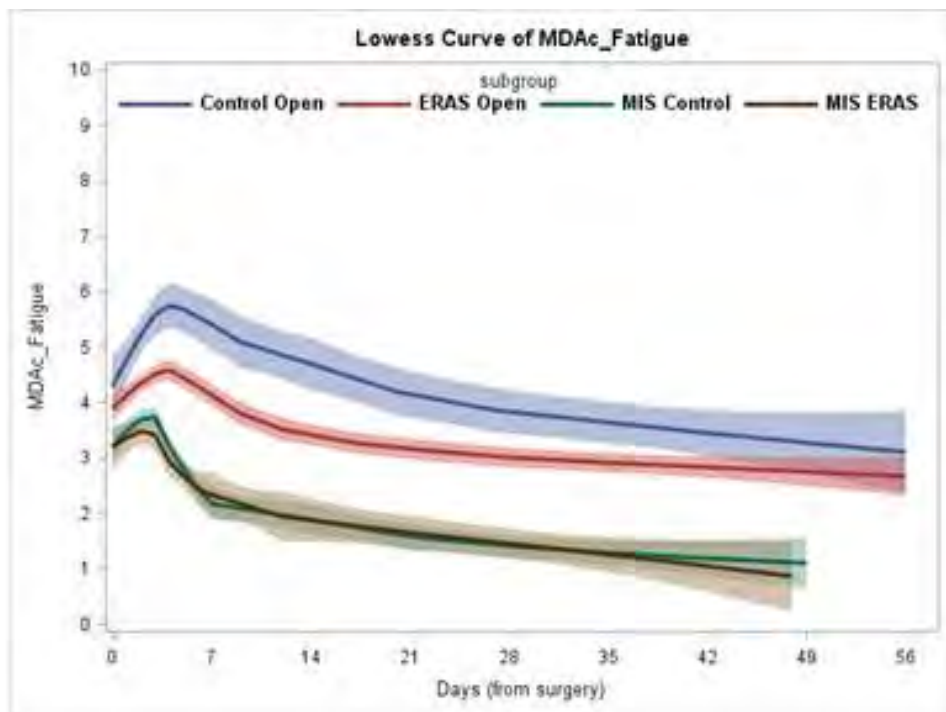


Fig. 1a. Patient reported fatigue over time. MIS ERAS referent group: Control open and ERAS open $P < .0001$, MIS control $P = .33$.

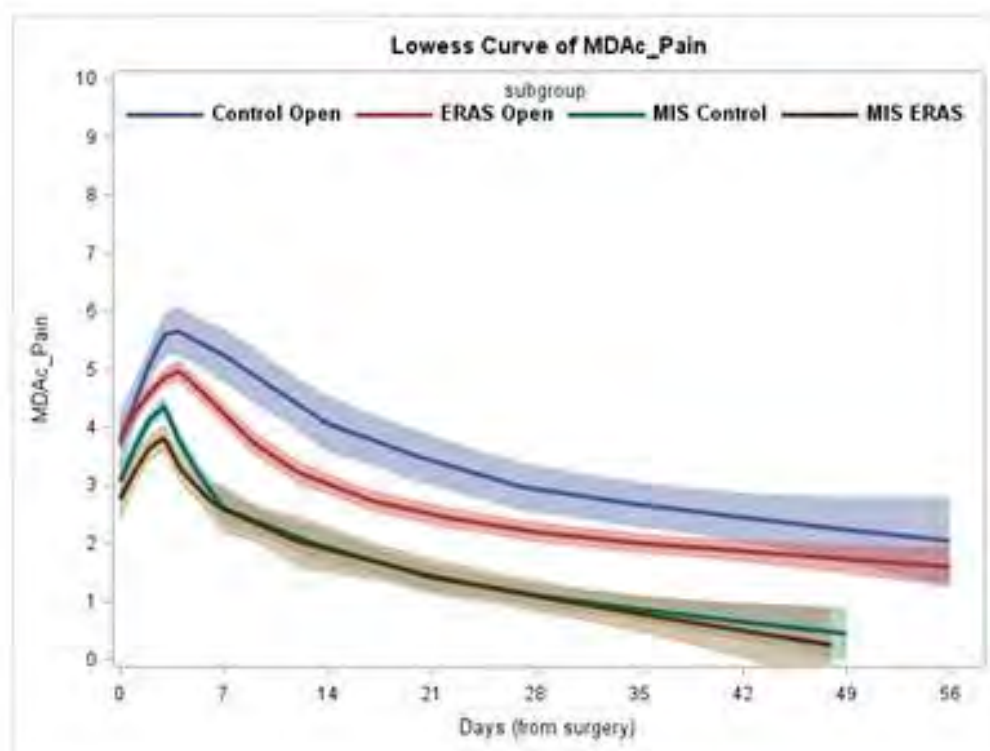


Fig. 1b. Patient reported pain over time. MIS ERAS referent group: Control open $P < .0001$ and ERAS open $P = .0014$, MIS control $P = .22$.

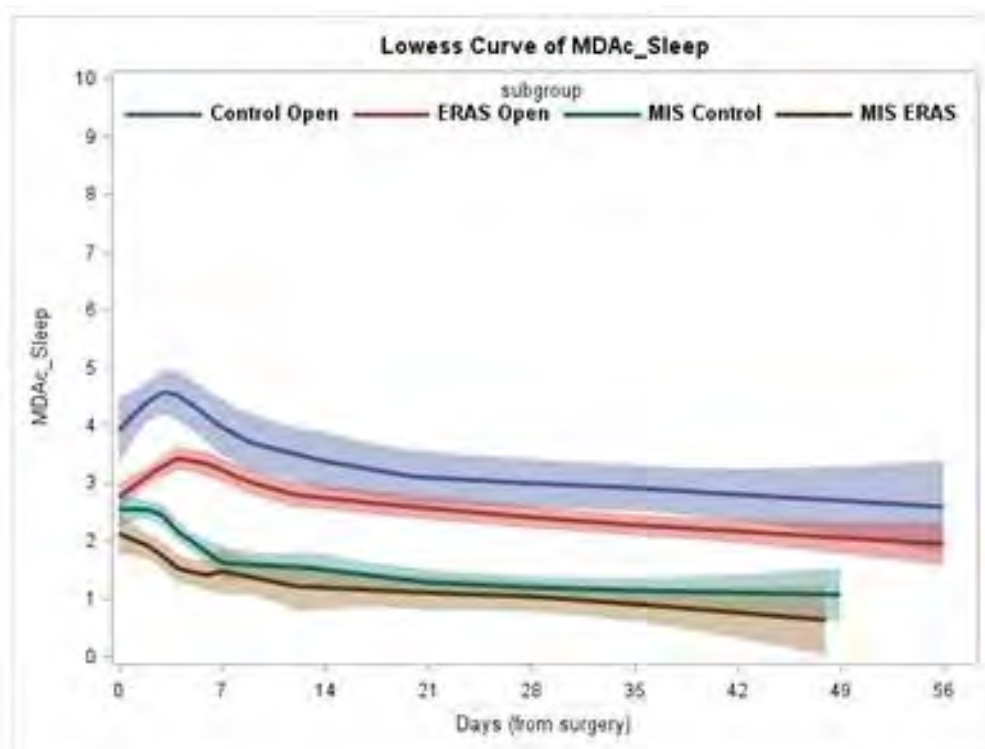


Fig. 1c. Patient reported sleep disturbance over time. MIS ERAS referent group: Control open and ERAS open $P < .0001$, MIS control $P = .03$.

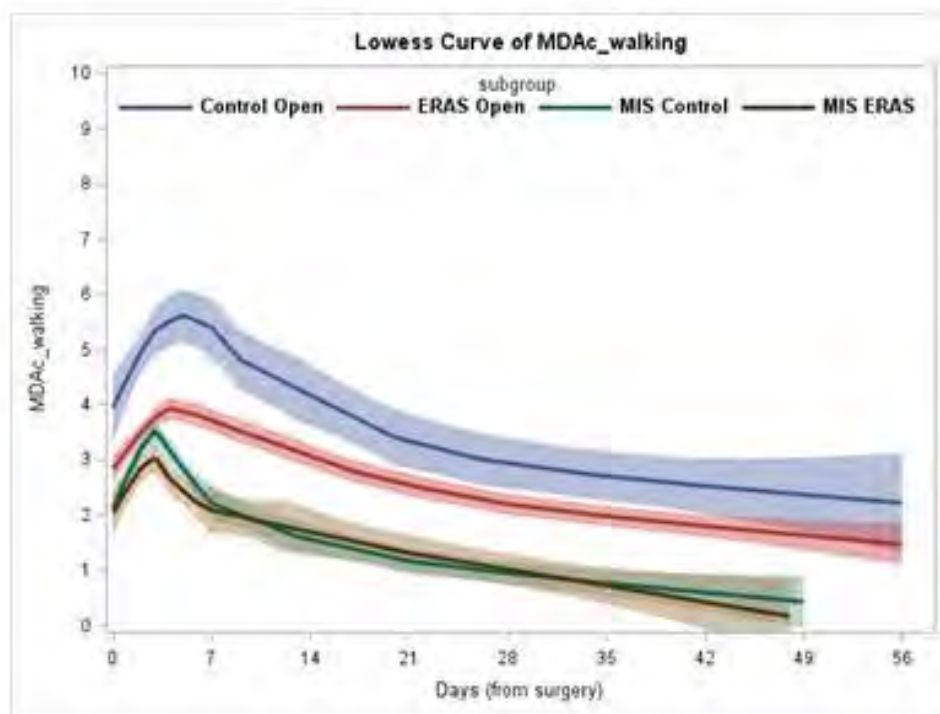


Fig. 1d. Patient reported interference with walking over time. MIS ERAS referent group: Control open $P < .0001$ and ERAS open $P = .003$, MIS control $P = .12$.

53 - Scientific Plenary

Gestational trophoblastic disease electronic consults: What do patients and physicians want to know?

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Objective: Given the rarity of gestational trophoblastic disease (GTD), specialized regional and national centers for GTD have been established. These centers serve at least 3 purposes: to improve care for women with GTD, enhance research through collaboration, and educate other clinicians about this rare disease. This study serves to understand the GTD knowledge gap by examining both patient and physician inquiries received at a specialized GTD center.

Method: All email consults received by specialists at our center between March 2016 and March 2017 were analyzed. Information collected included geographic location from which the consult came, source of inquiry, reason for the consult, type of GTD, and the advice/response provided. Descriptive statistics were used to analyze the major trends.

Results: Over 1 year, specialists at our institution received 102 electronic consults. Physicians sent 49 (48%), and patients sent 53 (52%) consults. The vast majority of electronic consults were sent by physicians and patients within the United States; however, 11% were directed from international locations. Among physicians, gynecologic oncologists were the most common specialty to consult our institution (65%), followed by medical oncologists (18%) and obstetrician gynecologists (18%). The majority of questions from gynecologic (62%) and medical oncologists (77%) concerned chemotherapy administration or alternative treatment regimens. This contrasted with general obstetrician gynecologists who more commonly asked about hCG monitoring (62%). Difficulties with appropriate FIGO staging and WHO risk score assignment were common themes that arose. Most of the confusion centered on the use of chest computed tomography rather than plain chest x-ray for assessment of lung metastases. Unlike physicians, patients were most concerned with the duration of hCG monitoring (51%) and when they could conceive.

Conclusion: This is the first attempt to quantify and describe electronic consults to a specialized GTD center. Both physicians and patients in the United States and abroad frequently utilize this platform to improve their knowledge about GTD management and follow-up. Although the types of inquiries from physicians and patients varied, they highlight fundamental gaps in understanding and potential opportunities for formal education in this rare disease.

54 - Scientific Plenary

It's like "magic": The mobile application for genetic information on cancer

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Objective: Current guidelines published by the National Comprehensive Cancer Network recommend that all women with ovarian, fallopian tube, or primary peritoneal cancers receive further genetic risk evaluation by a genetic counselor. Physicians however, continue to underrefer and women to underutilize genetic services. We seek to harness mobile phone technology as a means of promoting genetic counseling among ovarian cancer survivors. The overall study objective is to develop and assess the feasibility and effectiveness of a week-long and theory-based Mobile Application for Genetic Information on Cancer (mAGIC) intervention aimed to persuade ovarian cancer survivors to receive genetic counseling (GC).

Method: We developed the mAGIC intervention following Fogg's Behavior Model. After incorporating a Community Based Participatory Research approach and conducting focus groups to guide content development, this intervention consisted of 3 parts: (1) identifying barriers, (2) developing motivators, and (3) providing triggers to action. We then performed a prospective randomized trial in which women with a history of epithelial ovarian, primary peritoneal or fallopian tube cancer who had previously not received GC were randomized to either the app intervention or control. One week following the 7-day mobile app versus usual care, a telephone survey was performed to determine knowledge and intent to pursue GC. Uptake of GC at 3 months is being assessed by survey.

Results: Since February 2016 we have accrued 102 of a planned 104 women. Individuals randomized to the mAGIC intervention scored better on the knowledge quiz with mean scores of 9.4 ± 1.0 versus 7.1 ± 1.5 in the control group ($P < 0.0001$). At 1 week, significantly more individuals in the mAGIC group decided they wanted to have GC (63% vs 25% in the control group, $P = 0.001$). In addition, 84% of individuals in the intervention group had talked with their family about GC versus 65% in the control group ($P = 0.05$). See screen shots in Figure 1.

Conclusion: Our findings suggest that individuals randomized to the mAGIC app learned more, were more likely to pursue GC, and talked with their family about GC. Three-month survey results are pending. Our project provides important implications for extending this mHealth intervention to directly increase use of GC among high-risk patients and their family members.

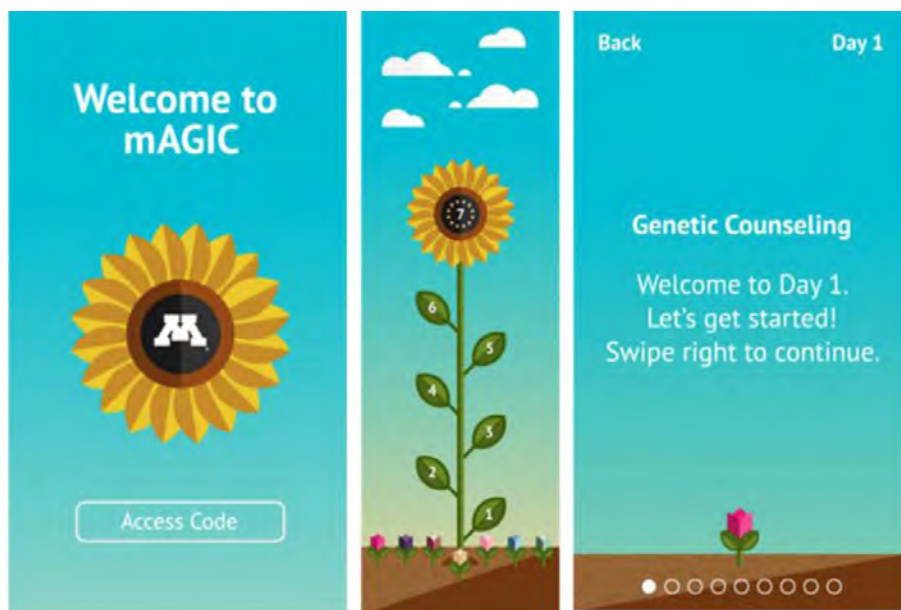


Fig. 1. Screenshots of mAGIC mobile app.

55 - Scientific Plenary

Rethinking cervical cancer screening guidelines in an aging U.S. population

S.E. Dilley, J.A. O'Donnell, H.J. Smith, S. Bae and W. Huh. *University of Alabama at Birmingham, Birmingham, AL, USA*

Objectives: The ACS/ASCP/ASCCP and USPSTF currently recommend cessation of cervical cancer screening after 65 years of age; however, recent studies suggest that age-related differences in cervical cancer incidence and outcomes warrant further attention. The objective of this study was to further quantify race- and age-related differences in cervical cancer incidence using nationwide databases, and to examine the potential benefits of cervical cancer screening in the over-65 years of age patient population

Methods: The Surveillance, Epidemiology and End Results (SEER-18) program database and National Cancer Data Base (NCDB) were queried to determine incidence of cervical cancer in participating registries and hospitals. Descriptive statistics and rates of cervical cancer by age quintile and decile over time were calculated using SAS.

Results: Using SEER-18 data, overall rates of cervical cancer cases have decreased over time, with a Kendall's Tau B of -0.85 ($P < 0.001$) for patients 20–49 years and -0.68 ($P < 0.001$) for those 75 years and older. In the SEER-18 database, 19.7% of cervical cancer cases were diagnosed in women 65 years or older from 2000 to 2014. This proportion did not change significantly over time. When stratified by race, non-Hispanic black women were even more likely than other racial/ethnic groups to be diagnosed after age 65 years (22.9%, $P < 0.001$). In the NCDB, 18.9% of cervical cancer cases were diagnosed in women over age 65 years from 2004 to 2014. When examined by age decile, only 5.1% of cervical cancer cases were diagnosed from age 20 to 29 years, while 8% were diagnosed from age 70 to 79 years in the NCDB. See Table 1.

Conclusion: Current guidelines for cervical cancer screening recommend cessation of screening after age 65 years and are based on theoretical modeling. Our data suggest that a considerable proportion of women are diagnosed with cervical cancer after age 65 years, which may suggest that patients are aging out of screening prematurely. An age-related disparity is especially present in non-Hispanic black women, a population already known to have disproportionately high cervical cancer incidence and mortality. Professional societies and the USPSTF should strongly consider extending the age limit for cervical cancer screening to improve outcomes and health equity, as 1 in 5 cases of cervical cancer occur after 65 years of age.

Table 1. Proportion of cervical cancer cases diagnosed by age group and race.

	NCDB 2004-2014 <i>n</i> (%)	SEER 2000-2014 <i>n</i> (%)
Age 65+	20213 (18.9%)	10,360 (19.7%)
Non-Hispanic Black	3,723 (22.1%)	1,680 (22.9%)
Non-Hispanic White	13,188 (19.0%)	5,807 (20.5%)
Hispanic	1,935 (14%)	1,704 (14.8%)
Other/Unknown	1,357 (19.9%)	1,167 (21.9%)

56 - Scientific Plenary

Patient-reported outcomes after surgery for endometrial carcinoma: Prevalence of lower extremity lymphedema after sentinel lymph node mapping (SLNM) compared to lymphadenectomy

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Objective: To compare the prevalence of patient-reported lower extremity lymphedema (LEL) in patients undergoing sentinel lymph node (SLN) mapping versus lymphadenectomy (LND) as part of surgery for newly diagnosed endometrial carcinoma.

Method: Patients from a single institution who had primary surgery for endometrial cancer between January 2006 and December 2012 and were still alive were mailed a survey that included a validated 13-item LEL screening questionnaire in August 2016, giving a minimum of 3 years and 8 months since surgery for all patients. The LEL questionnaire results in a score range of 0–52, with a cutoff of ≥ 5 predicting for LEL. Responses were excluded if 6 or fewer of the 13 items were answered or if patients responded that they had been diagnosed with LEL prior to surgery. Patients who had an SLN mapping with concurrent “backup” lymphadenectomy or who did not map and had a bilateral LND were included in the LND cohort. Patients who had a side-specific LND, as per our algorithm, were included in the SLN cohort. Medical records were reviewed for demographics, details of surgery, and adjuvant therapy. Appropriate statistical methods were used.

Results: Of the 1,275 potential participants identified, 623 (49%) responded to the survey. There were 599 evaluable responses (180 SLN, 352 LND, 67 HYST alone). Median BMI was similar in both cohorts ($P = 0.99$). External-beam radiation therapy (EBRT) was used in 10/180 (6%) SLN and 35/352 (10%) LND patients ($P = 0.1$). Self-reported LEL prevalence was 27% (49/180) in the SLN cohort compared with 41% (144/352) in the LND cohort (OR = 0.85, 95% CI 1.25–2.74, $P = 0.002$). LEL prevalence was 51% (23/45) in patients who received EBRT compared with 35% (170/487) in those who did not (OR = 1.95, 95% CI 1.06–3.6, $P = 0.03$). Increasing BMI was associated with the prevalence of LEL (OR = 1.04, 95% CI 1.02–1.06, $P = 0.001$). After controlling for EBRT and BMI, LND retained independent association with an increased prevalence of LEL compared to SLN (OR = 1.8, 95% CI 1.22–2.69, $P = 0.003$).

Conclusion: This is the first study to assess patient-reported LEL after SLN mapping for endometrial cancer. SLN mapping is independently associated with a significantly lower prevalence of patient-reported LEL compared with LND. Increasing BMI, as well as the use of adjuvant EBRT, is also associated with an increased prevalence of patient-reported LEL.

Scientific Plenary VIII: Last But Not Least....

Tuesday, March 27, 2018

Moderators: Elizabeth Jewell, MD, *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Renata R. Urban, MD, *University of Washington Medical Center, Seattle, WA, USA*

57 - Scientific Plenary

A novel site-specific proteomic screening test for ovarian cancer in a large prospective multi-institutional clinical study

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Objective: Despite advancements in ovarian cancer (OC) therapy, the greatest benefit in survival would be the discovery of an effective screening test that could accurately detect early-stage disease. This study's objective was to develop a site-specific proteomic-based triage test for OC using cervico-vaginal fluid (CVF).

Method: After institutional review board approval, more than 20 sites prospectively collected CVF from postmenopausal patients at initial visit to gynecologic oncologist prior to surgical evaluation of a pelvic mass. Specimens were stored/shipped in preservative liquid for mass spectrometry analysis. Specimens were blinded and randomly assigned for analysis using block randomization stratified by age and stage of cancer. Wilcoxon FDR and Area Under Curve (AUC) were set to determine peptides with $P < 0.01$. Peptides modeling was performed using "lasso" regression analysis with cross validation to determine the most accurate set of peptide predictors. Attention was given to negative predictive value (NPV), which allows a proper triage test for pelvic mass without cancer, and AUC, which allows proper screening test for all patients.

Results: A total of 442 specimens were collected with 25% ($n = 109$) being ovarian cancers, 58% ($n = 255$) benign pelvic masses, 6% ($n = 26$) borderline tumors of the ovary, and 5% ($n = 22$) cancers from other sites. Mean age was 63.3 years, and the majority of patients were white (80%). The majority of OC patients had stage I–II disease ($n = 70$, 64%), with the most common histology being serous ($n = 57$, 53%). For all histology/all stages versus benign, modeling determined NPV = 0.90 and AUC = 0.80 ($P = 1.4 \times 10^{-14}$). Subcohort analysis of serous histology/all stages versus benign, NPV = 0.96 and AUC = 0.87 ($P = 1.1 \times 10^{-14}$). For serous histology/early stage I–II versus benign, NPV = 1.0 with an AUC of 0.97 ($P = 5.4 \times 10^{-8}$) with a panel of 9 peptides. As such, this panel would correctly identify ~97% of all patients as having either early-stage I–II cancer or benign mass (Table 1).

Conclusion: Collectively, these data are promising both as a triage test that can accurately identify patients with a benign pelvic mass who are without cancer, and as a general screening test with sufficient areas under curves. Of note, ~65% of patients in this study had stage I–II disease, which may allow us to move this concept forward toward an effective screening test for early-stage disease.

Table 1. Models to Predict Ovarian Cancer vs. Benign.

All Histologies and All Stages								
Peptides	TP	TN	Sensitivity	Specificity	PPV	NPV	AUC	P Value
3	54	144	0.720	0.629	0.388	0.873	0.702	1.4e -07
7	50	173	0.667	0.755	0.472	0.874	0.744	2.3e -10
11	56	167	0.747	0.729	0.475	0.898	0.771	2.0e -12
17	56	172	0.747	0.751	0.496	0.901	0.796	1.4e -14
SEROUS Histology and All Stages								
Peptides	TP	TN	Sensitivity	Specificity	PPV	NPV	AUC	P Value
2	21	202	0.477	0.882	0.438	0.898	0.712	7.9e -06
4	29	190	0.659	0.830	0.426	0.927	0.760	5.0e -08
7	33	188	0.750	0.821	0.446	0.945	0.801	2.7e -10
11	34	188	0.773	0.821	0.453	0.949	0.837	1.4e -12
17	36	183	0.818	0.799	0.439	0.958	0.868	1.1e -14
SEROUS Histology and Early Stage 1 / 2								
Peptides	TP	TN	Sensitivity	Specificity	PPV	NPV	AUC	P Value
3	10	167	0.833	0.729	0.139	0.988	0.824	1.5e -04
6	9	218	0.750	0.952	0.450	0.986	0.906	2.1e -06
9	12	185	1.00	0.808	0.214	1.00	0.966	5.3e -08
18	12	229	1.00	0.996	0.923	1.00	1.00	5.5e -09

58 - Scientific Plenary

Evidence for synthetic lethality between bevacizumab and chemotherapy in advanced, p53 null endometrial cancers

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Objective: Mutations in p53, which are common in patients with advanced endometrial cancer, represent a platform upon which to design combinatorial regimens of molecular inhibitors + chemotherapy with the potential to result in synthetic lethality. GOG/NRG Study 86P, A Three Arm Randomized Phase II Study of Paclitaxel/Carboplatin/Bevacizumab (NSC#704865, IND#7921), Paclitaxel/Carboplatin/Temsirolimus (NSC#683864, IND#61010) and Ixabepilone (NSC#710428, IND# 59699)/Carboplatin/ Bevacizumab as Initial Therapy for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer, was one of the first attempts to combine molecular inhibitors such as bevacizumab or temsirolimus with chemotherapy in patients with advanced endometrial cancer.

Method: From the 250 patients enrolled and evaluable on this study, DNA sequencing of *TP53* and immunohistochemistry for p53 protein were performed in order to categorize cases from GOG/NRG Study 86P as p53 (1) wildtype, (2) loss of function (LOF) or null, or (3) gain of function (GOF) or oncogenic. We next examined the relationship between the p53 mutational class

and progression-free survival (PFS). The molecular mechanisms of action of the drugs were then studied in vitro using cell models of advanced endometrial cancer.

Results: We noted a marked improvement in PFS for patients with p53 mutations resulting in a p53 null state who were treated with bevacizumab + chemo compared to temsirolimus + chemo and compared to the other p53 mutational classes and treatments. The PFS for the p53 null or LOF mutations was 19.6 months compared to 12.2 months with p53 wildtype and 10.6 months compared to p53 oncogenic or GOF mutations when treated with carboplatin/paclitaxel + bevacizumab as noted in Table 1. Using cell models, the molecular mechanism of synthetic lethality was found to result from the ability of agents such as bevacizumab, which block signaling downstream of tyrosine kinases, to abrogate cell cycle checkpoints in the absence of p53. This causes the premature entry of cancer cells into vulnerable phases of the cycle where chemotherapeutic agents are most active.

Conclusion: We conclude that p53 null status may identify patients with advanced endometrial cancer who will particularly benefit from bevacizumab + chemotherapy.

Table 1. Progression-Free Survival (PFS) by Primary Tumor p53 Mutation and Treatment.

p53 mutation	Treatment	PFS (median) in months	95% CI (lower)	95% CI (upper)
WT	Bev + PC	12.2	10.1191	17.0513
WT	Tem + PC	10.2	8.3778	15.3758
GOF	Bev + PC	10.6	4.1396	15.0472
GOF	Tem + PC	8.6	2.6940	12.7146
LOF	Bev + PC	19.6	4.0411	25.0678
LOF	Tem + PC	8.9	2.2012	10.0554

59 - Scientific Plenary

Randomized trial of adjuvant chemotherapy versus concurrent chemoradiotherapy in early-stage cervical cancer after radical surgery: A Chinese Gynecologic Oncology Group study (CSEM-002)

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^aTongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, ^bWomen's Hospital, School of Medicine, Zhejiang University, Zhejiang, China, ^cQilu Hospital, Shandong University, Jinan, China

Objective: Radical hysterectomy (RH) including pelvic lymphadenectomy should be enough for local disease control in early-stage cervical cancer patients. Adjuvant chemotherapy alone after RH may be an alternative strategy for its efficacy for control of both microscopic local and distant metastatic diseases, preservation of ovarian function in young females, and avoidance of long-term serious radiation complications. It is worthy to conduct an RCT to evaluate the effects and toxicity of adjuvant chemotherapy after RH among early-stage cervical cancer patients with risk factors.

Method: Eligible patients with FIGO stage IB–IIA were randomly assigned in a 1:1 ratio to receive either adjuvant chemotherapy (CT group) or adjuvant concurrent chemoradiotherapy (CCRT group). In the CT group, paclitaxel plus cisplatin (TP) combination therapy was performed according to the risk factors. In the CCRT group, patients received external beam radiation therapy with cisplatin once a week; brachytherapy was given as necessary (Figure 1). The primary outcome was 2-year progression-free survival (PFS). Planned sample size was 345 patients to show noninferiority of postoperative adjuvant chemotherapy as compared with adjuvant CCRT with the threshold hazard ratio (HR) of 2.24.

Results: Recruitment was finished in November 2014. In July 2017, a total of 324 patients were enrolled in the trial from 7 hospitals around China. PFS was similar in both groups. The HR for relapse in the intention-to-treat population was 0.878 ($P = 0.731$) in favor of patients assigned to adjuvant chemotherapy (95% CI 0.418–1.845), excluding the predefined noninferiority boundary (Figure 2). Overall survival was similar to PFS. Patterns of recurrence in those patients whose disease recurred are summarized in Table 1. There was no statistically significant difference in the patterns of recurrence between the groups, although there was a greater trend toward a higher distant failure rate in the adjuvant CCRT group (Table 1). Subgroup analysis and treatment-related adverse events, ovarian function, and quality of life are under analysis.

Conclusion: Adjuvant chemotherapy was not inferior to adjuvant CCRT and could be a standard treatment option for patients with FIGO stage IB–IIA cervical cancer with surgically confirmed risk factors.

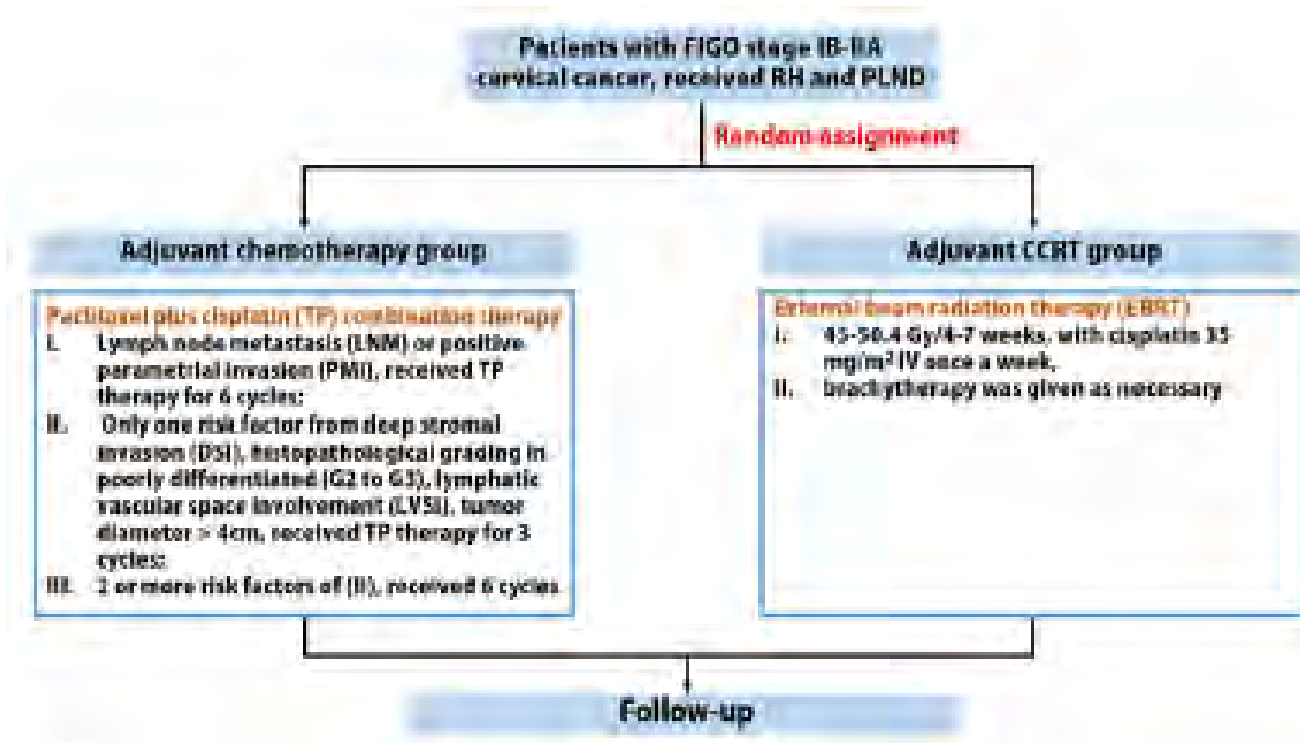


Fig. 1. Treatments of the groups.

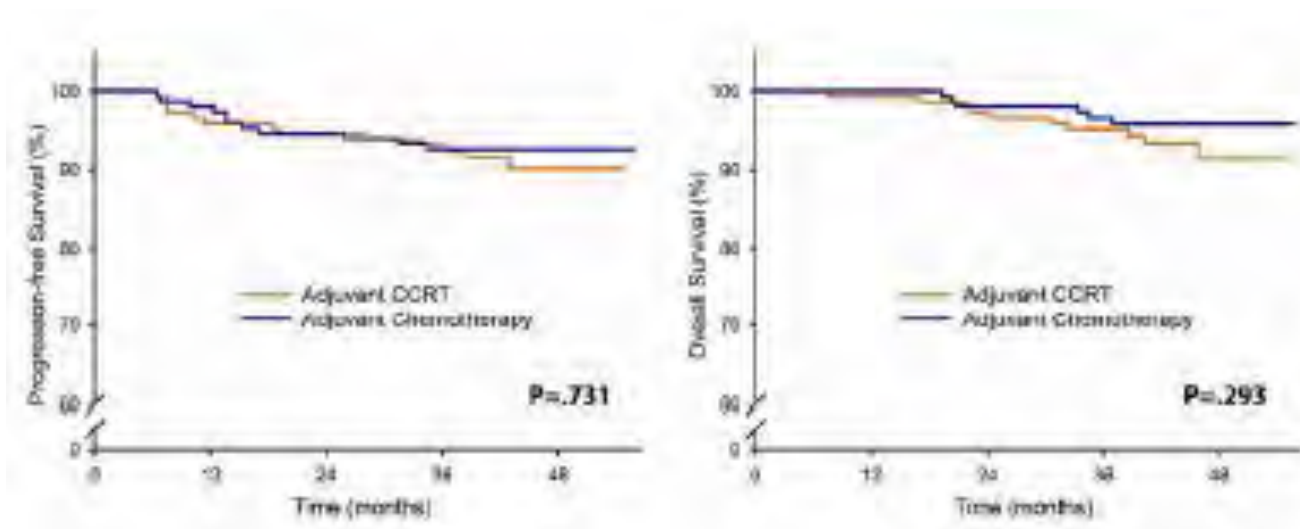


Fig. 2. PFS and OS of the groups.

Table 1. Recurrence and death patterns.

Treatment group	Adjuvant CT group (n = 13)	Adjuvant CCRT group (n = 13)	P value
Recurrence			0.151
Local	9	4	
Locoregional	3	5	
Distant	1	4	
Death	9	10	1.000

60 - Scientific Plenary

Come back in six months, or never? Defining surveillance and survivorship in gynecologic malignancies with an evidence-based approach

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Objective: Survivorship involves a multidisciplinary approach to both surveillance and the management of comorbid conditions and secondary cancers; however, practitioner roles and timing are based on arbitrary 5-year cutoffs. Here, we used a novel method analyzing overall survival hazards to systematically define these cutoffs for transitions of care.

Method: The SEER database was queried for survival data on women aged 18–100 years with a primary diagnosis of any uterine, endometrial, ovarian, cervical, vulvar, vaginal, and placental cancers. Women were excluded if they had a personal history of a nongynecologic cancer. Their immediate risk of death (so-called mortality hazard) was plotted over time. The point at which this hazard approached the baseline of age-matched controls defined a high-risk mortality period. The persistent elevated mortality above baseline was also noted. Finally, the point at which the hazard of cancer-related death fell below noncancer causes was also noted.

Results: Complete data were available for 291,624 women with the gynecologic cancers of interest. The high-risk mortality period was shortest among women with placental or vulvar cancers (3 years) followed by cervix, uterine, and vaginal cancers (4, 5, and 5 years, respectively) and longest among those with ovarian cancer (8 years). Elevated mortality in the follow-up period was undetectable in the placental site cancers and highest among ovarian cancers (1.2%). Most cancers (uterine, cervix, vulvovaginal, and placental) never had cancer mortality surpass noncancer mortality, while ovarian cancer mortality surpassed all other cause mortality for 9 years. See Figure 1.

Conclusions: These findings indicate that a standardized 5-year surveillance period is both inadequate for some cancers and excessive for others. Cancers of the uterus, vulva, and vagina had short high-risk mortality periods, and demonstrated that cardiovascular disease and other lifestyle-associated morbidities pose a greater risk than cancer mortality, suggesting we divert more resources to primary care-led survivorship care. In contrast, ovarian cancer requires the most resources with the longest high-risk period, and highest persistent baseline mortality risk, and the highest increased mortality, all arguing for longer follow-up with a gynecologic oncologist.

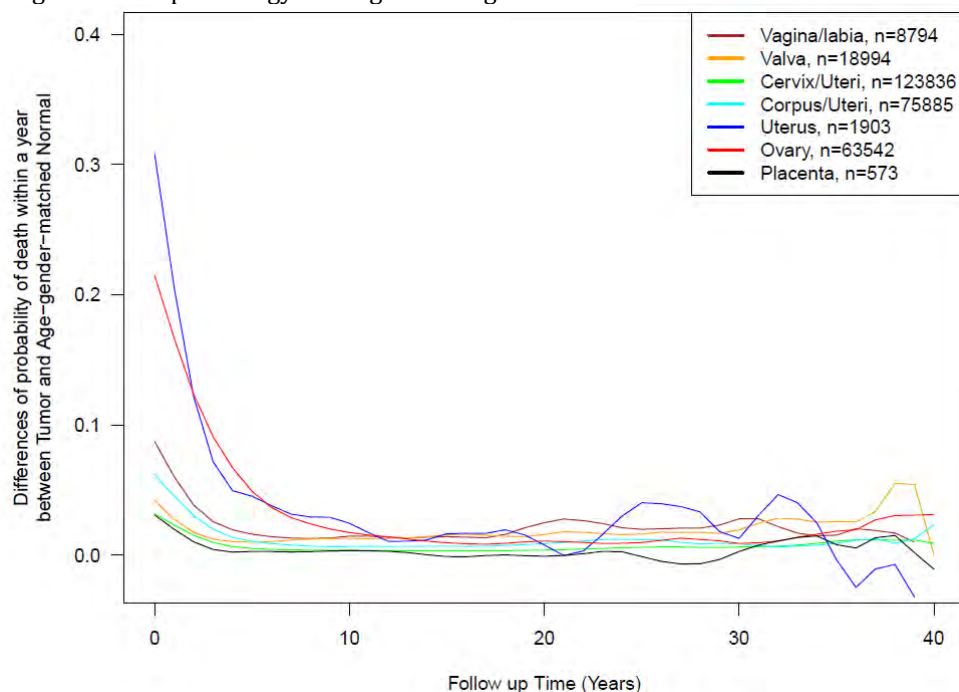


Fig. 1. Difference of probability of death within one year between tumor and normal in SEER data across women's cancers.

Featured Poster Session

61 - Featured Poster Session

Benign surgery performed by gynecologic oncologists: Is selection bias altering our ability to measure surgical quality?

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Objective: To compare the characteristics of women undergoing hysterectomy for benign disease with either a benign gynecologist or gynecologic oncologist and to assess for differences in complication rates with and without risk adjustment.

Method: Patients undergoing benign hysterectomy recorded in the National Surgical Quality Improvement Program (NSQIP) targeted hysterectomy file in 2015 were identified. The primary outcome was any postoperative complication. Stratified analysis was performed by route of surgery. Bivariate tests and modified Poisson regression were used to adjust for confounding by procedure type and patient characteristics.

Results: We identified 17,639 patients who underwent hysterectomy for benign indications, whose primary surgeon was a benign gynecologist (82%, $n = 14,550$) or a gynecologic oncologist (18%, $n = 3,089$). Patients who underwent surgery with gynecologic oncologists were older (51 vs 46 years, $P < 0.001$), had higher BMIs (32 vs 30, $P < 0.001$), had more prior abdominal surgery (29% vs 25%, $P < 0.001$), had larger uteri (299 vs 271 g, $P < 0.001$), and were more likely to be white race (73% vs 62%, $P < 0.001$). They were also more likely to be diabetic (10.6% vs 7.0%, $P < 0.001$), to be hypertensive (34% vs 25%, $P < 0.001$), and had higher ASA and Charlson comorbidity scores ($P < 0.001$ and $P < 0.001$, respectively). For laparoscopy, surgery with a gynecologic oncologist was associated with a decreased incidence of postoperative complication (RR = 0.80, 95% CI 0.66–0.98). This association persisted with adjustment for patient and operative characteristics (aRR = 0.77, 95% CI 0.63–0.94). However, for laparotomy, surgery with a gynecologic oncologist was associated with an increased risk of complication (RR = 1.18 95% CI 1.01–1.38). The direction of this relationship changed with adjustment (aRR = 0.90, 95% CI 0.76–1.07).

Conclusion: Strong selection bias exists between patients operated on by a gynecologic oncologist versus a benign gynecologist even for benign indications. This is reflected by the higher prevalence of known factors associated with complication and the change in association between specialty and complication with risk adjustment. Quality measurement should take this selection bias into account when comparing complication rates between benign gynecologists and gynecologic oncologists even for the same procedures.

62 - Featured Poster Session

Racial disparities in hereditary gynecologic cancer risk assessment: What and why?

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Objective: The aim of this study was to compare referral patterns, genetic testing, and pathogenic variant rates between black and white patients in a large southeastern gynecologic cancer risk assessment clinic.

Method: We performed a cross-sectional study of an institutional review board-approved prospective, cohort study of patients from a gynecologic cancer risk assessment clinic. Data evaluated included age, race, frequency of genetic testing, referral provider specialty, and indication, as well as frequency and types of pathogenic variants. Women reporting Hispanic or Jewish ethnicity as well as Asian, Native American, or Pacific Islander race were excluded.

Results: From 2010 to 2015, 588 (91.2%) white women and 57 (8.8%) black women were evaluated. Black women were younger (49.3 ± 12.5 years) than white women (54.2 ± 14.8 years, $P = 0.016$). Although approximately one-third of both black (36.0%) and white women (32.6%) were referred for family history alone, black women were more likely to be referred for a known pathogenic variant (20.0% vs 6.2%) and less likely to be referred for a personal history of ovarian cancer (24.0% vs 46.8%, $P = 0.0023$). While both groups were most likely referred by a gynecologic oncologist (black women 43.6% vs white women 63.0%), black women were more likely to be referred by a surgical oncologist (23.0% vs 12.8%) or a genetic counselor (12.8% vs 5.9%) than white women ($P = 0.0234$). Referral rates from primary obstetricians/gynecologists were similar (black women 15.3% vs white women 12.8%), while referral from other primary care providers was low in both groups (black

women 0% vs white women 2.9%). Both groups underwent similar rates of genetic testing (black women 82.4% vs white women 85.5%, $P = 0.5563$) and had similar rates of *BRCA1* mutations (12.7% vs 11.5%); however, black women were more likely to have *BRCA2* mutations (21.3% vs 9.5%, respectively, $P = 0.0194$).

Conclusion: Previous studies underrepresent black women in gynecologic cancer risk assessment clinics. Black women are more likely to be referred by a surgical oncologist or a genetics counselor than white women, suggesting that breast health clinics or services might be an entry point for black women for genetic counseling and testing. In addition, black women evaluated in our clinic were more than twice as likely as white women to carry a *BRCA2* mutation. Efforts should continue to increase awareness about the importance of referral of patients at the primary care level because this may help capture the subset of women who are not currently undergoing counseling and testing.

63 - Featured Poster Session

The utility of preoperative PET/CT in the detection of extrauterine disease in high-risk endometrial cancer: A prospective study

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Objective: The identification of extrauterine disease is critical in the management of high-risk endometrial cancer (EC). The purpose of this study was to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the detection of extrauterine disease on preoperative PET/CT when compared to pathological findings in high-risk EC patients.

Method: Women with high-risk EC were prospectively enrolled. High-risk EC included serous, clear cell, MMMT, grade 3 endometrioid, and grade 1/2 tumors with evidence of deep myometrial invasion or cervical involvement. They underwent preoperative PET/CT followed by primary surgery. Primary tumor factors including max SUV, peak SUV, metabolic tumor volume (MTV) SUV3, and MTV 40% were summarized and compared by lymph node status. Sensitivity, specificity, PPV, and NPV were calculated independently for the detection of lymphadenopathy and peritoneal disease by PET/CT.

Results: A total of 112 high-risk patients had a preoperative PET/CT between April 2013 and May 2016. On PET/CT, 25 patients (22%) had extrauterine disease; 16 (14%) had positive lymph nodes; and 9 (8%) had peritoneal disease. Median age was 62 (range 29–86) years. Median BMI was 30.8 kg/m² (range 15.8–64.3 kg/m²). There were 109 patients who underwent primary surgery, and 95 (87%) who underwent a complete pelvic and paraaortic lymphadenectomy (LAD). The sensitivity of PET/CT to detect positive nodes was 42.9% (95% CI 21.8–66.0); specificity, 90.5% (95% CI 81.5–96.1); PPV, 56.3% (95% CI 29.9–80.3); and NPV, 84.8% (95% CI 75.0–91.9%). There was no difference in primary tumor characteristics on imaging including median max SUV (18.1 vs 13.3, $P = 0.5$), peak SUV (15.8 vs 10.9, $P = 0.09$), MTV SUV3 (25.5 vs 23.9, $P = 0.72$), or MTV 40% (9.0 vs 18.9, $P = 0.14$) between patients with negative and positive lymph nodes, respectively. The sensitivity of PET/CT to detect peritoneal disease was 33.3% (95% CI 13.0–61.3); specificity, 97.9% (95% CI 91.8–99.6); PPV, 71.4% (95% CI 30.3–94.9); and NPV, 90.2% (95% CI 82.3–94.9).

Conclusion: Preoperative PET/CT did not reliably predict the presence of extrauterine disease in women with high-risk EC. However, given the high specificity of PET/CT in the detection of peritoneal disease, it could be considered in the preoperative treatment planning for patients with high-risk EC.

64 - Featured Poster Session

A comprehensive genomic analysis of neuroendocrine carcinoma of gynecologic and breast tumors

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Objective: Neuroendocrine carcinomas (NEC) of gynecologic and breast origin are aggressive histologic subtypes that confer a worse prognosis. We hypothesized that a single comprehensive genomic profiling (CGP) assay could better match breast and

gynecologic NEC subsets to mechanistically driven treatment modalities by simultaneously assessing tumor microsatellite instability (MSI), tumor mutation burden (TMB), and targetable genomic alterations (GA).

Method: CGP assay of 160 breast and gynecologic NEC from FFPE clinical specimens (53 cervical, 48 breast, 32 ovarian, 21 uterine, and 7 vaginal) was conducted by hybridization capture of up to 315 cancer-related genes (FoundationOne) and provided GA (short variants, indels, copy number alterations, and rearrangements). For 78 cases, TMB was calculated by counting mutations across a 0.8–1.1 Mb region (TMB-low, <6 muts/Mb; TMB-intermediate, 6–19.9 muts/Mb; TMB-high, ≥0 muts/Mb). MSI-high, MSI-intermediate, or MS-stable was assigned by a computational algorithm examining 114 intronic homopolymer loci for 57 cases. Clinically relevant GA (CRGA) were defined as GA associated with on-label targeted therapies and targeted therapies in clinical trials.

Results: GA were identified in >90% of NEC samples. Inactivating GA were most common in *TP53* in 50% (80/160) and *RB1* in 31% (50/160) of cases seen across tissue types except vaginal tumors (Table 1). Of 160 cases, 98 had at least 1 CRGA, with 52.0% (51/98) in the *AKT/PI3K/mTOR* pathway, 19.4% (19/98) in the *MEK* pathway, and 17.3% (17/98) with GA in the homologous recombination repair pathway. The median TMB was generally very low with uterine NEC being the highest at 4.5 mut/Mb. Uterine NEC had the highest prevalence of MSI-H tumors (4/19), and this accounted for 45% of the cases with elevated TMB. A comparison of GA in lung small-cell undifferentiated carcinomas to breast and gynecologic NEC demonstrates a much higher rate of *TP53* (91%) and *RB* (70%) GA and a much lower rate of CRGA.

Conclusion: This is the first description of CGP across the spectrum of NECs of the female genital tract and breast. TMB and MSI status varies across NEC primary site and may suggest utility of checkpoint inhibition in a subset of patients. GA in *TP53* and *RB1* are frequent, but less prevalent compared to lung NEC. Genomic profiling of rare tumors can guide clinical trial design for targeted therapies.

Table 1. The 10 most commonly identified GA in patients with neuroendocrine tumors of the female genital tract and breast and frequency breakdown by histology.

Gene	Overall	Breast	Cervix	Ovary	Uterus	Vagina
<i>TP53</i>	43%	62%	20%	46%	60%	0%
<i>RB1</i>	27%	38%	12%	25%	50%	0%
<i>MYC</i>	18%	19%	22%	11%	20%	0%
<i>PTEN</i>	17%	6%	18%	7%	50%	20%
<i>PIK3CA</i>	15%	17%	10%	7%	40%	0%
<i>FGFR1</i>	11%	30%	0%	0%	10%	0%
<i>ZNF703</i>	10%	30%	0%	0%	5%	0%
<i>ARID1A</i>	10%	4%	6%	11%	30%	20%
<i>CCND1</i>	9%	28%	0%	0%	5%	0%
<i>FGF19</i>	9%	28%	0%	0%	0%	0%

65 - Featured Poster Session

Development and validation of a risk calculator for adverse perioperative outcomes for women with ovarian cancer
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Objective: Cytoreductive surgery for ovarian cancer is associated with substantial morbidity. We utilized a nationally representative sample to determine the clinical and demographic factors associated with adverse outcomes to create a calculator to determine the predicted risk of serious perioperative morbidity and mortality.

Method: We examined patients undergoing surgery for primary ovarian, fallopian tube, or peritoneal cancer in the National Surgical Quality Improvement Program (NSQIP) database between 2005 and 2015. The database includes detailed clinical and demographic characteristics and outcomes of patients treated across the United States. To adjust for patients who had additional procedures for cytoreduction (pelvic exenteration, lymph node dissection, bowel, liver, bladder, or diaphragm resection), we assigned 1 point each to create a procedure score. Logistic regression models were created to select variables

statistically significantly associated with Clavian IV complications or 30-day mortality. A nomogram was developed, and internal validation was performed using bootstrapping methods of 1,000 resamples.

Results: A total of 7,940 patients were identified, 589 (7.4%) of whom experienced a Clavian IV complication or died. Among the 18 baseline variables assessed, increasing age, emergent surgery, ascites, bleeding disorder, low albumin, higher ASA, and a higher extended procedure score were significantly associated with serious perioperative morbidity and mortality (Figure 1). Of these factors, procedure score was the most strongly associated with a risk of an event, particularly for a score ≥ 3 (aOR = 4.77, 95% CI 3.24–7.03). Internal validation showed a strong discrimination with the distribution of predicted probabilities from the nomogram tracking closely to observed events across a spectrum of low- to high-risk groups indicating excellent calibration (C-index 0.72 indicating a 72% correct identification of the higher risk patients, Figure 1).

Conclusion: This perioperative ovarian cancer nomogram is useful for risk stratification for women with ovarian cancer when considering eligibility for surgery, the extent of a debulking surgery, or use of neoadjuvant chemotherapy. Future studies should be performed to externally validate this tool.

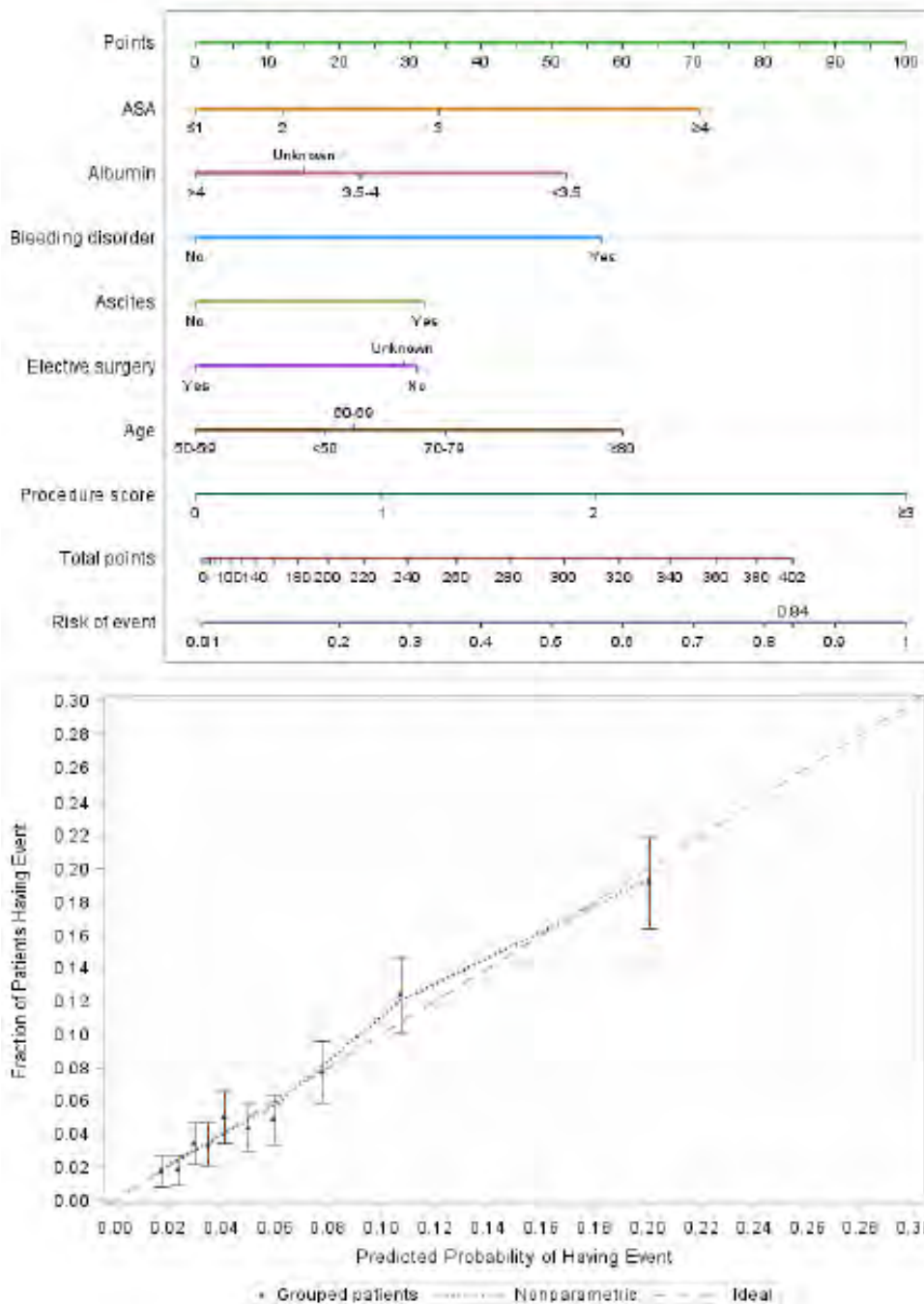


Fig. 1. Nomogram and the associated calibration plot to predict risk of perioperative Clavian IV complication or mortality in ovarian cancer debulking. Risk points for each variable are obtained by mapping the patient's value to the scale labeled "Points." The points are totaled across the variables and the corresponding value located on the scale "Total points" is then mapped to the scale "Risk of event" to obtain the predicted risk of serious perioperative morbidity and mortality. In the calibration plot the dashed line indicates ideal reference line where predicted probabilities would match the observed proportions. Triangles represent nomogram-predicted probabilities grouped for each of the ten decile groups, along with the respective 95% confidence intervals.

66 - Featured Poster Session

Nedaplatin and paclitaxel compared with carboplatin and paclitaxel for patients with platinum-sensitive recurrent ovarian cancer

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Objective: This cohort study was designed to evaluate the efficacy and safety of nedaplatin plus paclitaxel (NP) compared with carboplatin plus paclitaxel (CP) in platinum-sensitive recurrent ovarian cancer.

Method: Patients with recurrent interval >6 months after finishing platinum-based therapies between January 1, 2009, and December 31, 2014, were investigated. Patients received an intravenous infusion of NP (nedaplatin 80 mg/m² plus paclitaxel 175 mg/m²) or CP (carboplatin at an area under the curve of 5 plus paclitaxel 175 mg/m²) protocols every 3 weeks. Primary endpoint was progression-free survival (PFS); secondary endpoints were overall survival (OS) and toxicity.

Results: A total of 436 patients were enrolled in the study, containing 241 receiving the CP protocol and 195 receiving the NP regimen. With median follow-up of 63.5 months, PFS was 11.0 months with NP protocol versus 9.5 months with CP regimen ($P = 0.109$). Subgroup analysis indicated that PFS for the NP arm was statistically superior to that for the CP arm ($P = 0.048$) when recurrent interval was 6–12 months; median PFS was 10.0 versus 8.0 months, respectively. There was no significant difference in overall survival between the 2 groups. Grade 3–4 hematological toxicity was less frequent in the NP arm than in the CP arm ($P < 0.01$). The incidence of hypersensitivity in the CP and the NP arm was 21.9% and 5.6%, respectively, $P < 0.001$. See Figure 1.

Conclusion: NP protocol with decreased toxicity showed no inferiority to standard CP regimen in platinum-sensitive recurrent ovarian cancer. Compared to the CP arm, the NP arm obtained significant benefit in progression-free survival when the recurrent interval was between 6 and 12 months.

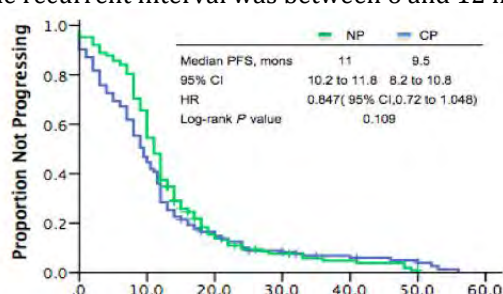


Figure 2A Progression-free Survival (months)

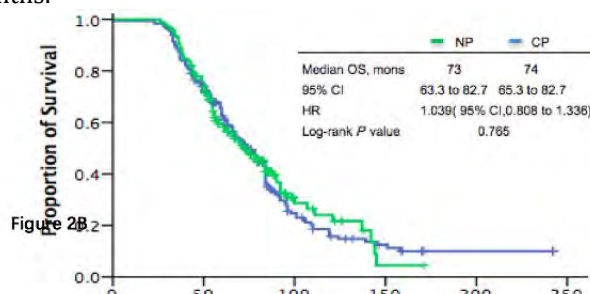


Figure 2B Overall Survival (months)

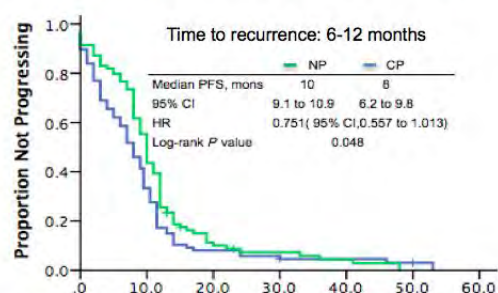


Figure 3A Progression-free Survival (months)

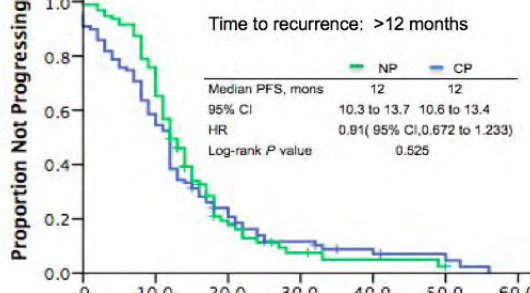


Figure 3B Progression-free Survival (months)

Fig. 1.

67 - Featured Poster Session

A subgroup of cases with a high immunogenic profile in homologous recombination-proficient high-grade serous ovarian carcinoma: Possible candidates for checkpoint blockade therapy

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Objective: There is increased evidence of the benefit of PARP inhibitors in patients with high-grade serous ovarian carcinoma (HGSC) who have homologous recombination (HR)-deficient tumors. However, there is a need to develop new treatment for patients with HR-proficient tumors. The aim of this study is to investigate the immunological background of HR-proficient HGSC by integrated molecular analysis to explore the subpopulation of patients who may be candidates for immunotherapy.

Method: A total of 80 cases of HGSC were analyzed in the study. Exome and RNA sequencing was performed for these tumors. Methylation arrays were also carried out to examine *BRCA1* promoter methylation status. Mutations, neoantigen load, antigen presentation machinery, and immune profile were investigated, and the relationships of these factors with clinical outcome were analyzed.

Results: We defined tumors with *BRCA1/2* or *RAD51C/D* mutations or *BRCA1* promoter methylation as HR-deficient. A total of 33 (41.3%) and 47 (58.8%) patients were classified as having HR-deficient and HR-proficient tumors, respectively. Increased numbers of mutations and neoantigens were observed in HR-deficient tumors ($P = 0.002$). However, 40% of the patients with HR-proficient tumors still had high numbers of neoantigens, and these patients had a better survival trend than those with fewer neoantigens in HR-proficient HGSC. Inclusion of HLA-class I expression status in the analysis showed that patients with both high neoantigens and high HLA-class I expression had improved survival ($P = 0.021$). Gene set enrichment analysis showed that the gene sets for effector memory CD8, TH1, interferon response, and inflammatory response were enriched in patients with high neoantigens and high HLA-class I expression in HR-proficient tumors, suggesting a T cell-inflamed phenotype.

Conclusion: Patients with HR-proficient HGSC with an increased number of neoantigens and high HLA-class I expression status had better survival and a high immunogenic profile. This subgroup of cases might be appropriate targets for immune checkpoint inhibitors, rather than PARP inhibitors.

68 - Featured Poster Session

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy as initial treatment of ovarian, fallopian tube, and primary peritoneal cancer: Preliminary results of a phase II randomized clinical trial

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Objective: Ovarian cancer is the deadliest of gynecologic cancers. Approximately 70% of patients present in advanced stages, and the majority eventually recur, resulting in a 50% 5-year overall survival with standard-of-care treatment. Studies have shown a 5-year OS of 63%–67% in recurrent ovarian cancer treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) after other therapies have failed. A prospective randomized trial was designed to evaluate CRS/HIPEC as a primary treatment for newly diagnosed, untreated advanced (stage III–IV) ovarian, primary peritoneal, and fallopian tube cancers.

Method: Between 2014 and 2017, patients were prospectively randomized into 1 of 2 groups. The intervention group underwent CRS/HIPEC (carboplatin 800 mg/m²) with adjuvant IV chemotherapy (carboplatin/paclitaxel × 6 cycles). The control group underwent CRS alone, with standard-of-care adjuvant chemotherapy (IV paclitaxel/IP cisplatin/IP paclitaxel × 6 cycles). Gynecologic and surgical oncologists operated together on each patient. Surgical complications, postoperative mortality, intraoperative (IOP) blood loss/transfusions, hospital length of stay (LOS), and delay in adjuvant chemotherapy were assessed as primary outcomes. Secondary outcomes included overall survival (OS) and disease-free survival (DFS).

Results: To date, 19 patients have enrolled: 11 in the CRS/HIPEC group and 8 in the control group. Clinical characteristics are shown in Table 1. DFS at 2 years was 69% for the CRS/HIPEC group and 59% for the control group ($P = 0.75$). OS at 2 years was 89% for the CRS/HIPEC group and 77% for the control group ($P = 0.75$).

Conclusion: This randomized trial directly compares CRS/HIPEC with conventional postoperative IP therapy as initial treatment for advanced ovarian cancer. At 3 years, statistical significance has not yet been observed between the study groups, except in the delay to adjuvant chemotherapy. This delay was expected in the CRS/HIPEC group because of IOP chemotherapy. There is an apparent advantage of CRS/HIPEC in terms of disease-free survival and overall survival. Enrollment of more patients and longer follow-up are needed in order to derive appropriate conclusions. Preliminary results are encouraging.

Table 1. Clinical characteristics of enrolled patients.

	CRS/HIPEC n = 11	Control n = 8	<i>P</i> value
Mean pre-operative PCI	26	25	0.79
Optimal cytoreduction (CC score 0-1)*	89%	100%	1.00
Mean IOP blood loss (ml)	1572	1012	0.35
Mean IOP transfusions (units PRBCs)	2.8	2.3	0.78
Mean hospital LOS (days)	15	11	0.18
Post-operative mortality (n)	1	0	1.00
Grade III/IV surgical complications**	44%	13%	0.29
Time from surgery to adjuvant chemotherapy (days)	65	45	0.01

*Optimal cytoreduction: <0.25 cm residual disease

**NCI – CTAE v.4

PCI: Peritoneal cancer index; CC: Completeness of cytoreduction; IOP: Intraoperative; PRBCs: Packed red blood cells; LOS: Length of stay; CRS/HIPEC: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.

69 - Featured Poster Session

Utilization of preoperative PET-CT and pelvic MRI reduces multimodality therapy in the care of women with early-stage cervical carcinoma

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Objective: Positron emission computed tomography (PET-CT) to evaluate pelvic lymph nodes and pelvic magnetic resonance imaging (MRI) to evaluate the parametria have been utilized to triage the management of women with early-stage cervical carcinoma. This study aimed to assess the performance of these tests over time.

Method: An institutional review board-approved, retrospective review of all women treated from 2003 to 2013 for stage IA1–IIA2 invasive cervical cancer at 2 academic centers was conducted. Patient charts were reviewed, and clinical variables were extracted. Associations between use of PET-CT or MRI and relevant clinical factors were analyzed utilizing *t* tests, χ^2 , logistic, and linear regression as appropriate. The Kaplan-Meier method was used to analyze survival.

Results: We identified 484 women treated for early-stage cervical cancer, of whom 183 (38%) and 188 (39%) underwent pretreatment PET-CT and MRI, respectively, with 28% of women undergoing both tests. Utilization of both PET-CT and MRI increased with time (both $P < 0.001$), and the use of radical hysterectomy decreased over time ($P = 0.025$). Use of MRI and PET-CT was positively associated with higher FIGO stage ($P < 0.001$). No true positive extracervical disease was detected in those women with stage IA disease. PET-CT identified disease outside the cervix in 20% of patients, and MRI identified positive parametria in 14%. Both positive parametria on MRI and positive lymph nodes on PET-CT were associated with reduced odds of radical hysterectomy (OR = 0.18, $P = 0.001$, and OR = 0.10, $P < 0.001$). Positive PET-CT was associated with decreased risk of both surgery and upfront radiation ($P = .003$). Positive MRI was not associated with combination upfront therapy ($P = 0.07$). Kaplan-Meier curves demonstrated reduced survival associated with either a positive PET-CT or positive MRI ($P < 0.001$ and $P < 0.002$ respectively; see Figures 1 and 2), controlling for age and FIGO stage. A multivariate Cox regression incorporating stage, age, and PET-CT positive nodes demonstrated that a positive PET-CT was independently associated with decreased survival (HR = 3.88, $P < 0.008$).

Conclusion: These data suggest that preoperative PET-CT and MRI have prognostic value and significantly altered treatment modality decisions over time for women with stage IB–IIA cervical carcinoma.

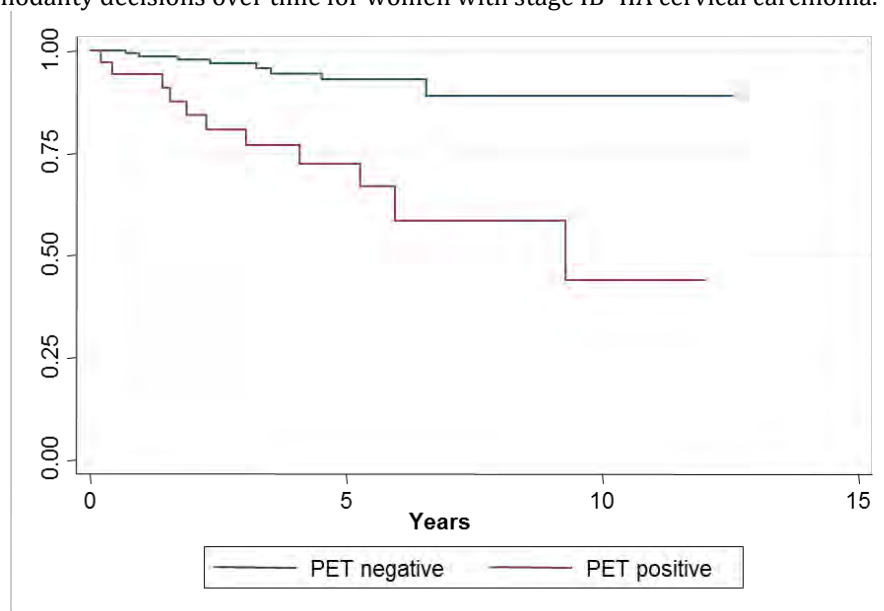


Fig. 1. Overall Survival by Pelvic Node Status in Women who underwent PET-CT. Positive lymph nodes on pre-treatment PET-CT associated with decreased survival ($P < 0.001$).

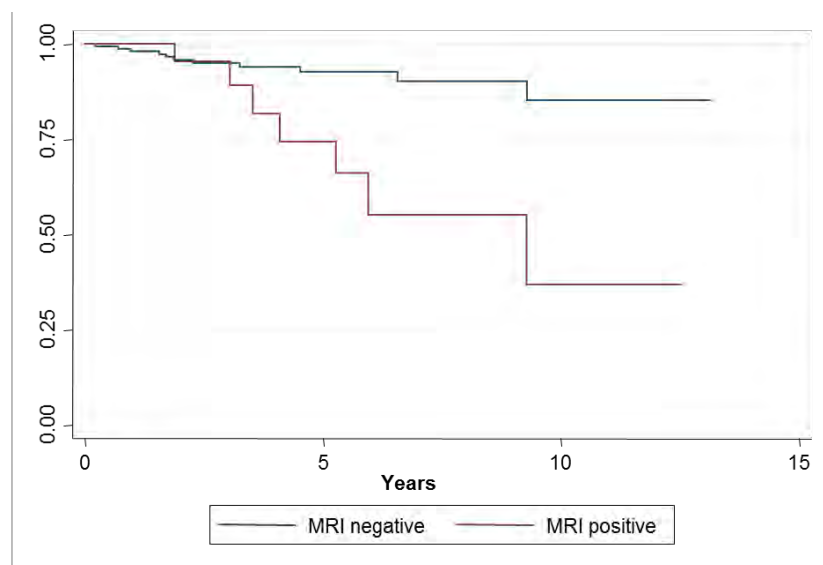


Fig. 2. Overall Survival by Parametrial Involvement in Women who underwent MRI. Positive parametria on pre-treatment MRI associated with decreased survival ($P < 0.002$).

70 - Featured Poster Session

Identification of ovarian cancer patients for immunotherapy by concurrent assessment of tumor mutation burden (TMB), microsatellite instability (MSI) status, and targetable genomic alterations (GA)

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Objective: In 2017, human tumors with high microsatellite instability (MSI-H) were approved for treatment with programmed-death 1 (PD-1) inhibitors. More broadly, recent studies suggest that tumor mutation burden (TMB) alone can predict response to PD-1 inhibitors. To identify ovarian cancer (OC) patients most likely to respond to treatment with PD-1

inhibitors, we have applied a single comprehensive genomic profiling (CGP) assay to simultaneously assess MSI status, TMB, and targetable genomic alterations (GAs) to a large cohort of OC patients.

Method: CGP assay of 4,140 formalin-fixed, paraffin-embedded OC specimens by hybridization capture of up to 315 cancer-related genes (FoundationOne) provided genomic alterations (SV, indels, CAN, rearr), TMB, and MSI. TMB was calculated by counting mutations across 1.21 Mb region and classified as high (TMB-H, ≥ 7.6 muts/Mb) or low (TMB-L, < 7.6 mut/Mb) using the top decile threshold. MSI-H or stable (MSS) status was assigned by computational algorithm examining 114 intronic homopolymer loci.

Results: A total of 2,872 specimens were of clear cell (CCOC), endometrioid (EOC), mixed OC, or high-grade serous OC (HGSOC) histology. TMB-H specimens (269, 9.37%) had average age 62.2 years and TMB 8.1–652.3 muts/Mb, median 9.9. TMB-L specimens had average age 59.5 years and TMB 0–7.2 muts/Mb, median 2.7. Examining by subtype for prevalence of TMB-H, there were 20.7% EOC, 9.0% CCOC, 9.7% mixed OC, and 7.8% HGSOC. Of the TMB-H specimens, 6.3% were identified as MSI-H (by subtype: 41.3% EOC, 13.0% CCOC, 22.2% mixed OC, and 0% HGSOC). There were 252 TMB-H and MSS cases, distributed across histologies: 7.9% CCOC, 6.7% EOC, 2.7% mixed OC, and 82.5% HGSOC. Among the specimens with TMB-H and MSS, GAs of note include *BRCA1*, *POLE*, *ARID1A*, *TP53*, *MLL2*, and *KRAS*. See Table 1.

Conclusion: EOC have the highest prevalence of MSI-H and high TMB among all histological types of OC. Therefore, EOC may represent the most responsive histological type, followed by CCOC and mixed OC, for treatment with PD-1 inhibitors. MSI testing alone to determine eligibility for treatment with anti-PD-1 inhibitors may miss a significant number of patients harboring hypermutated tumors secondary to other GAs (e.g., *POLE*) potentially responsive to immunotherapy. Recurrent OC patients should be screened for both TMB and MSI before being considered for treatment with PD-1 inhibitors.

Table 1: Summary of Data on Tumor Mutation Burden and Microsatellite Instability Status in Ovarian Carcinomas.

	<i>n</i>	<i>n</i> with TMB \geq 7.6 muts/Mb	%	<i>n</i> with MSI-H	<i>n</i> with MSI-H and TMB \geq 7.6 muts/Mb	% MSI-H of TMB \geq 7.6 muts/Mb
Clear cell ¹	254	23	9.06%	4	3	13.04%
Endometrioid ²	140	29	20.71%	13	12	41.38%
Carcinoma, Mixed ³	92	9	9.78%	2	2	22.22%
HG Serous ⁴	2655	208	7.83%	0	0	0

¹ Diagnosed as ovarian clear cell; mets from endometrial clear cell excluded

² Endometrioid carcinomas determined to be ovarian primaries or arising in extrauterine endometriosis; in some cases synchronous uterine primaries observed but metastases from uterus to ovary excluded

³ Carcinoma mixed = at least 2 distinguishable epithelial patterns observed/reported (e.g. serous + clear cell)

⁴ Serous Carcinoma High Grade/NOS: Serous histology which was not considered histologically low or was specifically designated high (includes FIGO grade 2 & 3 and NOS)

71 - Featured Poster Session

Evaluation of circulating tumor DNA in patients with endometrial cancer harboring somatic PIK3CA or KRAS mutations: A potential high-risk factor for recurrence

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Objectives: Circulating tumor DNA (ctDNA) has received attention not only as an important source for liquid biopsy to identify prognostic marker in cancer patients but also as a diagnostic for early detection of cancer. Our aim is to understand the clinical role of ctDNA detection in patients with endometrial cancer harboring somatic *PIK3CA* or *KRAS* mutations.

Method: Since somatic *PIK3CA* and *KRAS* mutations were among the most frequent mutated genes in endometrial cancer, tumor specimens and plasma samples (before surgery) of patients with endometrial neoplasms were investigated for *PIK3CA* and *KRAS* mutations using droplet digital PCR (ddPCR). We defined ctDNA detection to be positive when the corresponding mutations were detected in the plasma cell-free DNA.

Results: We screened 205 patients with endometrial neoplasms for somatic *PIK3CA* and *KRAS* mutations by ddPCR. A total of 74 patients with endometrial neoplasms were found to have somatic *PIK3CA* and/or *KRAS* mutations. In 74 patients, 68, 3, and 3 patients had endometrial cancer, synchronous endometrial and ovarian cancer, and atypical endometrial hyperplasia, respectively. The detection rate for ctDNA was 14.7% (10/68) in patients with endometrial cancer. *PIK3CA* and *KRAS* mutations in the plasma cell-free DNA were detected in 14.3% (5/35) and 13.3% (6/45), respectively, of patients with endometrial cancer. We investigated the relationship between ctDNA detection and clinicopathological features in endometrial cancer patients. The detection rate of ctDNA was associated with advanced stage ($P = 0.0084$) and lymphovascular space invasion (LVSI) ($P = 0.0022$). In addition, we examined the potential association of ctDNA detection with patient survival. ctDNA detection was associated with shorter recurrence-free and overall survival in endometrial cancer patients by log rank test ($P = 0.0010$ and 0.0036 , respectively). Multivariate Cox regression analysis revealed that ctDNA remained an independent indicator for overall survival ($P = 0.025$).

Conclusion: Our data suggest the presence of ctDNA (somatic *PIK3CA* and/or *KRAS* mutations) in plasma might be a high-risk factor for recurrence in endometrial cancer patients.

72 - Featured Poster Session

Tackling the opioid crisis: Reduced postoperative oral and intravenous opioid use after implementation of an enhanced recovery after surgery (ERAS) program in gynecologic oncology patients

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Objective: To evaluate opioid use of women undergoing open surgery for suspected gynecologic cancer before and after implementation of a comprehensive institutional enhanced recovery after surgery (ERAS) program.

Method: An ERAS program for women undergoing open abdominal surgery for suspected gynecologic cancer was implemented at a comprehensive cancer center. Multimodality perioperative analgesia was used including regional incisional infiltration of liposomal bupivacaine (Exparel) and scheduled acetaminophen and ibuprofen (for nonbowel anastomosis patients). A comparison group of patients prior to ERAS program implementation served as controls (pre-ERAS). Data on postoperative pain medication during hospitalization were obtained. Statistical analysis was performed using STATA.

Results: Over a 12-month period, 103 women were treated on the ERAS protocol (ERAS); all received liposomal bupivacaine injection intraoperatively. A comparison group was 118 patients (pre-ERAS) undergoing similar surgery over the prior 12 months; 75% had regional epidurals placed for postoperative pain control. Forty-nine percent had ovarian cancer; upper abdominal surgery was performed in 81% and bowel resections in 23% of patients. IV PCA narcotic use was significantly less in the ERAS group compared to pre-ERAS (4.6% vs 49%, $P < 0.0001$). Nineteen percent of ERAS patients required no IV narcotics postoperatively, and only 40% required IV narcotics after postoperative day 0. Oral narcotic use in hospital was less in the ERAS patients (82% vs 96%, $P = 0.002$). At discharge, 99% of patients were prescribed oral narcotics in both groups (oxycodone 5 mg or hydromorphone 2 mg), and average number of pills dispensed was significantly less for ERAS patients than for pre-ERAS (60 vs 77, $P = 0.005$). In addition, hospital length of stay was significantly shorter in ERAS patients (3.7 vs 4.8 days) with a stable readmission rate (2.9% vs 4.1%).

Conclusion: Implementation of a multimodality analgesia program including intraoperative incisional infiltration of liposomal bupivacaine significantly reduces patient postoperative IV and oral opioid use and decreases discharge provider opioid prescription amounts.

73 - Featured Poster Session

GOG 8035: Nuclear *BRCA1* loss may identify a poor prognostic subgroup of women with locally advanced cervical cancer treated with cisplatin-based chemoradiation: An NRG Oncology study

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Objective: Despite widespread adoption of chemoradiation for women with locally advanced cervical cancer, 30%–40% will recur. Interactions of *BRCA1* and *ERCC1* with other molecules in the homologous recombination/nucleotide excision repair pathways are well characterized, but their roles in the transcriptional response to DNA damage is poorly understood. *BRCA1* mutations confer a favorable prognosis in some subsets (high-grade serous ovarian cancer) but have also been associated with poor survival (breast). We studied *BRCA1* and *ERCC1* expression in pooled cervical cancer specimens from 2 NCI-sponsored studies of cisplatin-based chemoradiation.

Method: GOG 191 and 219 were phase III randomized trials that studied maintaining hemoglobin levels >12.0 g/dL) or incorporation of the hypoxic cell sensitizer tirapazamine, respectively. Pretreatment excisional biopsies were prospectively collected and assessed for *BRCA1* and *ERCC1* by immunohistochemistry (IHC). Nuclear staining was scored by blinded GOG pathologists as absent (0), weak (1), moderate (2), or strong (3). *BRCA1* was also given a composite score (nuclear + cytosolic). Associations of DNA repair proteins with clinical endpoints were evaluated in an exploratory analysis without adjustment for multiplicity.

Results: Of 516 evaluable patients, 375 submitted tissue. Adequate tumor was found in 358 cases for *BRCA1* and 329 for *ERCC1*. *BRCA1* scores were 0 ($n = 82$), 1 ($n = 128$), 2 ($n = 109$), 3 ($n = 39$) and were not associated with age, ethnicity, stage, or cell type. Nuclear staining (0 vs 1–3) for *BRCA1* tracked only with PFS (HR = 0.61, 95% CI 0.43–0.88; Figure 1) and OS (HR = 0.61, 95% CI 0.42–0.90). Patients with *BRCA1* 1–3 had twice the odds of maintaining local control versus those with no staining (OR = 2.0, 95% CI 1.1–3.7).

Conclusion: Intact genetic machinery may render cervical cancer more vulnerable to chemoradiation, while genetic chaos measured by absent *BRCA1* nuclear localization may be a poor prognostic factor. Prospective validation and exploration of *BRCA1*'s putative role as a tumor suppressor gene in this disease may be warranted. The therapeutic potential to exploit synthetic lethality using PARP inhibitors in molecularly categorized subsets of women with cervical cancer is implicit.

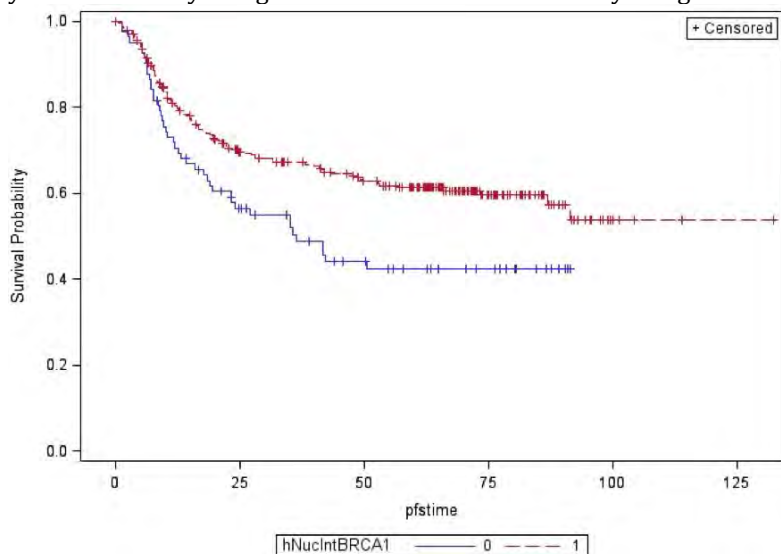


Fig. 1. Product-Limit Survival Estimates.

74 - Featured Poster Session

Initial safety and activity findings from a phase IB escalation study of mirvetuximab soravtansine, a folate receptor alpha (FR α -targeting antibody-drug conjugate (ADC), with pembrolizumab in platinum-resistant epithelial ovarian cancer (EOC) patients

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Objective: Mirvetuximab soravtansine is a folate receptor alpha (ADC), comprising an FR α -binding antibody linked to the tubulin-disrupting maytansinoid DM4. In preclinical studies, mirvetuximab soravtansine has been shown to activate monocytes and upregulate immunogenic cell death markers on ovarian tumor cells, providing a mechanistic rationale for combining this agent along with the modality of immune checkpoint blockade. Accordingly, mirvetuximab soravtansine is currently being evaluated in combination with pembrolizumab as part of the phase 1b/2 FORWARD II trial (NCT02606305) in patients with platinum-resistant epithelial ovarian cancer (EOC).

Method: Mirvetuximab soravtansine was tested in 2 doses in combination with pembrolizumab on day 1 of a 21-day cycle. The starting dose was 5 mg/kg (adjusted ideal body weight) and then escalated to 6 mg/kg, the phase 3 monotherapy dose; pembrolizumab dosing remained constant at 200 mg. Responses were assessed according to RECIST 1.1, and adverse events (AEs) were evaluated by CTCAE v4.0.

Results: A total of 14 heavily pretreated patients (median of 5 prior lines of therapy, range 2–7) were enrolled as part of dose escalation. Both doses of mirvetuximab soravtansine were well tolerated when combined with pembrolizumab, and the safety profile for the combination was consistent with the known profiles of each agent, with the most frequently observed AEs being fatigue, nausea, and diarrhea (predominantly grade 1 or 2). One patient discontinued due to a related AE (grade 1 pneumonitis). In the subset of patients with medium to high FR α expression levels by immunohistochemistry (i.e., $\geq 50\%$ of cells with $\geq 2+$ staining intensity, $n = 8$), confirmed partial responses were observed in 3 individuals; 2 are ongoing with at least 5 months on treatment; and the third had a duration of therapy of 7 months. Six patients in total are still being studied.

Conclusion: At full dosing, the combination of mirvetuximab soravtansine and pembrolizumab demonstrates favorable tolerability, with primarily mild to moderate (\leq grade 2) AEs observed. Further, preliminary signals of efficacy were observed in this heavily pretreated population of patients with FR α -positive EOC. Together, these findings support ongoing enrollment of a total of 35 patients in an expansion cohort to evaluate the combination in the setting of platinum-resistant disease.

75 - Featured Poster Session

Concordance of germline multigene panel testing with prior microsatellite instability and immunohistochemistry analyses in endometrial cancer patients

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Objective: Microsatellite instability (MSI) and immunohistochemistry (IHC) for the mismatch repair (MMR) proteins are recommended methods of screening for Lynch syndrome and eligibility for targeted therapy, but their sensitivity and specificity are each less than 90%. We aimed to assess the concordance of germline multigene panel testing (MGPT) results with prior MSI and/or IHC in endometrial cancer patients.

Method: Patients with endometrial cancer who had MGPT between 2012 and 2016 at a single laboratory and reported results of prior MSI and/or IHC were reviewed and classified as concordant if tumor testing matched MGPT results, discordant if they did not match MGPT results, and atypical if they had both concordant and discordant features.

Results: Of patients with IHC results ($n = 739$), concordance was high among those with normal IHC (96%, $n = 278$) and low among those with abnormal IHC (19.8%, $n = 89$). The largest percentage of cases with abnormal IHC were discordant cases for which *MLH1* methylation had not been ruled out (43.3%, $n = 195$). An additional 31.6% ($n = 142$) were discordant with methylation ruled out or not necessary, and 5.3% ($n = 24$) were atypical. Concordance rates further varied by IHC pattern (see

Table 1). Of note, 10 cases with concordant, normal IHC had a germline mutation in a non-MMR gene, and 7 of 11 discordant cases with normal IHC had a germline MMR mutation.

Conclusion: Sporadic *MLH1* promoter methylation is known to be common in endometrial cancer. These results highlight the importance of ruling this out in order to decrease discordant and/or inconclusive results. Other possible explanations for discordant results include 2 somatic MMR mutations, unclassified variants that are actually pathogenic, mutations not detected with current technology, and inaccurate tumor testing. Endometrial cancer patients with normal IHC will most likely have normal germline testing results; however, a small percentage may still have Lynch syndrome and, potentially, a MMR-deficient tumor eligible for a PD-1 inhibitor. *MLH1* methylation analysis, germline MGPT, and tumor MMR gene sequencing are likely to result in few discordant results and more conclusive answers for endometrial cancer patients with MMR-deficient tumors.

Table 1. Concordance of Endometrial Cancer Cases by IHC Pattern (*n* = 739)

IHC Results and Concordance	N	%
Normal IHC	289	39.1%
<i>Concordant</i>	278	96.2%
<i>Discordant</i>	11	3.8%
Abnormal IHC	450	60.9%
<i>Concordant</i>	89	19.8%
<i>Discordant</i>	142	31.6%
<i>Atypical</i>	24	5.3%
<i>Discordant-Methylation not ruled out</i>	195	43.3%
Loss of MLH1 (with or without PMS2)	245	54.5%
<i>Concordant</i>	36	14.7%
<i>Discordant</i>	15	6.1%
<i>Discordant-Methylation not ruled out</i>	195	79.2%
Loss of PMS2 only	37	8.2%
<i>Concordant</i>	4	10.8%
<i>Discordant</i>	33	89.2%
Loss of MSH2 (with or without MSH6)	71	15.8%
<i>Concordant</i>	22	31.0%
<i>Discordant</i>	48	67.6%
<i>Atypical</i>	1	1.4%
Loss of MSH6 only	65	14.4%
<i>Concordant</i>	27	41.5%
<i>Discordant</i>	38	58.5%
Atypical staining pattern*	32	7.1%
<i>Concordant</i>	0	0.0%
<i>Discordant</i>	8	25.0%
<i>Atypical</i>	23	71.9%
<i>Discordant-Methylation not ruled out</i>	1	3.1%

*Loss of two proteins that are not part of the same heterodimer, loss of three or more proteins, or equivocal, weak, or focal staining

76 - Featured Poster Session

Sentinel lymph node mapping (SLNM) in endometrioid endometrial cancer: Does it work in the real world?

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Objective: To investigate the utility of sentinel lymph node mapping (SLNM) for endometrioid endometrial cancer (EEC) in a community setting.

Method: We retrospectively studied women with EEC who underwent hysterectomy plus surgical staging during January 2011–March 2016. Data were extracted from our local cancer registry and confirmed via chart review. Patients underwent either traditional lymphadenectomy (TL) using standard anatomical borders or SLNM with subsequent dissection. Mapping was performed using near-infrared fluorescence imaging (NIRI) with indocyanine green (ICG) dye following the Sloan-Kettering protocol. Patient characteristics were compared between lymph node (LN) dissection methods using parametric and nonparametric tests. Differences in recurrence risk were assessed via proportional hazards regression.

Results: A total of 597 patients with EEC were identified; 57 patients were excluded because of multiple primaries, lymphadenectomy occurring on a later date than hysterectomy, stage IV disease, or tumor grade 4. Of the remaining 540 patients, 180 underwent TL, and 360 underwent SLNM. SLNM attempts were successful in 95% of 377 patients (83% with bilateral detection, 12% with unilateral detection). The total number of LNs dissected was significantly greater in the TL than in the SLNM group (median 17.0 vs 5.00, $P < 0.01$), as was the percentage of patients with positive nodes (10.6 vs 5.83%, $P = 0.04$). Pathology identified patients who underwent TL as higher risk based on standard risk factors, namely, greater tumor diameter (TD, median 40.0 vs 35.0 mm, $P < 0.01$), extent of myometrial invasion (MI, median 31.3% vs 20.0%, $P < 0.01$), and presence of lymphovascular space invasion (15.0% vs 8.61%, $P = 0.02$). While grade did not significantly differ by LN dissection method, a trend towards higher grade with TL was observed. Notably, recurrence risk was not associated with dissection method (HR = 1.04, 95% CI 0.48–2.27, $P = 0.91$) or number of LNs retrieved (HR = 1.01, 95% CI 0.98–1.04, $P = 0.45$). See Table 1.

Conclusion: SLNM using NIRI/ICG was highly successful (95%) in our community setting. Selection bias likely led to differences in risk level between TL and SLNM groups. For EEC patients with TD <50 mm, MI <33%, and grade 1-2, SLNM may be a feasible surgical staging option.

Table 1. Characteristics and outcomes of patients with endometrioid endometrial cancer who were treated in a community hospital setting.

Characteristic or Outcome	Traditional lymphadenectomy			Sentinel lymph node mapping and dissection		
	Overall <i>N</i> = 179	No SLNM attempted <i>n</i> = 163 (30.1%)	SLNM attempted but failed <i>n</i> = 16 (2.95%)	Overall <i>N</i> = 363	SLNM with unilateral detection <i>n</i> = 41 (7.56%)	SLNM with bilateral detection <i>n</i> = 322 (59.4%)
<i>Patient, Tumor, and Treatment Characteristics:</i>						
Age (years), mean (95% CI)	62.2 (60.6-63.7)	61.7 (60.0-63.3)	67.2 (62.0-72.3)	63.2 (62.3-64.2)	65.0 (61.7-68.3)	63.0 (62.0-64.0)
Age ≥70 years, <i>n</i> (%)	40 (22.4)	35 (21.5)	5 (31.3)	84 (23.1)	12 (29.3)	72 (22.4)
White NH race/ethnicity, <i>n</i> (%)	162 (90.5)	148 (90.8)	14 (87.5)	337 (92.8)	39 (95.1)	298 (92.6)
BMI (kg/m ²), mean (95% CI)	37.4 (35.9-38.8)	37.1 (35.6-38.7)	39.8 (35.3-44.2)	35.5 (34.6-36.4)	38.1 (35.1-41.2)	35.2 (34.3-36.1)
Obese (BMI ≥30 kg/m ²), <i>n</i> (%)	135 (75.4)	119 (73.0)	16 (100)	264 (72.7)	31 (75.6)	233 (72.4)

FIGO stage, <i>n</i> (%)						
I	150 (83.8)	136 (83.4)	14 (87.5)	317 (87.3)	38 (92.7)	279 (86.7)
II	4 (2.23)	4 (2.45)	0 (0.00)	14 (3.86)	2 (4.88)	12 (3.73)
III	25 (14.0)	23 (14.1)	2 (12.5)	32 (8.82)	1 (2.44)	31 (9.63)
Tumor diameter (mm), median (IQR)	41.0 (28.0-60.0)	41.0 (28.0-60.0)	41.5 (31.5-50.0)	35.0 (23.0-50.0)	40.0 (30.0-60.0)	35.0 (21.5-50.0)
Myometrial invasion (%), median (IQR)	31.4 (8.33-70.0)	31.0 (8.00-70.0)	40.9 (18.0-70.3)	20.0 (5.56-52.4)	25.0 (11.1-53.3)	20.0 (5.26-50.0)
Tumor grade, <i>n</i> (%)						
1 – well differentiated	103 (57.5)	93 (57.1)	10 (62.5)	221 (60.9)	22 (53.7)	199 (61.8)
2 – moderately differentiated	51 (28.5)	45 (27.6)	6 (37.5)	106 (29.2)	13 (31.7)	93 (28.9)
3 – poorly differentiated	25 (14.0)	25 (15.3)	0 (0.00)	36 (9.92)	6 (14.6)	30 (9.32)
Lymphovascular space invasion, <i>n</i> (%)	27 (15.1)	25 (15.3)	2 (12.5)	31 (8.54)	5 (12.2)	26 (8.07)
Radiation therapy received, <i>n</i> (%)	62 (34.6)	52 (31.9)	10 (62.5)	113 (31.1)	12 (29.3)	101 (31.4)
<i>Outcomes:</i>						
Total lymph nodes dissected, median (IQR)	17.0 (11.0-25.0)	17.0 (12.0-26.0)	14.0 (9.50-15.5)	5.00 (3.00-8.00)	4.00 (2.00-9.00)	5.00 (3.00-7.00)
Cancer positive in any dissected node, <i>n</i> (%) ^a	19 (10.6)	18 (11.0)	1 (6.25)	21 (5.79)	1 (2.44)	20 (6.21)
Cancer positive in sentinel nodes, <i>n</i> (%) ^a	NA	NA	NA	20 (5.51)	1 (2.44)	19 (5.90)
Local/regional cancer recurrence, <i>n</i> (%) ^b	11 (6.15)	11 (6.75)	0 (0.00)	11 (3.03)	0 (0.00)	11 (3.42)
Recurrence (local, regional, or distant), <i>n</i> (%) ^b	19 (10.6)	19 (11.7)	0 (0.00)	17 (4.68)	0 (0.00)	17 (5.28)
Length of follow-up (years), median (IQR)	3.60 (1.87-4.51)	3.71 (2.43-4.58)	0.64 (0.42-1.84)	1.63 (0.53-2.60)	1.52 (0.55-2.67)	1.63 (0.53-2.59)

Abbreviations: BMI, body mass index; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile range (25th percentile-75th percentile); NA, not applicable; NH, non-Hispanic; SLNM, sentinel lymph node mapping.

^a Refers to the number and percentage of patients with positive nodes.

^b Given never-disease-free status, 7 patients and 9 patients were excluded from the traditional lymphadenectomy and sentinel lymph node mapping/dissection groups, respectively, for purposes of computing percentages.

77 - Featured Poster Session

Germline *BRCA* mutation rate in Southern California Latina women

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Objective: Latinos are the largest ethnic group in California. Germline *BRCA* mutation and testing completion rates in Latinas are yet to be well described. The aim was to evaluate germline genetic testing prescribing and testing patterns while stratifying by patients' ethnic background.

Method: A total of 2,053 charts of new patients seen between July 2013 and July 2017 at a gynecologic oncology practice in southern California were reviewed. Data abstracted included referral for germline genetic testing in compliance with breast and/or ovarian cancer (HBOC) National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2017, testing completion rate, outcomes, racial/ethnic patient backgrounds. Data were analyzed with χ^2 tests.

Results: Of 2,053 patients, 571 met germline genetic testing criteria based on personal or family history. Testing was prescribed in 258/571 (45%) of all qualifying patients, regardless of presentation diagnosis. By ethnic background, prescriptions were given for 155/352 (44%) non-Hispanic white, 66/146 (45%) Latina, 17/38 (45%) African-American, and 15/25 (60%) Asian patients. Differences in testing prescriptions rates were nonsignificant. Testing was completed in 96/155 (62%) non-Hispanic white, 41/66 (62%) Latina, 11/17 (65%) African-American, and 10/15 (67%) of Asian patients ($P = NS$). Pathogenic *BRCA* mutations were identified in 31/96 non-Hispanic white (32%), 9/41 (22%) Latina, 5/11 (45%) African-American (45%), and 2/10 (20%) Asian patients. *BRCA* mutation rates were not statistically different. Of 571 (42%) of patients, 240 had personal history of breast, ovarian, fallopian tube, or primary peritoneal cancers; 53/240 (22%) of this cohort were Latina, and 145/240 (60%) non-Hispanic white. Genetic testing was prescribed in 132/240 patients (55%); by subgroup, in 26/53 (49%) of Latinas and 79/145 (54%) of non-Hispanic white ($P = NS$). See Figure 1.

Conclusion: At a southern California tertiary care center, 45% of patients meeting NCCN criteria for HBOC germline testing were prescribed, with a 62% testing completion rate. There was no difference by ethnic background in rates of testing prescription and completion or *BRCA* mutation rates. Of tested Latina patients, 22% were found to have *BRCA* mutations, indicating a high rate of *BRCA* germline mutations in this group. Further studies are underway to identify provider barriers to improving testing referral and completion and to further characterizing detected mutations.

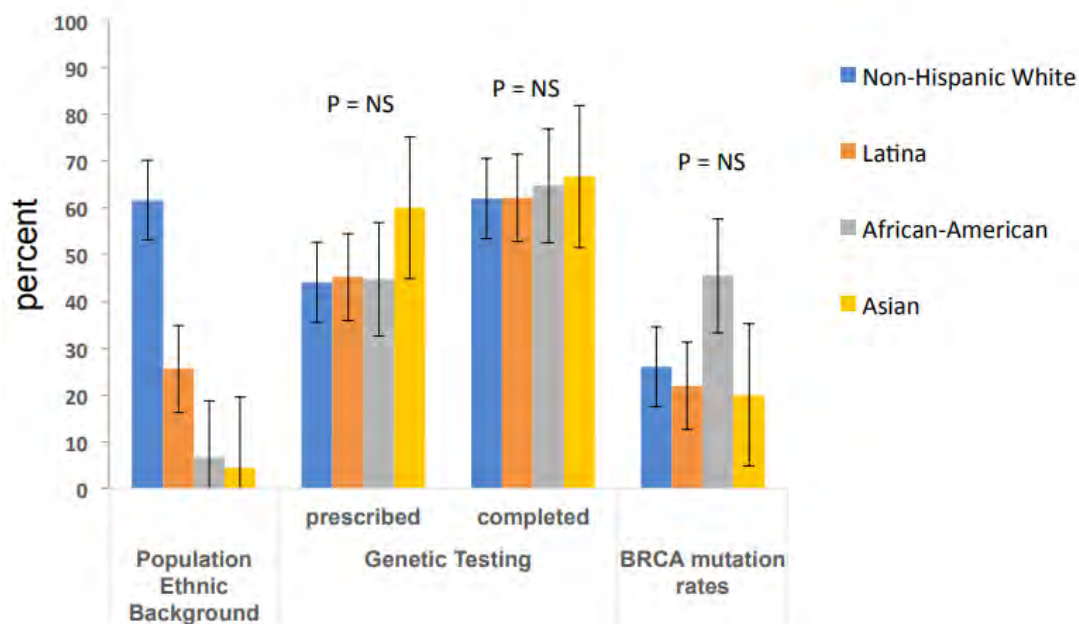


Fig. 1. Germline genetic testing results summary. Summary of germline genetic testing in Southern California gynecologic oncology patients. Twenty-five percent of women were Latina. Differences in prescription and completion of genetic testing, as well as rate of detected *BRCA* mutations were non-significant by ethnic background.

78 - Featured Poster Session

Phase I trial of Vigil® personalized engineered autologous tumor cells (EATC) in ovarian cancer

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Objective: To evaluate the safety and effectiveness of a novel immunotherapy vaccine constructed from autologous tumor harvest with tumor-specific neoantigen source in a phase I study of recurrent ovarian cancer (OC) patients.

Method: A nonrandomized open-label phase I study of Vigil monotherapy was performed in 29 recurrent OC patients using autologous tumor cells. After tumor acquisition, a personalized EATC vaccine was created incorporating two components: (1) *rhGM-CSF DNA* for enhanced antigen presentation combined with (2) bifunctional *shRNA_{furin}*, which inhibits endogenous immunosuppression via activation of TGFβ immunosuppressive isoforms. Vigil was given monthly at dose of 1×10^7 cells/injection up to 12 months. In order to determine immunotherapy activity as defined by T cell activation, a quantitative measurement of responding mononuclear γIFN release to patient autologous tumor (γIFN-ELISPOT) was used as a biomarker. Response and survival were compared by ELISPOT status, and patients were followed for 3 years.

Results: A total of 29 OC patients underwent tumor acquisition for Vigil vaccine creation, with ELISPOT testing determined in 25 patients (ELISPOT+, $n = 21$, and ELISPOT-, $n = 4$). Patients received monthly intradermal injections up to 12 doses for a total of 191 doses. No significant treatment-related adverse events (AEs) were noted, with only a single grade 3 AE of fatigue. The most common AE was injection site induration ($n = 89$ events), all grade 1. Three-year OS was achieved in 20 of 29 (69%) patients, with only 1 ELISPOT- patient achieving 3-year OS (Figure 1). Median OS of all patients was 41.3 months. When stratifying by ELISPOT biomarker status, median OS in ELISPOT- patients was 15.3 months versus ELISPOT+ patients in which median was not reached (Figure 1). Mean survival for ELISPOT- and ELISPOT+ was 23.2 versus 53.8 months, respectively ($P = 0.003$).

Conclusion: Personalized treatment with Vigil immunotherapy shows excellent tolerability with limited side effects. Survival was favorable for the entire cohort with subgroup analysis demonstrating γIFN-ELISPOT as a potential predictive biomarker for response and survival to personalized novel immunotherapy vaccine treatment.

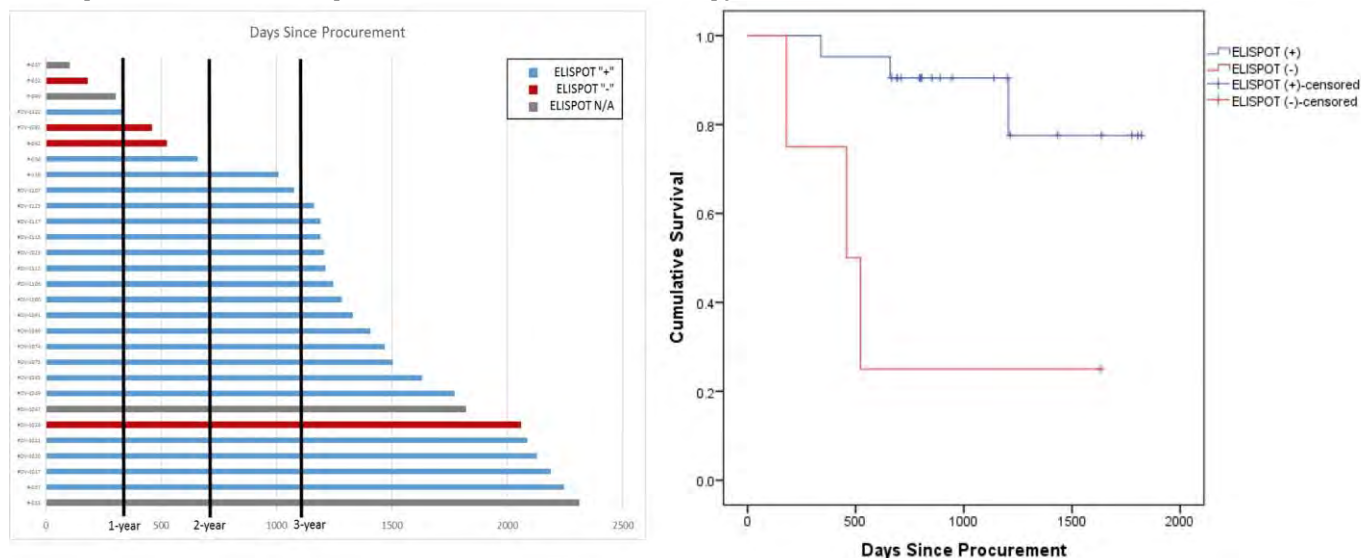


Fig. 1.

79 - Featured Poster Session

A prospective, randomized control trial evaluating the impact of backfill versus spontaneous voiding trial on discharge time for gynecologic oncology patients undergoing laparoscopic hysterectomy

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Objective: Same-day discharge (SDD) is feasible following laparoscopic hysterectomy (TLH) in gynecologic oncology patients, resulting in low readmission rates and postoperative complications. As the cost of care increases, SDD also results in a reduced cost compared to overnight and multiday admission. Backfill voiding trials have been described in the urogynecologic literature showing a reduction in discharge with a catheter following vaginal surgery. The aim of this study is to determine whether performing a backfill voiding trial leads to expedited discharge following laparoscopic hysterectomy in gynecologic oncology patients.

Method: Subjects scheduled for SDD TLH were enrolled and randomized to a backfill voiding trial or a spontaneous voiding trial following surgery. To detect a 30-minute difference in discharge time with 80% power, 117 patients were required to be enrolled. Voiding trials were performed per hospital protocol. The primary outcome was length of stay. Secondary outcomes included time to void, catheter replacement, admission to the extended recovery unit (ERU), and postoperative complications and readmission. Clinical and follow-up data were obtained from the longitudinal medical record.

Results: A total of 121 patients were randomized: 60 to a backfill voiding trial and 61 to a spontaneous voiding trial. There was a statistically significant reduction in median length of stay for patients undergoing backfill voiding trial versus spontaneous voiding trial (271.5 vs 329 minutes, $P = 0.015$). There was also a significant reduction in median time to void with the backfill versus spontaneous voiding trial (30 vs 289 minutes, $P < 0.001$). There was no difference in median pain score (2), catheter replacement, or admission to ERU between the two groups. See Figure 1.

Conclusion: There is a significant reduction in time to void and total length of stay in patients randomized to a backfill voiding trial following TLH with no increased patient discomfort. While the numbers of postoperative admissions were low and likely underpowered to detect a difference in admission rate, these data will help to streamline postoperative care and translate into a reduction in cost for SDD gynecologic oncology patients.

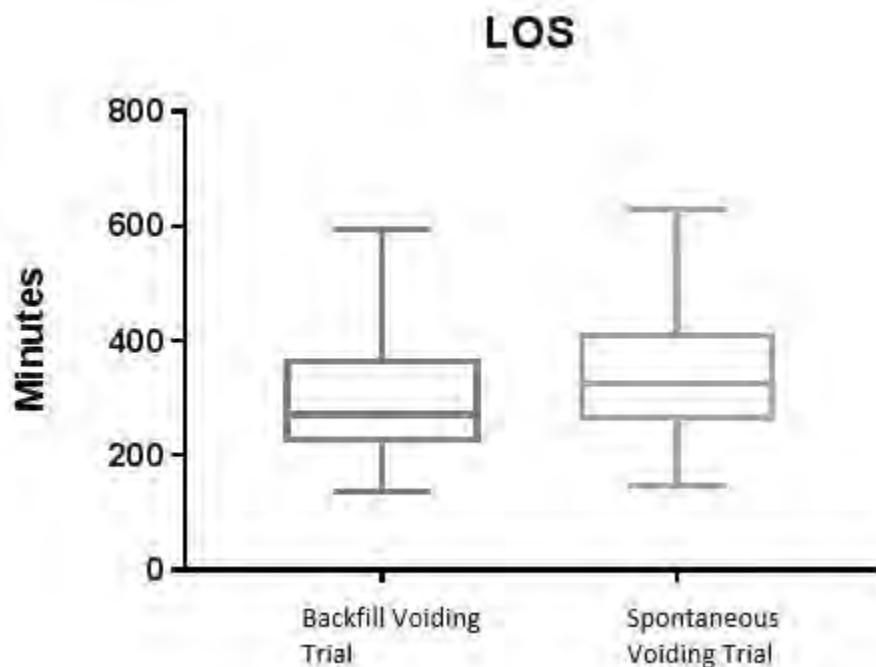


Fig. 1.

80 - Featured Poster Session

Adoptive dendritic cell transfer following platinum-based chemotherapy extends overall host survival in a preclinical model of metastatic ovarian cancer

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Objective: Chemotherapeutic drugs and surgery have proven only partially effective in treating advanced ovarian cancer, with 5-year survival rates (OS) remaining at less than 27%. Immunotherapy treatment using dendritic cell (DC) vaccination alone has shown minimal benefit in patients with advanced ovarian cancer. We examined whether therapeutic DC-based vaccination could enhance the efficacy of cytotoxic drugs in the treatment of primary metastatic ovarian cancer.

Method: Wildtype mice were injected intraperitoneally (IP) with 2.5 million *ID8* ovarian cancer cells to recapitulate the aggressive microenvironment of human metastatic ovarian cancer. Mice were divided into 4 treatment groups: untreated, cisplatin only, DC vaccination only, and cisplatin plus DC vaccination. Following confirmation of ovarian cancer dissemination at day 13, cisplatin (5 mcg/g) was administered IP every 2 weeks for 3 cycles, followed by weekly IP infusions of 3 million bone marrow-derived DCs. Mice were imaged using bioluminescence and weighed biweekly to monitor tumor burden and ascites accumulation. Survival analysis using log rank analysis and Kaplan-Meier data was preformed. Each group contained 8 mice to provide a 5% significance level and 95% power to detect differences in survival of 20% or greater.

Results: Metastatic ovarian cancer was developed in 32 mice. Untreated mice accumulated ascites significantly faster than mice in the treatment groups. No significant difference in median survival was observed between untreated mice and the group receiving therapeutic DC transfer alone (79 vs 83 days, $P = 0.4539$). Mice treated with cisplatin alone demonstrated a median survival of 128 days, which was significantly longer than that of the untreated group or the group treated with DCs alone ($P = 0.0023$). Notably, mice treated with cisplatin followed by adoptive DC transfer survived an average of 29 days longer than mice receiving cisplatin alone (128 vs 157 days, $P = 0.0002$).

Conclusions: Compared with chemotherapy alone, adoptive DC immunotherapy following cisplatin treatment significantly increased median survival rates in mice with ovarian cancer. DC-mediated antitumor effects are therefore enhanced in the setting of recent chemotherapy.

81 - Featured Poster Session

Vaginal brachytherapy is associated with improved overall survival in stage IB endometrioid endometrial carcinoma: A propensity matched, National Cancer Data Base study

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Objective: Randomized trials have failed to show an improvement in overall survival (OS) with adjuvant radiation therapy (RT) in stage I endometrioid endometrial cancer (EEC). This study evaluates trends in use of RT and its impact on OS in low-grade (1-2) and high-grade (3) stage I EEC.

Method: The National Cancer Data Base was queried to identify patients with stage I EEC who underwent hysterectomy from 2004 to 2013. Patients were classified as stage IA grade 1-2, stage IA grade 3, stage IB grade 1-2, and stage IB grade 3. Trends in the use of vaginal brachytherapy (VBT) and external beam radiation therapy (EBRT) were assessed. Overall survival (OS) was measured from surgery, summarized using the Kaplan-Meier method and analyzed using the Cox proportional hazards model. Propensity matched analyses were performed to evaluate the impact of RT on OS within each group.

Results: Of 349,404 women with EC considered for analysis, 132,393 (38%) met inclusion criteria. Overall, 81% of patients had stage IA (73% stage IA G1/2, 8% stage IA G3) and 19% had stage IB disease (15% stage IB G1/2, 4% stage IB G3). Only 18% of patients received adjuvant therapy: 52% VBT, 30% EBRT and 18% chemotherapy + RT. EBRT use decreased over time (8% in 2004-2005 versus 3% in 2012-2013), while VBT use increased (8% in 2004-2005 versus 12% in 2012-2013). Among stage IA G1/2 patients, 1% received EBRT and 5% received VBT versus 10% and 19% respectively of stage IA G3 patients. In contrast, 17% stage IB G1/2 received EBRT and 25% VBT versus 29% and 17%, respectively, of stage IB G3 patients. Five-year OS was 90% \pm 0.1% and decreased with increasing stage and grade. Stage IA, G1/2 did not benefit from either EBRT or VBT ($P = 0.09$ and 0.32 , respectively) (Figure 1A). VBT improved OS in stage IB G1/2 compared to no treatment ($P < 0.0001$). In both stage IB G1/2 and stage IA G3, VBT was superior to EBRT ($P = 0.0004$ and $P = 0.004$, respectively) (Figure 1B/1C). Stage IB G3 patients had improved OS with either VBT or EBRT versus no treatment (Figure 1D), but no difference in OS was seen with VBT compared to EBRT ($P = 0.94$) in this group.

Conclusion: Five-year OS in stage IA G1/2 is approximately 90% and is not improved by the use of adjuvant RT. In contrast, using propensity matching, VBT was associated with a 20% OS improvement in patients with stage IB G1/2 and IA G3 compared to EBRT. Despite a trend of increasing VBT and decreasing EBRT use, these findings demonstrate potential opportunities to reduce both overtreatment (use of EBRT) and undertreatment (omission of VBT) in stage I EEC patients.

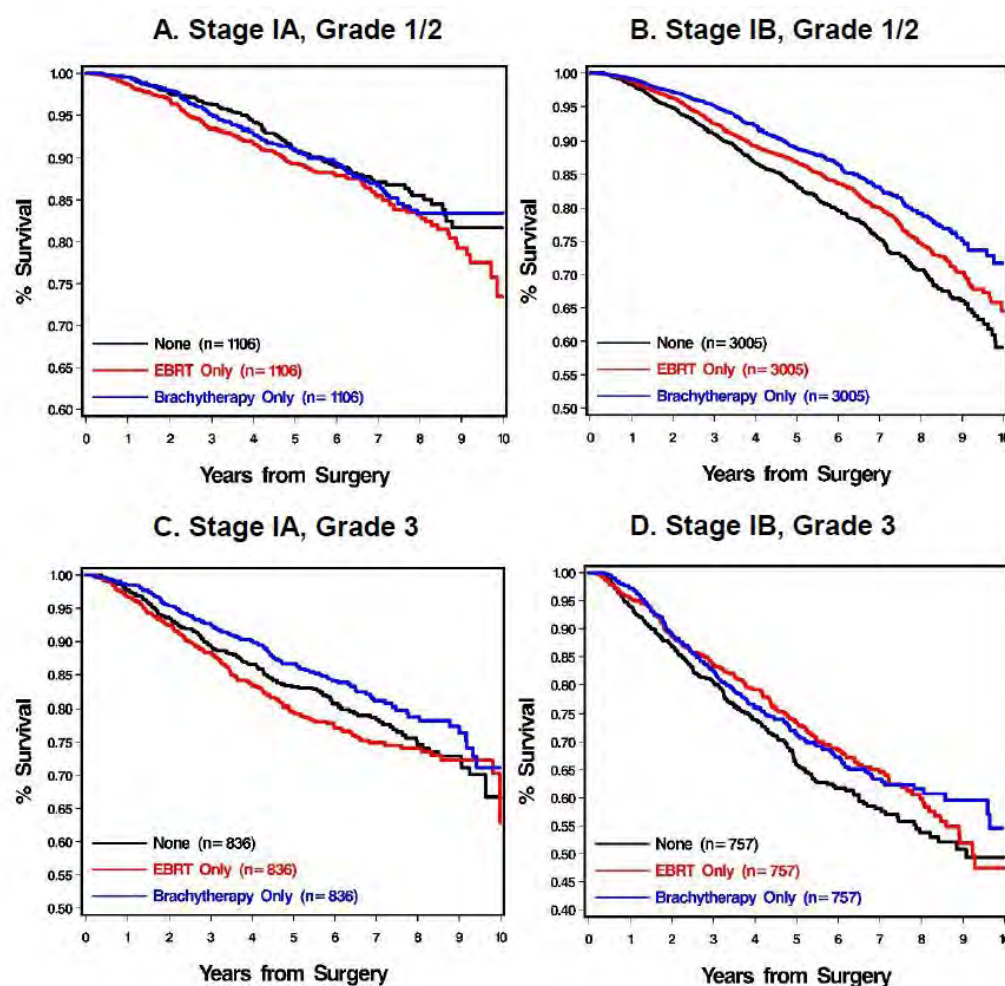


Fig. 1.

82 - Featured Poster Session

Favorable tumor immunophenotype is associated with homologous recombination deficiency in ovarian carcinoma

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Objective: Both the presence of tumor-infiltrating lymphocytes (TIL) and defects in homologous recombination (HR) are important prognostic factors in ovarian carcinoma, but their relationship to each other is not defined. We characterized the distribution of TIL in a cohort of ovarian carcinoma patients with and without HR deficiency (HRD).

Method: Subjects were prospectively enrolled in a gynecologic oncologic tissue bank at the time of cancer diagnosis. Included subjects had carcinoma of the ovary, fallopian tube, or peritoneum. Subjects who received neoadjuvant chemotherapy were excluded. Malignant neoplasm and serum samples were collected, and patients were followed longitudinally. Immunohistochemistry (IHC) was performed on 119 patients for CD3 and CD8 (intratumoral T cells), CD68 (tumor associated macrophages), and FoxP3 (regulatory T cells). Microvessel density (MVD) was assessed at both 20x and 40x. Damaging germline and somatic mutations in genes in the HR pathway were determined using BROCA sequencing. HRD was defined as a damaging mutation in one of 17 genes in the HR pathway or promoter hypermethylation in *BRCA1* or *RAD51C*.

Results: Forty-six of 119 (38.7%) subjects had either a mutation in the HR pathway or promoter hypermethylation and were classified as HRD. Tumor-infiltrating immune cells were significantly higher in carcinomas with HRD than in carcinomas without HRD (CD3, $P = 0.003$, and CD68, $P = 0.015$). CD8, FoxP3, and MVD were not statistically different among HRD groups.

Among subjects with a defect in HR, median overall survival (OS) was significantly longer (57.6 vs 37.3 months, hazard ratio = 0.57, 95% CI 0.37–0.86, $P = 0.006$).

Conclusion: Among a cohort of patients with ovarian carcinoma, subjects with HRD, defined by either mutation or hypermethylation of a key HR gene, had significantly higher tumor-infiltrating immune cells and a 20-month improvement in OS. Based on these findings, an additional 160 patients are currently being evaluated, and data for all 279 patients will be presented to determine the relative contribution of the presence of TILs or HRD to improved outcomes. HRD could lead to an immunostimulatory environment through an increased neoantigen load, by stimulating the innate immune system with damaged or free cytosolic DNA, or as-yet-unrecognized mechanisms.

83 - Featured Poster Session

Comparative efficacy and tolerability of the PARP inhibitors, olaparib 300 mg tablets BID, niraparib 300 mg capsules QD and rucaparib 600 mg tablets BID as maintenance treatment in *BRCAm*-mutated (*BRCAm*) platinum-sensitive relapsed ovarian

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Objective: Maintenance treatment with poly(ADP-ribose) polymerase inhibitors (PARPis) significantly increases progression-free survival (PFS) in patients with *BRCAm* PSROC following response to platinum-based chemotherapy. PARPis have varying incidence of grade 3–4 adverse events (AEs) such as liver toxicity and thrombocytopenia. Variance in drug tolerability thresholds has also been observed among PARPis. There are no head-to-head comparative studies. We present a mixed-treatment comparison (MTC) of olaparib tablets, niraparib capsules, and rucaparib tablets to evaluate comparative efficacy and tolerability in the *BRCAm* population.

Method: Bayesian MTC efficacy analyses evaluated investigator (INV) and independent review committee (IRC) PFS HRs, using SOLO2 ITT data and NOVA and ARIEL3 *BRCAm* data. Safety analyses investigated ORs of grade 3–4 AEs, treatment interruption, and dose reduction due to AEs. ITT data from ARIEL3 were used; *BRCAm* safety data have not been published.

Results: Respective INV PFS HRs for olaparib versus niraparib, olaparib versus rucaparib, and rucaparib versus niraparib were HR = 1.11 (95% CI 0.67–1.84), HR = 1.30 (95% CI 0.67–1.84), and HR = 0.85 (95% CI 0.50–1.48). IRC PFS HRs were 0.93 (95% CI 0.53–1.60), 1.25 (95% CI 0.71–2.18), and 0.74 (95% CI 0.40–1.40), respectively. There were no efficacy differences between PARPis. ORs of grade 3–4 AEs were olaparib versus niraparib, OR = 0.18 (95% CI 0.07–0.47); olaparib versus rucaparib, OR = 0.36 (0.17–0.76); and rucaparib versus niraparib, OR = 0.52 (95% 0.22–1.21). Treatment interruption ORs were 0.31 (95% CI 0.11–0.78), 0.23 (95% CI 0.11–0.52), and 1.3 (95% CI 0.50–3.21), respectively. ORs for dose reduction were 0.13 (95% CI 0.02–0.85), 0.43 (95% CI 0.10–2.18), and 0.32 (95% CI 0.06–1.27), respectively. Olaparib showed significant reduction in odds compared with niraparib and rucaparib in grade 3–4 AEs and treatment interruption and significant reduction in odds of dose reduction compared with niraparib. See Table 1.

Conclusion: MTC showed no significant efficacy difference between PARPis in maintenance therapy in *BRCAm* PSROC patients following response to chemotherapy. For grade 3–4 AEs and treatment interruption, olaparib demonstrated superior tolerability with reduced odds compared with niraparib and rucaparib, and superior tolerability versus niraparib for dose reduction.

Table 1. Summary data on efficacy and tolerability in respective PARPi Phase III studies in PSROC.

PARPi	Study	(HRs) Median PFS (IRC), months	(HRs) Median PFS (INV), months	Grade 3–4 AEs, %	Treatment interruption, %	Dose reduction, %
Olaparib 300mg tablets BID	SOLO2	(0.25[0.18-0.35]) 30.2 vs 5.5	(0.30[0.22-0.41]) 19.1 vs 5.5	36.9 vs 18.2	45.1 vs 18.2	25.1 vs 3.0

Niraparib 300mg capsules QD	NOVA	(0.27) [0.17-0.41] 21.0 vs 5.5	(0.27[0.18-0.40]) 14.8 vs 5.5	74.1 vs 22.9	66.5 vs 14.5	68.9 vs 5.0
Rucaparib 600mg tablets BID	ARIEL3	(0.2[0.13-0.32]) 26.8 vs 5.4	(0.23[0.16-0.34]) 16.6 vs 5.4	54.6 vs 13.8	63.7 vs 10.1	54.6 vs 4.2

84 - Featured Poster Session

Immune checkpoint expression, microsatellite instability, and mutational burden: Identifying immune biomarker phenotypes in uterine cancer

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Objective: Endometrioid endometrial cancer (EEC) is categorized on a histologic continuum from grade 1 to 3 (grade 1 or low grade, grade 2; grade 3 or high grade). Increasing grade is associated with aggressive behavior and poor prognosis. Treatment options for advanced/recurrent disease are limited. Herein we identify distinct immune “biomarker phenotypes” to identify patients who may benefit from immune therapy (IT).

Method: A total of 621 tumors were analyzed for immune biomarker phenotype by multiplatform profiling. NextGen sequencing was performed on 592 genes. Tumor mutational load (TML) was defined as high ≥ 17 mutations/megabase. Microsatellite instability (MSI) by NGS was ≥ 46 loci. PD-L1 positivity was $\geq 2+$, $>5\%$ by IHC. Data were compared using χ^2 tests.

Results: Overall, MSI-H was found in 33% (203/621) of EECs. High-grade tumors had the most frequent MSI-H status, followed by a progressive decline in grade 2 and grade 1 tumors that was statistically significant (grade 3, 37%, 58/156; grade 2, 32%, 55/172; and grade 1, 22%, 25/113; $P = 0.007$). TML-H was identified in 25% (152/619) of EECs. Similar to MSI-H status, TML-H was most common in high-grade tumors, with a statistically significant decline noted as tumor grade decreased (grade 3, 34%, 53/156; grade 2, 23%, 39/171; and grade 1, 13%, 15/113; $P = 0.006$). Overall, PD-L1 expression was found in 5.5% (33/603) of EECs. High-grade ECCs had the most frequent PD-L1 expression, with a statistically significant decrease in expression frequency as tumor grade decreased (grade 3, 12%, 18/153; grade 2, 3.0%, 5/169; grade 1, 0.9%, 1/107; $P < 0.0001$). Triple negative (TN) biomarker phenotype was evaluated as a potential surrogate marker of low tumor immunogenicity. We identified TN phenotype in 72% of grade 1 ECCs (77/107) compared with 60% in grade 2 (101/168) and 52% in grade 3 (80/153), suggesting a higher incidence of immunogenic drivers with increasing tumor grade. See Figure 1.

Conclusion: We evaluated TML, MSI, and PD-L1 expression in more than 600 EECs. High-grade tumors appear to be more immunogenic than low-grade tumors, and may preferentially benefit from IT providing a potentially powerful treatment option. Conversely, low-grade tumors are less likely to benefit from IT and other treatment options should be considered.

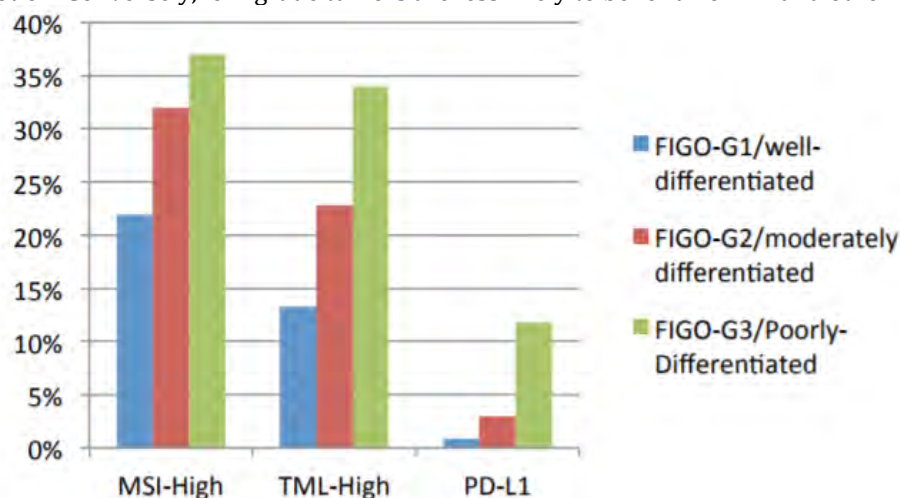


Fig. 1.

Table 1.

	MSI			TML			PD-L1		
	N		%	N		%	N		%
	High	Total	MSI-High	TML-High	Total	TML-High	Positive	Total	PD-L1
FIGO-G1/well-differentiated	25	113	22%	15	113	13.30%	1	107	0.90%
FIGO-G2/moderately-differentiated	55	172	32%	39	171	22.80%	5	169	3.00%
FIGO-3/Poorly-Differentiated	58	156	37%	53	156	34.00%	18	153	11.80%

85 - Featured Poster Session

Mutational burden, tumor immune checkpoint expression, and microsatellite instability in gynecologic malignancies: Implications for immune therapy

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Objective: Limited data exist in gynecologic oncology literature regarding immune therapy (IT). We studied "biomarker phenotypes" to identify patients who may benefit from IT in addition to, or in lieu of, traditional options.

Method: A total of 5,588 tumors were analyzed by multiplatform profiling. NextGen sequencing (NGS) was performed on 592 genes. Tumor mutational load (TML) was defined as high as ≥ 17 mutations/megabase. Microsatellite instability (MSI) by NGS was ≥ 46 loci. PD-L1 positivity was $\geq 2+$, $>5\%$ by IHC. Data were compared using χ^2 tests.

Results: A total of 3,223 ovarian, 1,989 uterine, 284 cervical, 49 vulvar, and 19 vaginal cancers were analyzed. MSI-high was found in 16% of uterine cancers (33% endometrioid, EM; 10% neuroendocrine, NE; 8% squamous, SQ; 7% clear cell, CC; 5% carcinosarcoma, CS; 3% serous; 2% leiomyosarcoma, LMS; 2% stromal sarcoma, SS); 1% of ovarian cancers (8% germ cell, 6% EM, 3% low grade, 2% mucinous, 2% CC, 1.2% CS, 0.7% serous); and 2% cervical and 0% of vulvar and vaginal cancers. TML-H was noted in 13% of uterine cancers (25% EM, 17% SQ, 10% NE, 5% serous, 5% CC, 5% SS, 4% CS, 3% LMS); 2% of ovarian cancers (9% germ cell, 6% EM, 3% low grade, 7% mucinous, 4% CC, 3% CS, 1% serous); 6% cervical; 6% vulvar; and 21% of vaginal cancers. PD-L1 expression was observed in only 7% of uterine and ovarian tumors but in 28% cervical, 63% vulvar, and 47% of vaginal cancers. By histology, MSI and TML were highly correlated ($P < 0.0006$). There was limited correlation between TML/PD-L1 (except in ovarian CC and serous and uterine LMS) and MSI/PD-L1 (except in uterine serous, ovarian mucinous, and serous). There was no significant correlation for MSI/TML/PD-L1 except in ovarian serous and CC ($P < 0.05$). Triple negative phenotype was identified in more than 85% of uterine serous, CS, LMS, and SS and ovarian serous, CS, LMS, and LG. Single or double positive markers were $\geq 15\%$ in the following cancers: cervical; uterine SQ, CC, EM; ovarian CC, EM, germ cell; and vulvar and vaginal. Triple positive was $<5\%$ in all cancers studied. See Figure 1.

Conclusion: We evaluated TML, MSI, and PD-L1 expression in 5,588 gynecologic cancers. Certain histologies appear better suited for IT: cervical, vulvar, vaginal, uterine EM and CC, and ovarian EM, CC, mucinous, low grade. and germ cell cancers. Given each cancer demonstrates its own phenotype, panel results are key in directing therapy.

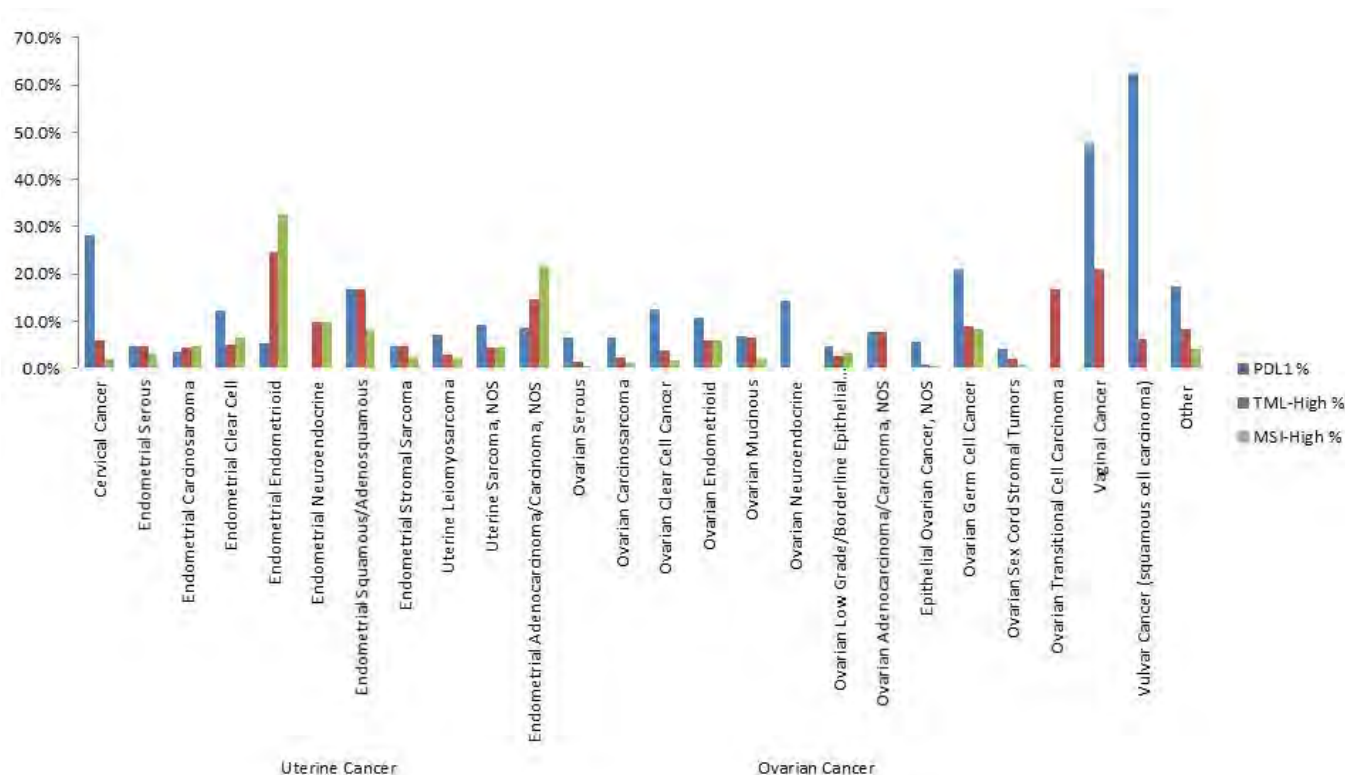


Fig. 1.

86 - Featured Poster Session

Improving the efficacy of PARP inhibition with a novel ATR inhibitor, ATRN119, in ovarian high-grade serous cancers

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Objective: PARP inhibitors (PARPi's) inhibit the repair of single-stranded breaks (SSBs), leading to DSBs at replication forks. ATR responds to replicative stress by stabilizing replication forks leading to cell cycle arrest, allowing DNA to repair. ATR inhibition (ATRi) is synthetically lethal with many genetic alternations found in ovarian HGSCs including *CCNE1* over-expression, and *BRCA1/2* and *TP53* mutations. While ATRi's are in early clinical trial development, improvement in specificity to minimize off-target effects and toxicity are needed. We hypothesize that ATRi, using a new selective small molecule inhibitor (ATRN119), in combination with PARPi will increase tumor regression compared to PARPi monotherapy with acceptable toxicity.

Method: ATRi (ATRN119), carboplatin, and PARPi (AZD2281, olaparib) were evaluated in PEO1 (*BRCA2*-mutant), JHOS4 (*BRCA1*-mutant), PEO4 (*BRCA* wildtype), and WO-24 primary ovarian cells (*BRCA* wildtype, Cyclin E high). Viability and colony formation were assessed. Drug effects on target and off-target pathways were performed. Drugs were tested as monotherapy and in combination using an orthotopic ovarian cancer patient-derived xenograft (PDX) model.

Result: ATRN119 treatment alone significantly decreased cell viability (<20%) in *BRCA*-mutant, *CCNE1*-over-expressing HGSOC cells that were PARPi-resistant and platinum-resistant. Similarly, ATRN119 was synergistic in decreasing cell survival (<10%) when in combination with AZD2281 in these cell models. ATRN119 targeted ATR by decreasing pCHK1 at nanomolar concentrations with no effect on mTOR/ATM, showing selectivity. Increases in pCHK1 with PARPi treatment were overcome with ATRi using ATRN119. ATRN119 alone had similar antitumor effects as PARPi alone in a *BRCA2*-deficient PDX model. Combination of ATRN119 with PARPi was tolerable and resulted in complete tumor regression unlike monotherapy in a *BRCA2*-mutant PDX model.

Conclusion: ATRN119 is a new ATRi that shows increased selectivity and potency compared to older ATRi. ATRN119 is as effective as PARPi monotherapy, resulting in tumor suppression in *BRCA*-mutant PDXs. However, ATRN119 combined with PARPi is tolerable and results in complete tumor regression, suggesting combination therapies may make PARPi more effective in the recurrent setting.

87 - Featured Poster Session

System-wide implementation of a perioperative practice-changing bundle to lower surgical site infections in gynecologic oncology: Outcome effect and impact of variations in compliance

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Objective: To investigate the effect of implementation of a perioperative practice-changing surgical bundle on the incidence of surgical site infection (SSI) in gynecologic oncology surgeries and to study the impact of bundle compliance on SSI rates.

Method: A quality improvement project involving implementation of a perioperative practice-changing bundle to reduce SSI was adopted by the gynecologic oncology division in 2012 and carried through the second quarter of 2017. The bundle included unified appropriate perioperative antibiotic choice, dosage, and intraoperative redosing; specific antibacterial vaginal and abdominal surgical site skin preparation including appropriate dry time; and maintenance of tight glycemic control and normothermia perioperatively. All data regarding bundle compliance and SSI were prospectively hospital-collected and validated. Bundle compliance was expressed as a percentage of the total number of items complied with. SSI rates included SSIs within 6 weeks postoperatively and were collected overall and for hysterectomies. Compliance and SSI rates were reported each quarter.

Results: A total of 5,331 gynecologic oncology procedures occurred during the study period, including 2,220 hysterectomies. The median patient age was 62 years, and the mean BMI was 36. The overall rate of SSI per 100 procedures was 2.21 for hysterectomies and 1.12 for all procedures. The hysterectomy SSI rates are shown in Figure 1. At bundle implementation in 2012, the SSI rate was 6.41% for hysterectomies and 3.23% overall; the last quarter of 2017, these rates dropped to 1.65% and 1.21%, respectively. The overall average bundle compliance rate after the first quarter of implementation was 77.4% (20% to 95%). Overall, a rise in bundle compliance corresponded with a drop in SSI, and vice versa (Figure 2). Bundle compliance was reinforced in the first quarter of 2015 after a high rate of SSI. This reinforcement led to lower SSI in subsequent quarters.

Conclusion: Implementation of a perioperative SSI reduction bundle remarkably lowered SSI. Compliance with the perioperative bundle is linked with SSI, and higher compliance led to lower SSI.

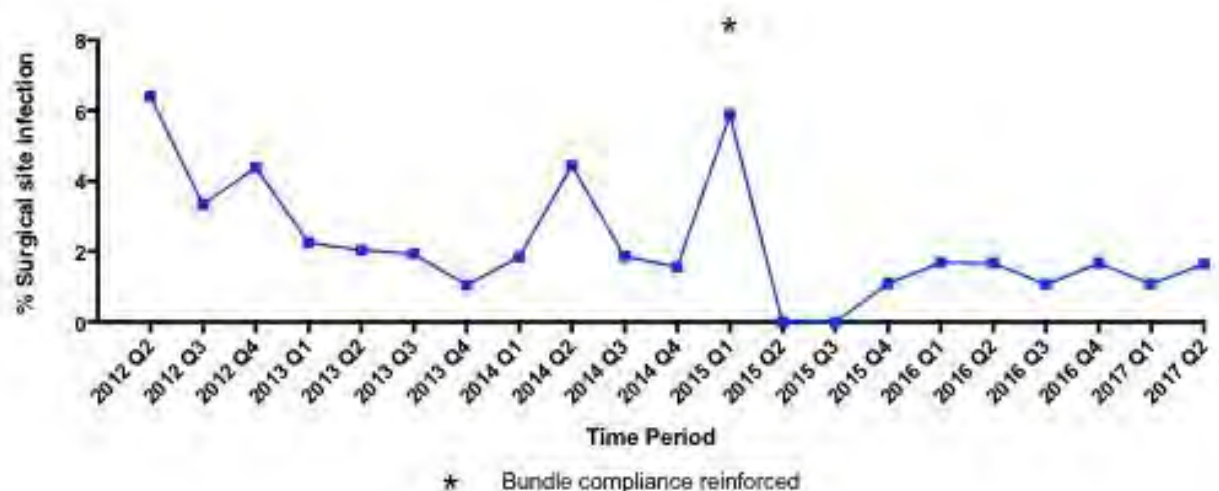


Fig. 1. Rate of surgical site infection in hysterectomy procedures by quarter.

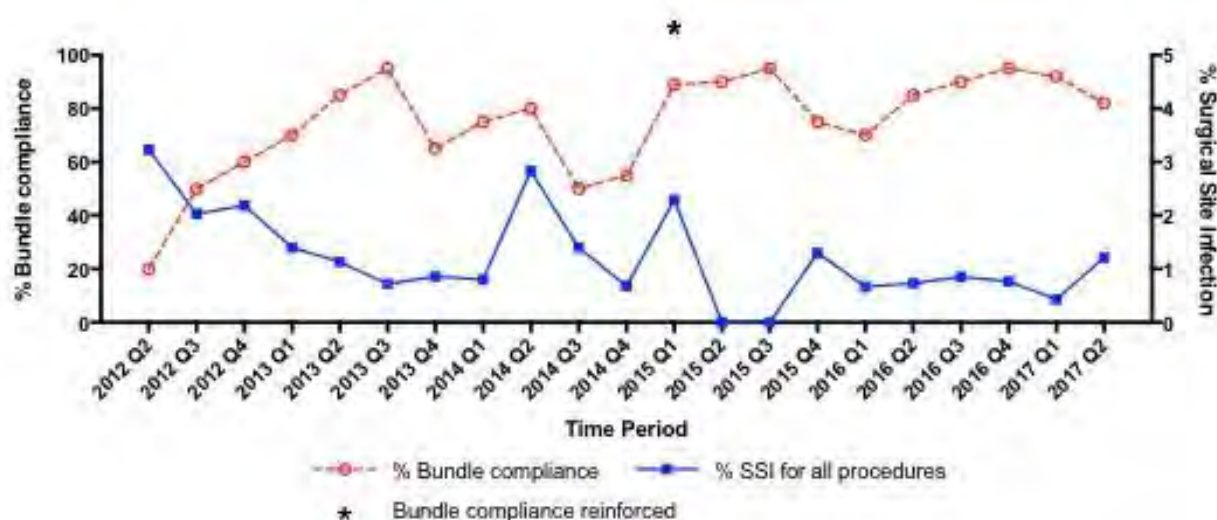


Fig. 2. Overall rates of bundle compliance and surgical site infection by quarter.

88 - Featured Poster Session

CA-125 is a useful predictor of disease status in uterine carcinosarcoma

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Objective: Uterine carcinosarcoma is a rare and aggressive tumor with poor outcomes. CA-125 is routinely used to track the disease course in ovarian cancer and has been suggested as a biomarker in other aggressive forms of uterine cancer. We sought to characterize CA-125 as a potential biomarker of disease status in uterine carcinosarcoma.

Methods: After obtaining institutional review board approval, we identified patients who had surgical staging for a pathologically confirmed uterine carcinosarcoma at our institution from January 2000 to March 2014. Clinical and pathological data were abstracted. Sign rank was used to compare changes in CA-125. χ^2 and Fisher exact tests were performed to identify predictors of elevated CA-125. Elevated CA-125 (>35) as a predictor of survival was assessed with linear regression.

Results: A total of 153 patients were identified. Median age was 65 (range 40–87) years, and the majority were Caucasian (88.9%). Of the 153 patients, 79 had a CA-125 drawn preoperatively (median 28.8 U/mL, range 6–771); 74 had a posttreatment level (median 8.0 U/mL, range 1–472); 37 had a level at the time of disease recurrence (median 30.0 U/mL, range 2–8,122); and 19 had a level at all 3 timepoints. A total of 28 (36%) had an elevated CA-125 (>35 U/mL) preoperatively. An elevated preoperative CA-125 was significantly associated with stage IV disease ($P = 0.003$). Analysis of the 51 patients with both pre- and posttreatment values found a significant drop in CA-125 ($P < 0.001$, sign-rank test). In the 30 patients who had end-of-treatment and recurrence levels, a significant increase was noted ($P = 0.001$). There was no significant trend in the 23 patients who had CA-125 drawn preoperatively and at time of recurrence ($P = 1.0$). In patients with all 3 timepoints, there was a significant difference between end-of-treatment CA-125 and recurrence ($P = 0.014$) but not between preoperative and end-of-treatment ($P = 0.073$) or recurrence ($P = 0.445$) CA-125 levels. Elevated preoperative CA-125 was not associated with overall survival ($P = 0.12$); elevated end-of-treatment CA-125 was associated with a worse overall survival ($P < 0.001$). See Figure 1.

Conclusion: Based on this dataset, elevated CA-125 does not correlate with presence of disease; however, the statistically significant drop at the end of treatment and rise at the time of recurrence would suggest a utility in trending CA-125. Prospective data is needed to confirm this trend.

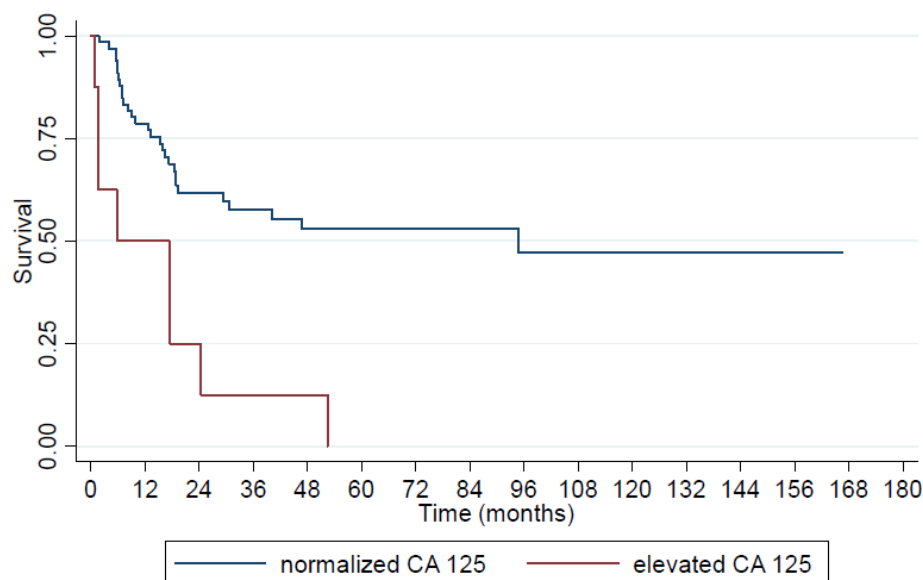


Fig. 1. Overall survival in patients with uterine carcinosarcoma and an elevated CA 125 at the end of treatment. Patients with an elevated CA-125 at the end of treatment have a significantly worse survival compared to patients with a normalized value ($P < 0.001$).

Poster Session

89 - Poster Session

Prognostic implication of programmed cell death 1 protein and programmed cell death 1 ligand 1 expression in endometrial cancer

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Objective: Monoclonal antibodies targeting programmed cell death-1 (PD-1)/programmed death ligand 1 (PD-L1) demonstrated promising clinical response, and the predictive/prognostic value of PD-1/PD-L1 immunohistochemistry (IHC) has been evaluated in many cancer types (1-3). However, the prognostic value of PD-1/PD-L1 IHC has not been evaluated in endometrial cancer (EC).

Method: We conducted a retrospective study to quantify the IHC expression of CD8, PD-1, and PD-L1 in immune cells (IC) at center of tumor (CT), invasive margins (IM), and/or tumor cells (TC) in 183 primary-EC samples from a single cohort, followed by their reciprocal combinations, including compartmental differences, and correlated them with overall survival (OS) and progression-free survival (PFS).

Results: In repeated Cox multivariable models adjusted by clinicoimmunopathologic factors, high CT-PD-L1 was an independent adverse prognostic factor for PFS (HR = 3.719, 95% CI 1.350–10.244) in all patients and for both OS (HR = 8.899, 95% CI 1.159–68.336) and PFS (HR = 4.135, 95% CI 1.440–11.871) in the microsatellite-stable subgroup. Immune marker ratios revealed independently shorter PFS for high CT-PD-L1/CT-CD8 ratio (HR = 4.653, 95% CI 1.675–12.927) and for high CT-PD-L1/CT-PD-1 ratio (HR = 4.874, 95% CI 1.361–17.447). Compartmentally different PD-L1 expression with a higher CT-PD-L1/IM-PD-L1 ratio showed independently poor OS (HR = 26.643, 95% CI 1.394–509.147) and PFS (HR = 11.448, 95% CI 2.336–56.093). Classification of EC into 4 groups based on CT-CD8 and CT-PD-L1 revealed significantly different survival among groups.

Conclusion: Compartmentalized analysis of PD-L1, as well as its combination with PD-1 and CD8, confers significant prognostic value and would provide insights for the tumor microenvironment in EC and potential predictive value for immunotherapy enabling more-refined-precision medicine in EC patients.

90 - Poster Session

AXL inhibition improves chemoresponse in gynecologic serous cancers

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Objectives: Genetic inhibition of AXL decreases invasion, migration, and metastasis in gynecologic serous cancers. We sought to determine how therapeutic inhibition of AXL affects treatment response in in vitro and in vivo models of serous cancers.

Method: Taxane- and platinum-resistant serous cell lines were used for in vitro cell viability (XTT) assays. Western blotting was used to detect protein expression and activation. Selective small molecule inhibition of AXL was achieved using BGB324. Single and combined therapy was assessed in in vivo subcutaneous models, utilizing the uterine serous cancer (USC) cell line *ARK1* in addition to patient-derived high-grade serous ovarian cancer xenografts (PDX). Statistical significance ($P < 0.05$) and IC₅₀ determination were assessed using Prism7.

Results: Western blot confirmed AXL over-expression in patient samples as well as in gynecologic serous cell lines. XTT assays demonstrated increased resistance to carboplatin and paclitaxel in AXL-expressing serous cells. Upon AXL inhibition with BGB324, the USC cell line *ARK1* demonstrated a dose-dependent sensitization to paclitaxel therapy (39%–72% decrease in IC₅₀). While BGB324 therapy did not decrease tumor burden alone in mouse models, combined paclitaxel and BGB324 therapy decreased tumor volume by 51%–67% when compared to treatment with single therapies or vehicle control ($P < 0.05$). Tumor proliferation rate was also significantly halted by combined AXL inhibition and paclitaxel therapy. In PDX models, BGB324 therapy improved tumor response to combined carboplatin and paclitaxel therapy when compared to chemotherapy alone, inhibitor alone, or vehicle control (77%, 87%, and 88% decrease in tumor volume, respectively, $P < 0.0001$).

Conclusion: In addition to being associated with more aggressive cancer phenotypes in gynecologic cancers, AXL contributes to platinum and taxane chemoresistance. Therapeutic inhibition of AXL with BGB324 restores chemosensitivity in gynecologic serous cell lines and patient-derived xenograft models.

91 - Poster Session

S-nitrosoglutathione, a physiologic nitric oxide carrier, reduces immunosuppression in ovarian cancer

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Objective: S-nitrosoglutathione (GSNO) is a physiological nitric oxide (NO) carrier that mediates a variety of NO signaling via trans-S-nitrosylation mechanisms. GSNO seems to play a role in regulating the effector function of various immune cells. We have previously shown the novel role of GSNO in inhibiting EOC growth in vitro and in vivo. Our aim was to investigate whether the antitumor effect of this physiological substance correlates with a modulation of the immune response.

Method: Immunocompetent B6 mice were used to grow intraperitoneal ID8 syngeneic mouse epithelial ovarian tumors. Mice were orally treated with GSNO (1 mg/kg body weight) or vehicle daily. Mice were sacrificed at day 60 for tumor burden evaluation. Quantification of various immune cells was performed by fluorescence-activated cell sorter (FACS) using specific cell surface markers. Interferon gamma (IFN γ) was measured by ELISA.

Results: GSNO treatment in ID8 tumor-bearing mice slowed down ovarian cancer progression as reflected by lower ascites volume ($P < 0.001$), tumor burden in the various organs, and Ki-67 expression ($P < 0.05$). Immune cell profiling showed significantly decreased number of immunosuppressive MDSCs (CD11b⁺Gr1⁺) in GSNO-treated mice ($P < 0.01$), including both granulocytic (CD11b⁺Gr1^{high}) and monocytic (CD11b⁺Gr1^{low}) subpopulations. Furthermore, intracellular IFN γ -producing CD4 and CD8 T cell populations were increased in tumor-bearing mice treated with GSNO compared to controls ($P < 0.01$). MDSCs isolated from the GSNO-treated group exhibited decreased ability to suppress CD3 cell proliferation ($P < 0.01$) and enhanced IFN γ production ($P < 0.01$).

Conclusion: GSNO, an endogenously available NO carrier, inhibits EOC progression possibly by reducing the immunosuppressive MDSCs and enhancing cytotoxic T cells activity. Thus, GSNO has a therapeutic potential in ovarian cancer and will be tested with other immunotherapeutic approaches.

92 - Poster Session

Targeting vitamin D receptor (VDR)/immune checkpoint inhibitor receptor ligand PD-L1 axis for immunotherapy of ovarian cancer

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Objective: VDR is highly over-expressed in epithelial ovarian cancer (EOC) and correlates with worse survival rate of patients. Cause and pathologic impact of VDR over-expression in EOC are not known. Our ongoing studies indicate that VDR expression activates PD-L1, which promotes immune evasion in tumors via deactivation of cytotoxic T-cells. We propose to study outcome of VDR/PD-L1 interactions and to determine whether targeting VDR/PD-L1 axis via a novel VDR antagonist MeTC7 can restore antitumor immunity and reduce tumor burden.

Method: The R2 Genomics Analysis and Visualization platform was used to establish the correlation of VDR expression with overall survival rate among EOC patients. Relative VDR over-expression in normal ovarian, benign, and serous and endometrioid EOC tissues was confirmed by fluorescence histochemistry. Stable VDR over-expressing SKOV-3 EOC cell clones were generated by transfection with hVDR DNA plasmid and antibiotic-mediated clonal selection. Stable VDR knockdown clones of SKOV-3 cells were generated via transfection with shRNA. PD-L1 expression was measured by flow cytometry. SKOV-3 and ES-2 cells were xenografted in nude or NSG mice and treated with MeTC7, a small molecule VDR antagonist.

Results: VDR over-expression was strongly associated with worse overall survival in EOC. Stable VDR over-expression in SKOV-3 cells led to strong activation of immune suppressive ligand PD-L1. VDR and PD-L1 colocalized in EOC tissues and SKOV-3 and OVCAR-8 EOC cells. Anti-VDR antibody showed immunoprecipitation with PD-L1 in SKOV-3 and OVCAR-8 EOC cells. Stably VDR knockdown (via shRNA) SKOV-3 cells showed reduced tumor burden in nude mice compared to wildtype and scrambled control cells. MeTC7 treatment reduced tumor burden in both SKOV-3 and a high PD-L1 expressing ES-2 cell derived xenografts in nude or NSG mice. MeTC7 reduced PD-L1 expression in SKOV-3 and OVCAR-8 EOC cells, M2 type macrophages, and in an irradiation-induced PD-L1 activation model of colorectal cancer in animals.

Conclusion: Our studies suggest that VDR over-expression and its interactions with PD-L1 may promote immune evasion in EOC. Targeted inhibition of VDR via MeTC7 can block PD-L1 expression, reduce tumor burden, and may promote antitumor immunity. Study of the effect of MeTC7 treatment on immune milieu of ovarian tumors in a syngeneic rat EOC model is in progress.

93 - Poster Session

STAT3 modulates the energy metabolism of ovarian cancer cells

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Objectives: STAT3 (Signal Transducers and Activators of Transcription 3) is associated with tumor progression, metastasis and chemo-resistance in ovarian cancer. STAT3 is constitutively activated in patient-derived ovarian cancer cells. High STAT3 expression is a predictor of poor prognosis in ovarian cancer. Apart from its function as a transcription factor, recently STAT3 has been shown to modulate mitochondrial function to promote carcinogenesis. The aim of our study was to investigate whether STAT3 activation can modulate cellular metabolism of ovarian cancer cells.

Methods: Stable clones expressing STAT3 were generated in A2780 ovarian cancer cells, along with empty vector (pcDNA) clones. The proliferation potential was estimated by MTT and colony formation assays. Nude mice were used to create xenografts, and STATTIC treatments were done via intraperitoneal injections. Seahorse XF Extracellular Flux analyzer was used to measure the bioenergetic phenotype. Real-time measurements of glycolysis and mitochondrial oxidation were done using the outputs of extracellular acidification rate (ECAR) and oxygen consumption rate (OCR), respectively

Results: Ectopic expression of STAT3 in A2780 ovarian cancer cell line resulted in increased proliferation ($P < 0.01$) and colony formation ability ($P < 0.001$) in vitro and led to large ovarian tumors ($P < 0.01$) compared to parental and pcDNA controls. Bioenergetic profiling showed higher mitochondrial respiration (OCR) and glycolysis (ECAR) in STAT3 clones compared to parental and pcDNA clones. Ratio of ECAR/OCR in the STAT3 over-expressing cells placed them in the "metabolically active" phenotype, while parental A2780 and pcDNA clones were in the "metabolically less active" phenotype. A selective inhibitor of STAT3, STATTIC, inhibited the STAT3-mediated growth of A2780 cells both in vitro ($P < 0.01$) and in vivo ($P < 0.01$). In addition, STATTIC treatments reversed the metabolically active state of STAT3 overexpressing clones to a lower

metabolic state, placing them in the same category as the control cells. In addition, STAT3 inhibited the cell proliferation of other ovarian cancer cell lines (*PEO4*, *C200*, and *OVCAR3*) that display a metabolically active phenotype.

Conclusion: STAT3 is capable of inducing metabolic changes in ovarian cancer cells and may be a survival mechanism that enhances the cellular fitness of the ovarian cancer cell resulting in increased oncogenic abilities.

94 - Poster Session

Comparative proteomic profiles of cervical cancer and paired paracancerous tissue and the potential effects of DUSP7 over-expression through inhibiting Ras pathway on the biological characteristics of human cervical cancer cell line

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Objective: To compare the protein profiles between paired samples of cervical cancer and paracancerous tissue and identify a series of differentially expressed proteins (DEPs) through quantitative proteomics.

Method: Proteomic profiles of three paired samples of cervical cancer and paracancerous tissue were detected and compared through quantitative proteomics. A candidate gene plasmid was inserted into pWSLV-08 vector with GFP (green fluorescent protein) as the reporter gene. The lentiviral particles containing candidate gene were transfected into SIHA cells. A variety of in vivo and in vitro tests were performed to evaluate the candidate gene on the biological characteristics of SIHA.

Results: According to the TMT (Tandem Mass Tags) ratios (≥ 1.5 or ≤ 0.5), three DEPs, including HRAS, DUSP7, and PLD1, and ERK1/2, participating in the RAS pathway, were selected for further evaluation. A stable cell line with over-expression of DUSP7 was established successfully. The CCK8 assay growth curves showed that DUSP7-SIHA cells proliferated slower than NC-SIHA cells, based on a clear delay in the doubling time. Colony formation assay showed that the number of colonies formed by DUSP7-SIHA cells was significantly less than those formed by NC-SIHA cells. At both the mRNA and protein levels, the expression of caspase-3, Beclin 1, and LC3B was increased, but Bcl-2 expression was reduced in DUSP7-SIHA cells. In the Matrigel invasive/migratory assay, DUSP7-SIHA cells demonstrated the weaker ability to invade and migrate through the membrane. Wound-healing assays showed that the migration area of DUSP7-SIHA cells was smaller than that of NC-SIHA cells. In addition, E-cadherin increased, but Vimentin was reduced in DUSP7-SIHA cells, which demonstrated that over-expression of DUSP7 had a potential role in inhibiting EMT process of SIHA cells. ELISA-VEGF assay showed that the VEGF level secreted in the supernatant of DUSP7-SIHA cultures was lower. The ability of HUVECs to form endothelial tube decreased when transfected with DUSP7 DNA plasmid. After subcutaneous injection, DUSP7-SIHA tumors were observed much later than NC-SIHA tumors.

Conclusion: Up-regulating the expression of DUSP7 may be useful for the prevention or treatment of cervical cancer, which was possibly achieved through dephosphorylation of the ERK1/2 and inactivation of the RAS pathway.

96 - Poster Session

Single cell exome sequencing reveals somatic *BRCA1* heterogeneity in a patient with *BRCA1* germline mutation

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Objective: Technological advances now allow for the analysis of tumor genomes and transcriptomes at the single-cell level. This technique was used previously to demonstrate the heterogeneous composition of tumors in high-grade serous ovarian cancer (HGSOC) using RNA sequencing. In this study, we performed exome sequencing from viable intraoperatively acquired primary HGSOC in a patient with a known *BRCA1* germline mutation.

Method: This patient was recruited for a prospective precision medicine program in ovarian cancer. An intraoperatively obtained viable specimen was enzymatically digested and depleted of immune infiltrating cells. Twelve individual tumor cells were isolated using the Fluidigm C1 and sequenced using Illumina HiSeq. The entire exome was sequenced, including 25 probes covering the *BRCA1* locus. Single nucleotide variants (SNV) were prioritized using SNPEffect after filtering using the OMNI1000 SNP database.

Results: Sequencing produced 255 million reads (21 million/cell) for an average coverage of 139x. Using SNPEffect, we identified a total of 1,211,689 SNVs (~250,000/cell). Coverage within the *BRCA1* gene locus was variable. Seven cells had <5

exons sequenced, while 5 cells had between 7 and 19 exons sequenced. Exon coverage within the *BRCA1* locus ranged tenfold from 36x to 3,600x. Within the *BRCA1* locus, we detected 74 SNVs. As expected, cells with high exon coverage had more SNVs (>10/cell), while the low coverage exons had fewer than 5 SNVs/cell. Of the 74 identified SNVs, 19 were detected in multiple cells. Of these, 18 SNVs were clonal, while 1 SNV was homozygous mutant in 1 cell and wild-type in a second cell. A *BRCA1* founder mutation was detected in 2 of 12 cells, and we did not detect any previously identified *BRCA1* reversion mutations.

Conclusion: Sequencing of only 12 cells within a *BRCA1* mutant ovarian cancer sample identified heterogeneity within the *BRCA1* locus. Of 19 SNVs detected in multiple cells, 5% (1/19) were variable between the cells. This rate of heterogeneity in somatic mutations may explain differences in duration of response to PARP inhibition among patients because of pre-existing reversion mutations within a bulk tumor population. Single-cell DNA exome sequencing will allow for better characterization of tumor cell populations and patients in the quest for a “precision medicine” approach to ovarian cancer treatment.

97 - Poster Session

Effectiveness of pegylated liposomal doxorubicin maintenance therapy for platinum-sensitive recurrent epithelial ovarian cancer

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Objective: To examine the effectiveness of pegylated liposomal doxorubicin (PLD) maintenance therapy (40 mg/m² every 4 weeks) after first-line salvage chemotherapy for platinum-sensitive recurrent epithelial ovarian cancer.

Method: This retrospective cohort study examined women with a first recurrence of platinum-sensitive epithelial ovarian cancer between January 1, 2005, and December 31, 2015. Eligible cases had PLD maintenance following the first-line salvage chemotherapy (*n* = 21). Outcomes of interest included adverse events related to PLD therapy and survival outcome after the first recurrence.

Results: The most common chemotherapy regimen for first-line salvage therapy prior to PLD maintenance therapy was carboplatin/PLD (*n* = 14, 75.0%) followed by carboplatin/gemcitabine (*n* = 5, 23.8%). The median platinum-free interval was 13.0 months (range 7.0–30.4 months). The median number of PLD maintenance cycles was 6 (range 3–24 cycles), and 4 (19.0%) women received 12 or more cycles. The median cumulative dose for PLD maintenance was 435 mg/m² (range 120–1,200 mg/m²); 14 (75.0%) women received ≥400 mg/m². There were 13 (61.9%) women who developed any grade of adverse event, including 3 (14.3%) women who developed grade 3–4 adverse events. The most common adverse event was mucositis (*n* = 7, 30.0%). Dose reduction due to adverse events occurred in 12 (57.1%) women including 2 (9.5%) women with discontinuation due to toxicity; the remaining 10 (42.9%) women tolerated the reduced dose well. No women developed cardiotoxicity or secondary malignancies. Median PFS and OS after the first recurrence were 16.6 (95%CI 11.2–22.0) and 46.9 (95% CI 34.7–59.1) months, respectively.

Conclusion: Compared to historical controls, our study suggests that PLD maintenance may possibly improve survival of women with recurrent platinum-sensitive epithelial ovarian cancer. This regimen is well tolerated overall with the use of dose reduction to manage toxicity. Once response is established, routine dose reduction to 30 mg/m² every 4 weeks is advisable.

98 - Poster Session

p53 and L1 cell adhesion molecule (L1CAM) protein expression and mRNA transcriptome analysis in endometrial cancer

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Objective: Both p53 and L1 cell adhesion molecule (L1CAM) immunohistochemical (IHC) staining have been shown as prognostic markers of poor outcome in endometrial carcinomas. Few studies have looked at correlation of these markers with protein expression and mRNA transcriptome levels. This study aims to investigate the overlap in protein expression and transcriptome profiles of these two prognostic markers in endometrial cancer.

Method: Primary tumor specimens were obtained from a consecutive cohort of 110 women with newly diagnosed endometrial cancer of any stage, 110 of which were stained for p53 expression and 103 for L1CAM expression. mRNA transcriptome analysis was then performed on 110 fresh frozen tumor specimens using Agilent gene expression arrays. Median follow-up time was 60.5 months. Correlations between p53 and L1CAM staining and transcriptome profiles were analyzed. Pathway analysis using PARADIGM was performed.

Results: Of the 110 specimens, 22 (20%) stained positive for p53 and 23 (22.3%) stained positive for L1CAM. L1CAM and p53 IHC staining were strongly correlated ($P < 0.0001$). L1CAM and p53 mRNA transcriptome profiles were also highly correlated, with a correlation coefficient of 0.5388 ($P = 0.0005$). KRAS-associated pathways were associated with these cases.

Conclusion: The strong correlation between p53 and L1CAM in protein expression and mRNA transcription profiling indicates possible similarities in pathogenesis and prognostic value. As p53 has been shown to be more highly expressed in uterine papillary serous carcinomas, L1CAM may be a marker of serous-like endometrioid tumors, detecting small subpopulations in otherwise low-risk cancers. These biomarkers could further assist in the identification of molecularly high-risk endometrial cancers in the quest to individualize and improve outcomes for these patients.

99 - Poster Session

Preclinical activity and safety of STRO-002, a novel ADC targeting folate receptor alpha for ovarian cancer

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Objective: Folate receptor alpha (FolRa) is a cell-surface glycoprotein, highly expressed in ovarian and endometrial adenocarcinoma, and is thus a promising target for cancer therapy using antibody drug conjugates (ADCs). We have employed an *E. coli* cell-free expression system (XpressCF™) and site-specific conjugation technology to generate STRO-002, a novel, site-specific, and homogenous FolRa-targeting ADC.

Method: We have conducted preclinical studies demonstrating antitumor activity, optimal ADC stability, and favorable safety profile of STRO-002. In vitro cytotoxicity assays and in vivo efficacy studies were conducted to evaluate the activity of STRO-002 in multiple ovarian cancer cell lines and xenografts. Exploratory toxicology studies were conducted to determine the safety profiles for STRO-002 and its metabolite SC209 in cynomolgus monkeys and rats, respectively.

Results: Potent in vitro cytotoxicity ($EC_{50} = 0.1-3$ nM) was observed in multiple ovarian cancer cell lines treated with STRO-002. STRO-002 exhibits dose-dependent tumor growth inhibition in Igrov-1 tumor xenografts at a single dose (Figure 1), and complete regression is achieved in Igrov-1 and OVCAR-3 tumors with a single dose at 10 and 5 mg/kg, respectively. In addition, administration of STRO-002 in combination with carboplatin confers added benefit in efficacy in Igrov-1 tumors. Exploratory toxicology studies show favorable safety profiles for STRO-002 and SC209. The main toxicity finding in monkeys dosed up to 10 mg/kg consists of reversible hematopoietic/lymphoid tissue toxicity, which is considered antigen-independent and is consistent with the antiproliferative effects of SC209 observed in single-dose toxicology studies in rats. No signs of ocular toxicity were observed. In addition, the drug-linkage in STRO-002 is highly stable in circulation, and the released warhead, SC209, is a very weak substrate for drug-resistant efflux pumps within the cell and is cleared rapidly from plasma.

Conclusion: STRO-002 is an ADC with minimal drug moiety release in circulation and the potential for an improved safety and activity profile, and a reduced risk of tumor drug resistance. These data support advancing STRO-002 to IND-enabling studies as a potential treatment of FolRa expressing malignancies such as ovarian and endometrial cancer.

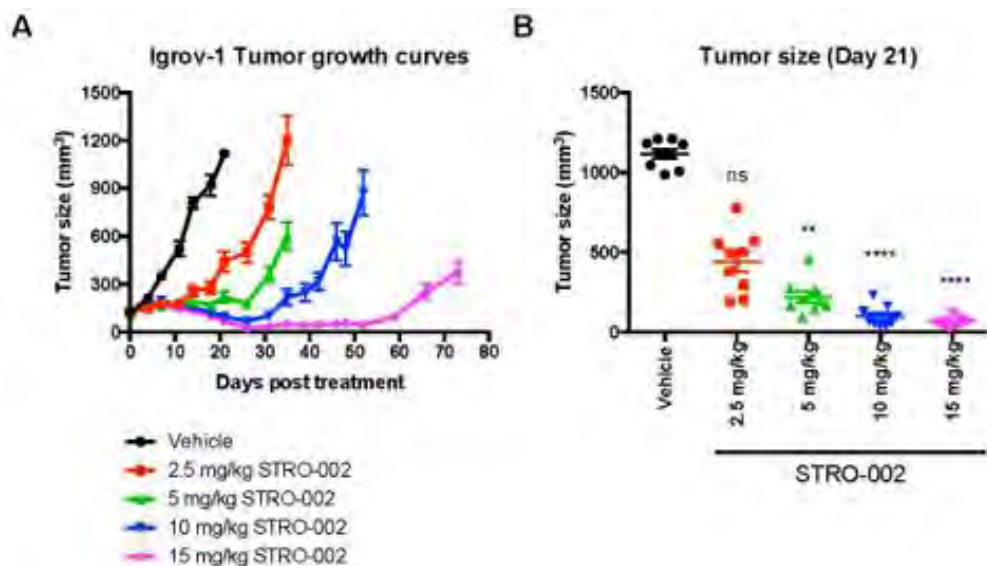


Fig. 1. Dose Dependent Effect of STRO-002 on Igrov-1 Tumor Growth.

100 - Poster Session

Preliminary data on the use of combination carboplatin, paclitaxel and pembrolizumab therapy for ovarian cancer

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Objective: The anti-PD1 antibody pembrolizumab is approved for the first-line treatment of select solid tumors. Pembrolizumab has previously demonstrated antitumor activity in heavily pretreated platinum-resistant ovarian cancer. This phase II trial (in progress) is evaluating the combination of carboplatin, paclitaxel, and pembrolizumab in patients with ovarian cancer and suboptimal cytoreduction. This represents our preliminary data.

Method: Patients with the diagnosis of stage III/IV epithelial ovarian cancer and any residual disease at the time of cytoreductive surgery meeting inclusion criteria were eligible to participate. Treatment consisted of carboplatin AUC 6 day 1; paclitaxel 80 mg/m² days 1, 8, and 15; and pembrolizumab 200 mg day 1 q 21 days. Alternatives to weekly paclitaxel were also administered and included paclitaxel 135 mg/m² day 1 or docetaxel 75 mg/m² day 1 q 21 days. The primary objectives were progression-free survival and tolerable safety profile.

Results: Seven patients consented. One patient screen failed. Six patients were treated. One patient was withdrawn due to treatment-related toxicity. Six patients were evaluable for toxicity. A total of 28 cycles of combined therapy were administered: 13 cycles of carboplatin AUC 6 day 1/paclitaxel 80 mg/m² days 1, 8, and 15, and pembrolizumab 200 mg day 1; 9 cycles of carboplatin AUC 5/paclitaxel 60 mg/m² days 1, 8, and 15, and pembrolizumab 200 mg day 1; 5 cycles of carboplatin AUC 5/docetaxel 75 mg/m² and pembrolizumab 200 mg day 1; 1 cycle of carboplatin AUC 5/paclitaxel 135 mg/m²; and 8 cycles of pembrolizumab 200 mg day 1. Six cycles of pembrolizumab maintenance therapy were administered. The most common adverse events for any grade were fatigue (83%), neutropenia (66%), anemia (66%), and thrombocytopenia (50%). The most common adverse events for grade 3 or 4 were neutropenia (33%), anemia (16%), congestive heart failure (16%), enteritis (16%), and pneumonitis (16%). The grade 4 pneumonitis was believed to be immune-related. Patients came off trial because of progression of disease (1) and grade 4 pneumonitis (1).

Conclusion: Pembrolizumab combination with carboplatin and paclitaxel even on a weekly schedule is safe and tolerable. The most common grade 3–4 adverse events were cytopenias likely related to cytotoxic therapy, similar to previous trials using carboplatin and taxol.

101 - Poster Session

Cytokine-induced memory-like natural killer cells demonstrate enhanced effector functions against ovarian cancer

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Objective: Natural killer (NK) cells are preactivated lymphocytes well-suited for adoptive immunotherapy because of their ability to kill tumor cells without prior sensitization. Early attempts with adoptive NK cell immunotherapy against ovarian cancer have proven unsuccessful, with the main limitations including failure of NK cells to expand *in vivo* and diminished NK cell effector function. Our objective was to investigate whether short-term incubation of NK cells with interleukin (IL)-12, IL-15, and IL-18 could produce cytokine-induced, memory-like (CIML) NK cells capable of enhanced *in vitro* and *in vivo* function against ovarian cancer.

Method: NK cells from healthy donors were incubated for 16 hr with IL-12, IL-15, and IL-18, washed to remove cytokines, rested on low-dose IL-15, and then placed against ovarian cancer targets at varying time points to assess phenotype and function via flow cytometry. NK-cell-mediated tumor-killing assay was performed comparing CIML versus control NK cells. CIML NK cells were injected intraperitoneal (IP) into a xenogeneic ovarian cancer mouse model. Healthy donor NK and NK cells derived from ovarian cancer ascites underwent proliferation and functional assays in both normal and immunosuppressive microenvironments. Student t tests and ANOVA were used to compare differences when appropriate.

Results: CIML NK cells demonstrate enhanced cytokine (IFN- γ , TNF- α) production ($P < 0.05$ on four independent lines) and NK-cell-mediated killing ($P < 0.05$ at 12 and 40 hr) of ovarian cancer. CIML NK cells decreased tumor burden (ANOVA, $P < 0.01$, $P < 0.0001$) and were associated with higher IP NK cell counts (mean 6,724 vs 815, $P < 0.0592$) on day 25 following injection *in vivo*. Healthy donor CIML NK cells proliferate more ($P < 0.05$) and are more functional ($P < 0.01$) compared to control NK cells in the suppressive soluble microenvironment of patients with ovarian cancer.

Conclusion: CIML NK cells have enhanced functionality and persistence against ovarian cancer *in vitro* and *in vivo*, even when exposed to ascites fluid. These findings suggest a potential strategy for NK cell-based therapy to circumvent the immunosuppressive nature of ovarian cancer.

102 - Poster Session

Novel immunooncology agent, small-molecule rory agonist lyc-55716: Tumor selection process for phase IIa expansion and rationale for clinical evaluation in ovarian cancer following phase I dose finding

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Objective: Translational and bioinformatics assessments were performed to support the inclusion of ovarian cancer (OC) patients in a phase 2a trial of the retinoic acid receptor-related orphan receptor γ t (ROR γ) agonist LYC-55716. ROR γ is the master transcription factor regulating type 17 effector T cell differentiation and function. Synthetic ROR γ agonists modulate gene expression in immune cells to enhance effector functions and decrease Treg and checkpoint pathways. ROR γ agonists have shown activity as mono- and combination therapy in syngeneic tumor models.

Method: Transcriptional profiling of murine and human T cells treated with and without ROR γ agonists was used to derive a gene signature. OC patient data in The Cancer Genome Atlas (TCGA) and other public datasets evaluated (1) ROR γ and ROR γ -inducing cytokine expression; (2) genes associated with ROR γ biology and surrogate markers of endogenous ROR γ ligands and correlations with prognosis; and (3) tumor microenvironment (TME) immune profiles. Tumor-infiltrating lymphocytes (TILs) and peripheral blood mononuclear cells (PBMCs) from OC patients were assessed for ROR γ expression and response to an ROR γ agonist.

Results: OC tumors expressed genes indicating infiltration of immune cells and high expression of ROR γ -inducing cytokines IL-23 α and IL-1 β . RNA sequence data showed >25% of TCGA OC samples expressed moderate to high levels of ROR γ , indicative of type 17 cells in the tumor. Consistent with this, TILs isolated from OC patients confirmed ROR γ expression in CD4⁺ TILs. OC tumors in TCGA expressed low levels of sterol efflux genes, suggestive of low endogenous agonist levels in the TME. Importantly, in OC samples, high ROR γ levels were significantly correlated with longer survival, and IL17A, an ROR γ target gene, was associated with favorable prognosis. Preliminary results from phase 1/2a clinical evaluation of LYC-55716 (NCT02929862) showed attainment of biologically active dose exposures and a well-tolerated safety profile in heavily pretreated patients, including patients with advanced gynecologic malignancies.

Conclusion: Preclinical activity in syngeneic tumor models, bioinformatics analyses of ROR γ expression and biology, and their correlation with improved survival support the inclusion of OC in a phase 2a clinical trial of LYC-55716.

103 - Poster Session

Single cell sequencing identifies distinct immune cell profiles in primary ovarian cancer

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Objective: Advances in sequencing technologies allow analyses to be conducted at the single-cell level. The purpose of this study was to investigate immune cell profiles in general, and natural killer (NK) cells in particular, for a tumor using single-cell sequencing.

Method: We generated transcriptome data from viable single cells from 4 primary ovarian cancers using the 10X Genomics platform and Illumina HiSeq. Multiple clustering techniques, including graph-based clustering, principal component analysis (PCA), t-Distributed Stochastic Neighbor Embedding (tSNE), and clustering through imputation and dimensionality reduction (CIDR), were used to define groups of cells with similar gene expression patterns. A total of 141 "immune signature" genes previously obtained from bulk sequencing were used to further define subsets of cells. Marker genes granulysin (GNLY) and natural killer cell granule protein 7 (NKG7) were used to identify NK cells. On 3 of the 4 patients, peripheral blood mononuclear cells (PBMCs) and ascites fluid cells were characterized for NK cells using flow cytometry.

Results: Transcript expression was characterized for an average of 3,425 (range 1,802–4,638) cells per patient with a mean of 92,662 (range 51,252–138,199) reads per cell in the 4 patients. The set of 141 "immune signature" genes was highly enriched in 1 cluster in 2 of the 4 tumors. The percentage of NK cells in the two immune-enriched samples was 1.52% and 1.51%, respectively. The percentage of NK cells in the PBMCs and ascites fluid for the enriched samples was 9.11% and 9.24% for tumor 1 and 8.25% and 30.3% for tumor 2.

Conclusion: Single-cell sequencing can provide a new means of investigating detailed immune profiles within ovarian cancer. Current NK cell and immunotherapy-based trials in ovarian cancer can benefit from these analyses to identify patients most likely to benefit from such treatment strategies.

104 - Poster Session

Resolution of recurrent, radiation-refractory, HPV+ squamous carcinoma of vulva and cervix following intratumoral vaccinations of quadrivalent HPV-L1 vaccine (GardasilTM) and topical TLR-7 agonist imiquimod (AldaraTM): A report of two

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Objective: The human papillomavirus is a significant global cancer burden. Few curative therapies are available for women with recurrent, radiation-refractory cancers of the lower genital tract. We report the "off-label" use of intratumoral injections of the quadrivalent HPV vaccine with serial application of topical imiquimod in 2 patients with recurrent, radiation-refractory, HPV+ lower-genital-tract cancers resulting in complete resolution of disease. We discuss how so-called "failed radiation" most likely altered the tumor producing these unlikely responses.

Method: Each patient was approved for compassionate use by our institution's BioEthics committee. Written consent was obtained, and "off-label" medications were free of charge. Patient A, a 90-year-old black female originally diagnosed with stage 2 vulvar squamous cell carcinoma, presented with 11 x 11 cm right inguinal tumor and symptomatic pulmonary metastases. Palliative groin radiation was initiated to the groin but stopped after 10 fractions (1,200 cGy total) because of progression (13 x 13 cm). Seven days after radiation, she began intratumoral HPV- L1 peptide vaccination (75 µg vaccine in 2 mL of normal saline) followed by 3 days of topical 5% imiquimod cream after each vaccination. Patient B, a 45-year-old who completed chemo-radiation (8,500 cGy) 28 days earlier for stage IIIB, squamous carcinoma of cervix, presented with a 4-cm central recurrence. Following histologic and PET imaging confirmation, immune therapy began while preparing for exenterative surgery. Immune therapy began 7 days after radiation by intratumoral vaccination as above and intravaginal 0.2% imiquimod vaginal suppositories. A second intratumoral vaccination was given 2 weeks later.

Results: Patient A demonstrated complete resolution of groin tumor and pulmonary symptoms. She lived 9 months after treatment. Patient B underwent examination under anesthesia on the day of exenterative surgery. Cervical tumor resolved changing operation to radical hysterectomy. Pathology was completely negative for cancer. HPV testing and PET/CT imaging 3 months postoperatively was also negative. The patient is 5 years without disease.

Conclusion: We report the use of 2 FDA-approved drugs used “off-label” to treat recurrent, radiation-refractory, HPV+ cancers of the lower genital tract.

105 - Poster Session

Inhibiting the wnt/ β -catenin pathway modulates immune response in ovarian cancer

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Objective: The Wnt/ β -catenin pathway mediates chemoresistance in ovarian cancer (OVCA) and is associated with immune exclusion via the non-T-cell-inflamed tumor phenotype across cancer types. Our objective was to investigate the inhibition of Wnt signaling in malignant human ascites cells and the immunomodulatory effect of Wnt inhibition using a syngeneic mouse model.

Method: Human OVCA cells obtained from the ascites of 53 patients were treated with 1 μ M of WNT974, a porcupine inhibitor, for 7 days, and ATP levels were assessed using the ATPlite assay. Ten samples with the highest reduction in ATP (>20%) were designated responders, and those with the lowest reduction in ATP (<10%) nonresponders. RNA-seq libraries were constructed before and after treatment to identify genes that (1) were differentially expressed among all treated compared to untreated samples and (2) predicted WNT974 response. The differentially expressed genes (DEGs, $n = 187$) between the responders and nonresponders were compared to the T-cell-inflamed and non-T-cell-inflamed groups from the OVCA TCGA database. C57BL/6 mice were injected subcutaneously with 7×10^6 ID8 OVCA cells and were treated with WNT974 ($n = 10$) or control ($n = 10$). WNT974 was given by oral gavage twice a day (5 mg/kg for 7 days followed by 2.5 mg/kg for 7 days). Mice were euthanized at days 7 ($n = 4$) and 14 ($n = 2$), and tumors were harvested for gene expression analysis using NanoString®.

Results: Of the 187 DEGs, 161 ($P < 0.05$) overlapped in RNA expression difference with the inflamed OVCA TCGA T-cell gene signature. Two Wnt pathway genes decreased after treatment ($P < 0.05$), but did not meet genome-wide significance. Mice treated with WNT974 had a gene expression profile on days 7 and 14 that more closely resembled an inflamed signature compared to untreated mice. In addition, WNT974 affected the expression of several genes that regulate T-cell function (Cd4, Cd8, Ifg, Cd274 (PDL1), Ctl4, and Lag3) on days 7 and 14.

Conclusion: Human OVCA ascites cells with a non-T cell-inflamed signature were more sensitive to WNT974, and the inhibition of the Wnt pathway in a syngeneic OVCA mouse model significantly affected immunomodulatory genes. Gene expression also shifted towards a T-cell-inflamed signature, indicating that Wnt inhibition leads to an increased immune response and could be used to enhance response to immunotherapy in OVCA.

106 - Poster Session

Effect of chemotherapy on immune infiltration status and immune pathway activation in high-grade serous ovarian cancer

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Objective: The impact of chemotherapy on the tumor-immune microenvironment (TIME) in high-grade serous ovarian cancer (HGSOC) is not well characterized. In this study, we evaluate the effect of neoadjuvant chemotherapy (NACT) on immune infiltration status and pathway activation in ovarian cancer.

Method: Twenty-eight paired tumors were identified from patients with HGSOC. Samples were acquired prior to NACT and at interval debulking surgery. Eight patients had tissue samples available from the same anatomic site before and after treatment. RNA was extracted using the Qiagen RNEasy kit and microarray performed in collaboration with Affymetrix using the Clariom D platform. Microarray expression data were analyzed using single-sample gene set enrichment analysis (ssGSEA) and then clustered using t-Distributed Stochastic Neighbor Embedding (t-SNE) analysis. Comparisons between enrichment scores of untreated and treated samples were performed using paired t tests or Wilcoxon.

Results: Estimated immune and stromal scores were significantly higher in matched samples after NACT treatment ($P = 0.02$ and $P = 0.05$), whereas non-site-matched paired samples did not show a significant difference ($P = 0.66$ and $P = 0.4$). Cytotoxic

T-cell enrichment score (ES) was higher in site-matched samples, but no difference was detected in paired nonmatched samples. There is increased activation of cell stress pathways across the cohort (Figure 1). The two patients who showed greater activation of proliferative pathways and less cell stress experienced clinically poorer outcomes, with progression-free survival of 166 and 328 days and overall survival of 176 and 661 days, respectively, significantly shorter than the medians for the remainder of the cohort (450 and 1,242 days, respectively). The Wnt signaling gene set ES was higher in samples with low immune ES, consistent with published data associating Wnt pathway activation with immune cell exclusion.

Conclusion: These findings show that carboplatin and taxane-based NACT frequently increases immune activation and cell stress in HGSOC. Overall, these findings serve to contribute to a better understanding of the TIME in high-grade serous cancer and suggest Wnt pathway inhibition may represent a rational target to improve immune infiltration.

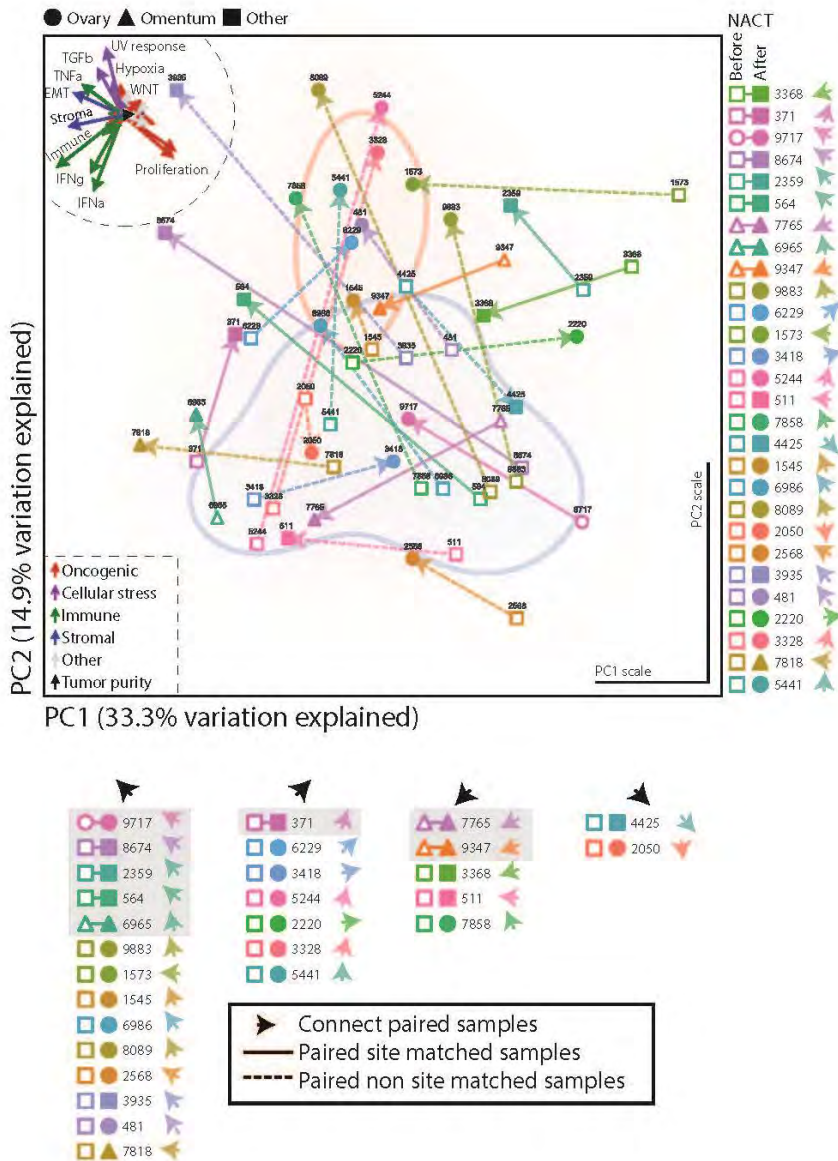


Fig. 1.

107 - Poster Session

Combination immune checkpoint blockade and MEK inhibition in a platinum-resistant ovarian cancer model

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Objective: PD-L1 blockade prevents PD-L1/PD-1 interaction and is currently explored as immune therapy of solid tumors. Here we investigate a combination therapy utilizing anti-PD-L1 together with a MEK inhibitor (AZD6244). The Ras pathway is frequently altered in a subset of ovarian cancers, and we have previously demonstrated that activation of oncogenic Kras leads to tumor PD-L1 upregulation in preclinical models. We hypothesize that Ras pathway inhibition with AZD6244 will lower PD-L1 expression on tumor cells and anti-PD-L1 will further decrease PD-L1 activity on both tumor cells and on other immune suppressor cells, both increasing antitumor immunity.

Method: Murine tumor cells derived from an orthotopic tumor isolated from a triple transgenic MUC1⁺/Kras/Pten mouse underwent prolonged in vitro propagation with increasing cisplatin doses to develop a cell line that served as our model for platinum-resistant ovarian cancer. Mice ($n = 32$) were injected with 5×10^6 tumor cells and divided into 4 treatment groups: weekly anti-PD-L1 antibody, daily AZD6244, combination anti-PD-L1, and AZD6244 or isotype control. Primary endpoint was survival to end of protocol. Secondary outcomes included tumor burden, ascites volume, and changes in immune gene expression. Tumors were evaluated with IHC and immune gene profiling.

Results: Treatment with anti-PD-L1 or AZD6244 each resulted in an upward trend in survival. However, the combined therapy showed no additive benefit ($P = 0.40$). All treatment groups demonstrated a decrease in tumor burden compared to control ($P = 0.05$), but no significant differences from one another. Therapies including anti-PD-L1 showed significantly lower ascites volumes ($P = 0.02$). In vitro we confirmed that activation of the Kras pathway upregulates PD-L1 and demonstrated this effect is reversed by AZD6244. In addition, IHC-revealed tumors treated with anti-PD-L1 demonstrate dense T cell infiltration.

Conclusion: We saw trends toward improved survival and decreased tumor burden in all treatment groups, but combination therapy did not improve survival. However, anti-PD-L1 containing regimens did produce a significant reduction in ascites. We hypothesize the impact of decreasing PD-L1 expression with AZD6244 and targeting PD-L1 receptors on tumor cells to increase antitumor immunity is redundant, rather than an additive effect.

108 - Poster Session

Exosomal expression of toll-like receptor 8-activating mir-146a-3p is upregulated by paclitaxel in chemoresistant epithelial ovarian cancer cells

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Objective: Recent studies have demonstrated the ability of epithelial ovarian cancer (EOC) cell-derived microRNAs (miRs) to confer chemoresistance via exosomal delivery through an unknown mechanism. Because our group has found that the TLR/MyD88 pathway is required for EOC chemoresistance, the objective of this study was to evaluate cellular and exosomal expression of TLR8-activating miRs in response to paclitaxel in chemosensitive (MyD88⁻) and chemoresistant (MyD88⁺) EOC cells.

Method: The EOC cell lines TR182 (paclitaxel-sensitive, MyD88⁻) and R182 (paclitaxel-resistant, MyD88⁺) were treated with or without paclitaxel (2 μ M) for 24 to 48 hours. Cellular and exosomal RNA was isolated, and expression of TLR8-activating miRs miR-146a-3p, miR-21a-5p, and miR-29a-5p was analyzed by qRT-PCR using snU6 as a control. Cell-free supernatants were analyzed for the proinflammatory marker IL-8 by ELISA.

Results: Cellular expression of TLR-activating miRs miR-146a-3p, miR-21a-5p, and miR-29a-5p was significantly higher in MyD88⁺ cells compared to MyD88⁻ cells by 5962.5-fold, 4.3-fold, and 5.6-fold, respectively ($P < 0.05$). Exosomal expression of miR-146a-3p was 36.1-fold higher in MyD88⁺ cells compared to MyD88⁻ cells ($P < 0.05$). While not significant, exosomal miR-21a-5p and miR-29a-5p were 2.3- and 2.9-fold higher, respectively, in MyD88⁺ cells. This correlated with a 95.7-fold higher basal IL-8 secretion in MyD88⁺ cells compared to the MyD88⁻ cells ($P < 0.05$). Treatment with paclitaxel significantly upregulated exosomal expression of miR-146a-3p by 1.3-fold in the MyD88⁺ cells ($P < 0.05$), while exosomal miR-146a-3p was not altered by paclitaxel in the MyD88⁻ cells.

Conclusion: These results demonstrate the presence and differential expression patterns of TLR8-activating miRs in chemoresistant and chemosensitive EOC cells, and that exposure to paclitaxel preferentially upregulates miR-146a-3p in the exosomal compartment of chemoresistant EOC cells. Thus, miR-146a-3p may have a potential role in EOC cell physiology as a mediator of exosomally conferred chemoresistance, and may represent a putative biomarker in the detection of paclitaxel-

resistant ovarian cancers.

109 - Poster Session

HE4 sabotages cytotoxic mononuclear cells via inducing dual specificity phosphatase 6 secretion

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Objective: To examine the role of secretory glycoprotein human epididymis protein-4 (HE4) in immune evasion and establish a preliminary mechanism of HE4-mediated immune failure in ovarian cancer.

Method: Modified subtractive hybridization was performed using the PCR-Select™ cDNA Subtraction Kit to create differential cDNA library. Effect of dual specificity phosphatase 6 (DUSP6) expression in PBMC in response to HE4 was confirmed by quantitative PCR, flow cytometry, and ELISA. In order to identify effector cells for the HE4-induced DUSP6, 2-color flow cytometry using antibodies against phosphor-Erk1/2 (pErk1/2) and CD4, CD8, CD14, CD19 and CD56 was performed. To evaluate the impact of HE4 on PBMC cytotoxicity on cancer cells, the human ovarian tumor cell line, SKOV3, was cocultured with PBMCs.

Results: Dual specificity phosphatase 6 (DUSP6) emerged as the most upregulated gene in PBMCs upon in vitro exposure to recombinant human HE4. CD8⁺ cells and CD56⁺ cells were found to be sources of the upregulated DUSP6. The HE4 exposure enhanced Erk1/2 phosphorylation specifically in these cell populations, and the effect was erased by coinubation with DUSP6 inhibitor, (E)-2-benzylidene-3-(cyclohexylamino)-2,3-dihydro-1H-inden-1-one (BCI). In coculture with PBMC, HE4-silenced SKOV3 exhibited enhanced proliferation with exposure to the external HE4; this effect was partially attenuated by adding BCI to the culture. In addition, the reversal effects of BCI were erased in the coculture with CD8⁺/CD56⁺ cell-deprived PBMC.

Conclusion: These findings show that DUSP6 is a suppressor of the cytotoxicity of the CD8⁺ and CD56⁺ lymphocytes, and HE4 enhances tumorigenesis of ovarian cancer through the compromised cytotoxicity of the CD8⁺ and CD56⁺ cells by upregulation of self-produced DUSP6, which acts as an autocrine factor.

110 - Poster Session

HE4 in tumor immune suppression and its potential as a therapeutic target in ovarian cancer

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Objective: To determine the impact of HE4 expression on the tumor-immune microenvironment and to identify HE4 as a viable therapeutic target in ovarian cancer.

Method: Tumor cells were transfected with an HE4-over-expression vector or null vector. This was done in human lines (SKOV3, 2008), a rat cell line (NuTu19), and a mouse cell line (ID8). PD-L1 expression was measured by RT-PCR, Western blot, flow cytometry, and immunohistochemistry. HE4 inhibition was performed with HE4-antisense or nonsense (control) oligonucleotides. MMP protein levels were determined by Western blot, and activity was assessed with zymography. Tumor models included mouse xenografts, the ID8 model, and the NuTu19 model. Tissues were analyzed with flow cytometry.

Results: HE4 induces PD-L1 expression in ovarian tumor cells and TAMs in vitro and in vivo. This enhanced PD-L1 expression is posttranscriptionally mediated through HE4's inhibition of matrix metalloproteases. In addition, HE4 over-expression reduces the number of tumor-infiltrative cytotoxic T cells in our rat model of ovarian cancer, which confirms patient data showing higher tumor expression of PD-L1 as a correlate of lower cytotoxic T cell infiltration. In vivo HE4 inhibition with antisense oligonucleotides resulted in delayed tumor growth.

Conclusion: HE4 induces PD-L1 expression on tumor cells and TAMs and reduces cytotoxic T cells within ovarian tumors, making it a promising therapeutic target for ovarian cancer treatment. Preclinical testing confirms that HE4 inhibition can delay ovarian tumor growth.

111 - Poster Session

Combined PD1 blockade and depletion of myeloid derived suppressor cells produces a synergistic antitumor effect in a murine model of ovarian cancer

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Objective: Monoclonal antibodies (mAb) that target programmed death (PD1) pathway may have a therapeutic role in epithelial ovarian cancer (EOC) by releasing the immune blockade caused by the PD1–PD-L1 interaction. On the other hand, myeloid-derived suppressor cells (MDSCs) represent a heterogeneous population of immature myeloid cells that are increased in ovarian tumors and create an immunosuppressive environment by inhibiting the T cell function. Our aim was to investigate whether depletion of MDSCs enhances the antitumor activity of PD1.

Methods: The intraperitoneal ID8 syngeneic mouse epithelial ovarian cancer cell model in B6 mice was used. The ID8-luciferase tumor-bearing mice were divided into 5 treatment groups: (1) a control group that received vehicle, (2) a second control group treated with isotype IgG2b mAb control (100 µg/dose/mouse), (3) group 3 treated with anti-Gr1 mAb that depletes MDSCs (100 µg/dose/mouse twice a week), (4) group 4 treated with anti-PD1 mAb (100 µg/dose/mouse twice a week for 3 weeks), and (5) group 5 treated with combination of anti-Gr1 and PD1 mAb. The mice were imaged using Xenogen IVIS to monitor tumor growth. Mice were sacrificed at day 40 for tumor burden evaluation. Quantification of immune cells was performed by fluorescence-activated cell sorter (FACS) using specific cell surface markers and by immunohistochemistry (IHC).

Results: The progression of ovarian cancer was significantly slower in mice treated with combination of anti-Gr1 and anti-PD1 when measured by bioluminescence images and ascites volume when compared to the control groups as well as those receiving single agent therapy. The reduced tumor burden in the combination group was validated by H&E tumor measurements and Ki-67 index ($P < 0.01$). Overall the combination group showed an increased Kaplan-Meier survival compared to single treatments ($P < 0.05$) or untreated/IgG2b ($P < 0.001$) groups. Anti-Gr1 treatment resulted in decreased MDSCs ($P < 0.01$), and combination with anti-PD1 resulted in increased antitumor immunity as seen by increased IFN-gamma-producing CD4 and CD8 T cells ($P < 0.01$).

Conclusions: Our data suggest that reducing MDSCs can improve the antitumor immune response of anti-PD1 immunotherapy by reshaping of the tumor microenvironment and making it less immunosuppressive.

112 - Poster Session

Focal adhesion kinase (FAK) controls programmed death-ligand-1 (PD-L1) expression and promotes tumor immune evasion in a syngeneic murine model of epithelial ovarian cancer

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Objective: FAK is a cytoplasmic tyrosine kinase that promotes tumor cell proliferation in ovarian cancer and has recently been linked to immune checkpoint regulation in other cancers. Our objective was to explore the effect of FAK on tumor cell number, tumor-infiltrating lymphocytes (TILs), and programmed death-1 (PD-1)/PD-L1 expression in a syngeneic murine model of epithelial ovarian cancer.

Method: An aggressive ovarian cancer cell line (*ID8-IP*) was derived from ID8 cells, and using the CRISPR/Cas9 system, a FAK knockout cell line was generated (*ID8-IP FAK KO*). To determine the effect of FAK on tumor cell proliferation and to evaluate for an interaction between FAK and T cells, tumor cells were injected intraperitoneally into immunocompetent (C57Bl6) mice. Tumor cells and immune cell populations were identified using flow cytometry.

Results: There were significantly more tumor cells in the *ID8-IP* group compared to the *ID8-IP FAK KO* group (61.4% vs 24.4%, $p < 0.0001$) and significantly fewer leukocytes (19.9% vs 48.3%, $P = 0.0003$). Although relative numbers of T cells and their subpopulations (T regulatory, CD4+, or CD8+) did not differ, there were significantly more PD-1 positive CD8+ cytotoxic T cells in the *ID8-IP* group relative to the *ID8-IP FAK KO* group (38.18% vs 14.26%, $P = 0.038$). To determine whether FAK regulates tumor-intrinsic PD-L1 expression in vitro, a third cell line (*ID8-IP FAK reexpressing*) was created by reintroducing FAK in the *ID8-IP FAK KO* cell line, and PD-L1-expressing tumor cells were identified using flow cytometry. Significantly more *ID8-IP* cells expressed PD-L1 in vitro relative to *ID8-IP FAK KO* cells (81.4% vs 39.7%, $P < 0.0001$), with the highest proportion of PD-L1 expression in the *ID8-IP FAK reexpressing* cells (88.5%).

Conclusion: Our study demonstrates that FAK is associated with aggressive tumor cell proliferation while promoting tumor evasion, as evidenced by higher PD-1 expression among CD8+ T cells. In addition, FAK significantly increases tumor-intrinsic PD-L1 expression. Experiments are in progress to establish a connection between these two novel findings in ovarian cancer.

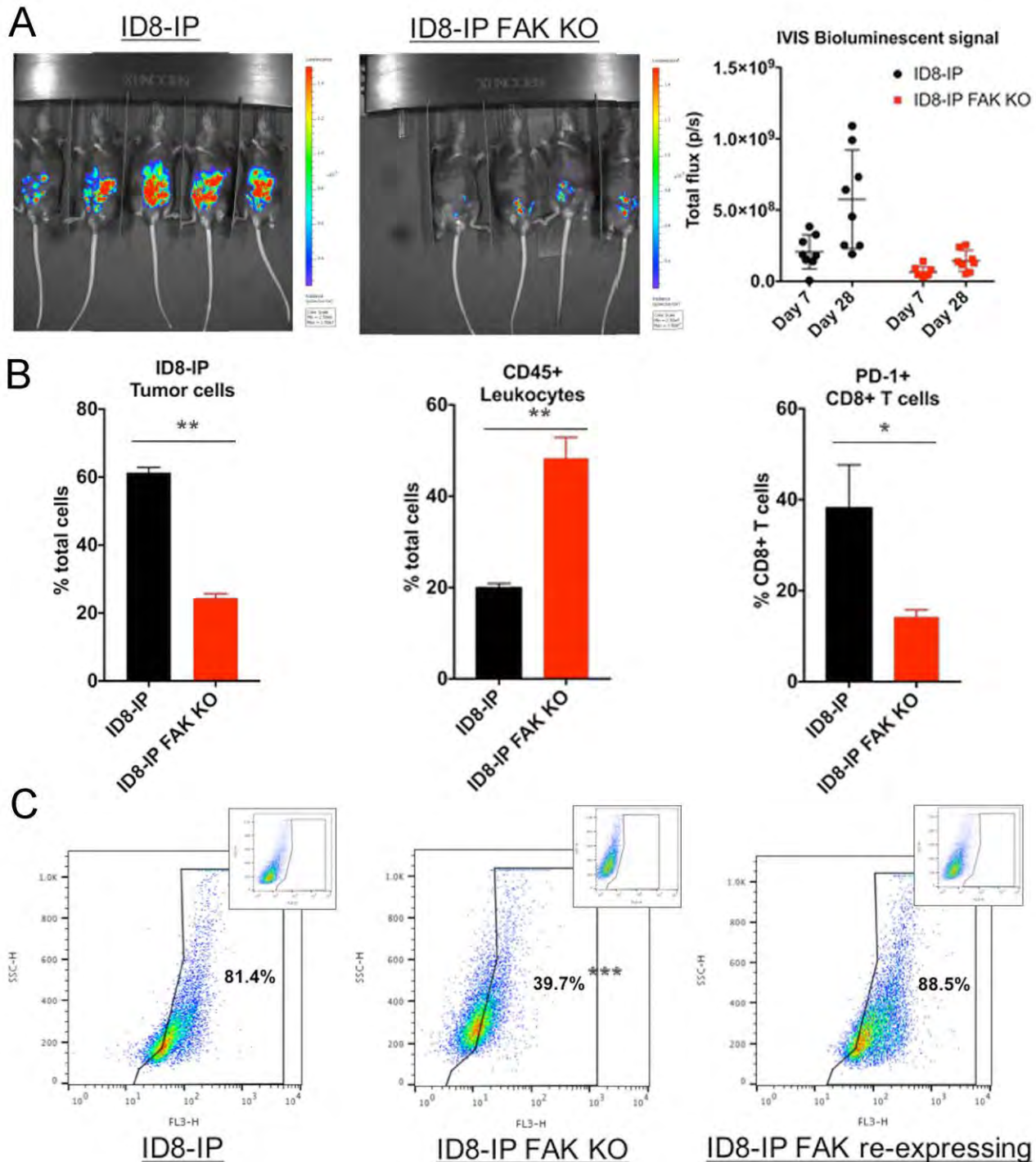


Fig. 1. (A) Representative IVIS images 28 days after injection with dTomato-luciferase-labeled ID8-IP or ID8-IP FAK KO tumor cells. Semiquantitative bioluminescent signal at Day 7 and Day 28 following injection. (B) Tumor cells and leukocytes expressed as percentage of ascites-associated cells harvested on Day 32. PD-1-positive cells expressed as percentage of total CD8+ T cells. * $P = 0.038$ (t-test), ** $P < 0.001$ (t-test). (C) Dot plot of anti-PD-L1 staining analyzed using FloJo software. Inset images are unstained controls used for gating each sample. Cells grown in non-adherent conditions *in vitro* for 5 days. *** $P < 0.0001$ (t-test) for ID8-IP FAK KO relative to ID8-IP and ID8-IP FAK re-expressing cells.

113 - Poster Session

TIGIT ligands CD155, CD112, and galectin-9 are associated with immune infiltration and increased overall survival in ovarian cancer

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Objective: Therapeutic targeting of PD-1 has demonstrated limited efficacy in ovarian cancer. Additional immune checkpoint pathways could be utilized for combination immunotherapy. In this study we investigate TIGIT pathway ligands and examine the association with tumor microenvironment and clinical outcome.

Method: Immunohistochemistry (IHC) staining was performed for TIGIT ligands CD155 (PVR), CD112 (Nectin-2), Galectin-9, PD-L1, CD3, and CD8. Staining was carried out on a previously described ovarian cancer tumor microarray (TMA) of 244 patients (204 primary samples, 140 synchronous metastatic samples, 107 matching pairs) with clinical follow-up. TMA slides were digitally scanned using ImageScope (Aperio), and standard image analysis algorithms for IHC quantification were applied to quantify the density of lymphocytes and calculate the semiquantitative H score for each core. K-means clustering was performed based on immune infiltration and TIGIT ligand expression, and subsequently cluster associations with overall survival were tested. Survival probabilities were estimated using the Kaplan-Meier method, and statistical significance was determined by the log rank test.

Results: Expression levels of TIGIT ligands clustered together, with either high or low expression of all three ligands. While expression levels of TIGIT ligands in primary tumor deposits were not prognostic, metastatic T cell infiltration and TIGIT expression were associated with overall survival (OS, $P = 0.037$); patients with low TIL infiltration had the lowest OS (34.9 months, 95% CI 24.9–44.8) regardless of TIGIT expression. High TIGIT ligand expression was associated with long OS (median 61.1 versus 39.9 months), with highest survival for high TIGIT ligand expression and immune infiltration. Metastatic sample PD-L1 expression was stronger in the tumor compartment (Spearman rho = 0.44, $P < 0.001$) than the stroma (rho = 0.26, $P = 0.002$). See Figure 1.

Conclusion: TIGIT ligands CD155, CD112, and Galectin-9 are expressed in ovarian cancer and, together with immune infiltration, predict increased OS versus immune infiltration and low TIGIT expression. This could reflect persistent immune infiltration in the face of TIGIT immune checkpoint inhibition. Further study of TIGIT ligand expression in ovarian cancer is warranted.

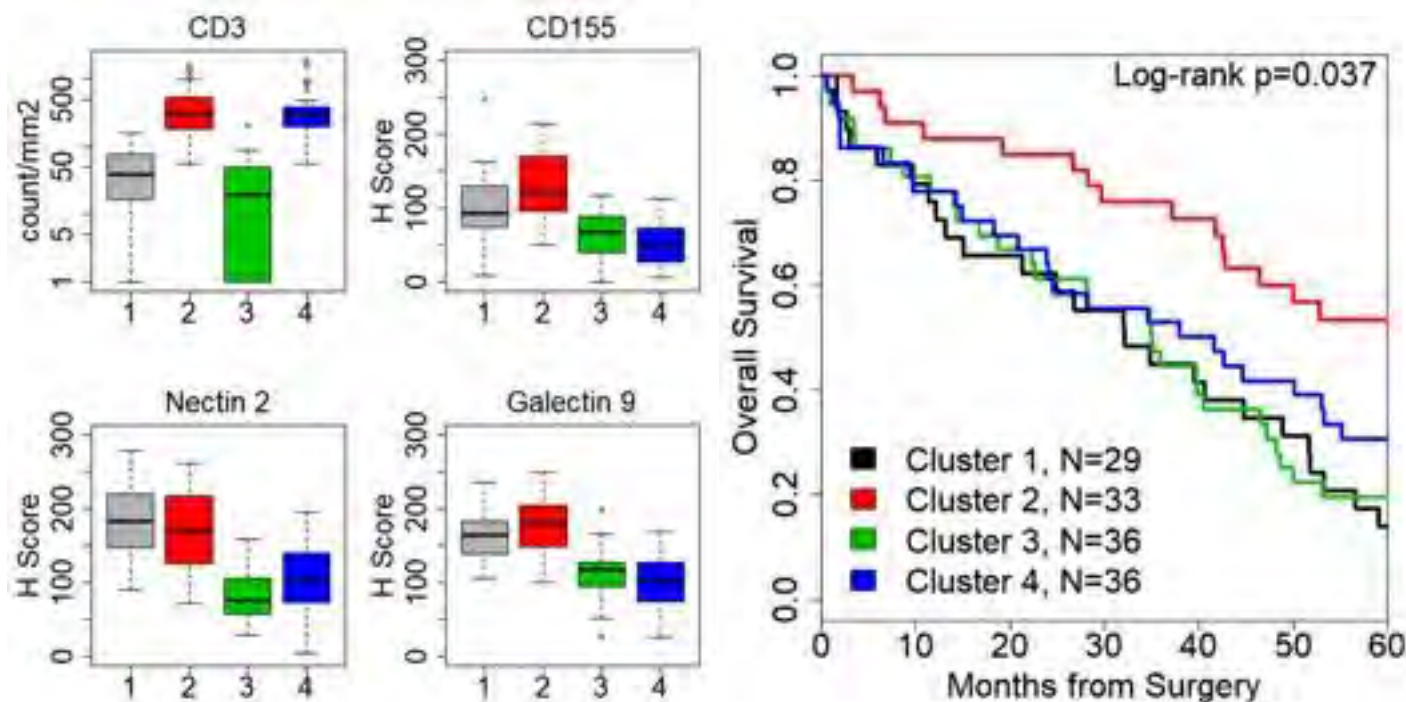


Fig. 1.

114 - Poster Session

A phase II trial of TPIV200 (a polypeptide vaccine against folate receptor alpha) plus durvalumab (anti-PD-L1 antibody) in patients with platinum-resistant ovarian cancer

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Objective: The primary endpoint (EP) of this study was assessment of overall response rate. The coprimary EP was progression-free survival at 6 months. Secondary EPs evaluated in the study were safety and tolerability of the combination and disease control rate. Exploratory correlative EPs included expression of PD-L1 and FR α , as well as both tissue and circulating immune signatures.

Method: This phase II clinical trial was based on a Simon 2-stage design. Patients with platinum-resistant or refractory ovarian cancer (OC) were enrolled over a 10-month period. Patients were treated with TPIV200 and GM-CSF on day 1 of cycles 1–6 and durvalumab on days 1 and 15 of cycles 1–12. Radiologic assessments were conducted every 3 cycles. Treatment was continued until evidence of clinical or radiologic progression, intolerance, or withdrawal. Neither PD-L1 nor FR α expression was required. There was no limit on prior therapy; 14 (14/27) patients had ≤ 3 prior treatments and 13 (13/27) had ≥ 3 priors.

Results: Between June 2016 and April 2017, 27 women between ages 42 and 76 (median 64) years were enrolled. Of these patients, 85% (23/27) had high-grade serous OC. The remainder had clear cell (2), endometrioid (1), and mixed (1) histologies. There were no grade 3 or 4 treatment-related adverse events (AEs). There were 2 grade 2 immune-related AEs in the form of autoimmune type I diabetes and pneumonitis. Both patients were successfully managed with insulin and drug discontinuation, respectively.

Conclusion: TPIV200/huFR-1 and durvalumab can be safely combined in heavily pretreated patients with platinum-resistant refractory OC. Analysis for the primary EP is ongoing and will be presented.

115 - Poster Session

Carbon nanoparticles compared with indocyanine green (ICG) in sentinel lymph node (SLN) detection in gynecologic oncology, which is better? A retrospective single-center study in 134 cases of cervical cancer and endometrial cancer in China

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Objective: To evaluate the feasibility and clinical value of identifying SLN and to compare different techniques in both cervical cancer and endometrial cancer.

Methods A retrospective single-center study of 134 cases (71 with cervical cancer and 63 with endometrial cancer) was conducted in our department. All patients underwent SLN biopsy with tracers of indocyanine green (ICG) and/or carbon nanoparticles. Excision of all mapped SLN was conducted and followed by procedures such as systematic pelvic lymphadenectomy and hysterectomy according to National Comprehensive Cancer Network (NCCN) guidelines. All the lymph nodes were examined postoperatively for the routine paraffin section of hematoxylin and eosin (H&E) staining. Detection rate, sensitivity, and negative predictive value of SLN were calculated, and factors associated with the detection rate were analyzed.

Results: The overall detection rate of 134 cases enrolled was 93.5%, with 75.0% bilaterally. The detection rate of SLN with the combined technique was significantly higher than the single technique of carbon nanoparticles ($P < 0.05$). The difference in SLN detection rate between ICG and carbon nanoparticles was not significant ($P > 0.05$). The difference in SLN detection rate between cervical and endometrial cancer patients was not significant ($P > 0.05$). SLNs were mostly recognized in external iliac and obturator areas in both cervical and endometrial cancer in the study. Among 94 patients who underwent systematic pelvic lymphadenectomy, sensitivity of SLN detection was 7%, and the negative predictive value was 97.9%. The sensitivity and negative predictive value were both 100% in patients with successful bilateral mapping of SLN. See Tables 1 and 2.

Conclusion: The overall detection rate of SLN in cervical and endometrial cancer was the highest with the combined technique of ICG and carbon nanoparticles. The detection rate and located regions of SLN are similar between cervical and endometrial cancer and SLN are mostly recognized in the external iliac and obturator areas. The sensitivity and negative predictive value of SLN detection are high, especially when SLN are bilateral mapped. SLN biopsy other than systematic pelvic lymphadenectomy seems to be a safe and effective strategy for early stage patients with specific condition.

Table 1. Comparison of SLN detection rate with different methods.

Method	Overall Detection Rate, %	Bilateral Detection Rate, %
ICG	86.3	56.9
Carbon nanoparticles	81.5	51.6
Combined	93.5	75.0

Table 2. Comparison of sensitivity and negative predictive value of SLN with different methods.

Method	SLN Metastasis	Pelvic Lymph Node		Sensitivity, %	Negative Predictive Value, %
		Positive	Negative		
ICG	Positive	7	0	77.8%	95.9%
	Negative	2	47		
Carbon nanoparticles	Positive	9	0	90.0%	98.4%
	Negative	1	60		
Combined	Positive	6	0	85.7%	97.9%
	Negative	1	47		

116 - Poster Session

Identifying susceptibilities and pharmacodynamic biomarkers for mirvetuximab soravtansine in high-grade ovarian and endometrial cancer

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Objective: High-grade endometrial and serous ovarian cancers share similarities at a molecular level. Folate receptor alpha (FR α) expression is found in the majority of these cancers. Mirvetuximab soravtansine (IMGN853) developed by ImmunoGen is an antibody-drug conjugate which consists of a FR α -targeting antibody linked to a potent tubulin-acting agent, DM4. The objective of this study was to show that IMGN853 has sufficient antitumor activity in high-grade endometrial and ovarian cancer patient-derived xenograft (PDX) mouse models and to identify therapeutic susceptibilities and candidate pharmacodynamic biomarkers of this compound.

Method: Two high-grade endometrial cancer PDX models (OV42 and OV150) and two high-grade serous ovarian cancer PDX models (OV17 and OV262) shown to express FR α were utilized. When tumor volumes reached 100 mm³, mice were randomly assigned to a single-tail vein injection of 5 mg/kg of IMGN853 (treatment) or phosphate-buffered saline (control) at day 0. Tumor growth was evaluated twice per week using a caliper, and mice were sacrificed by day 30. Tumors were harvested for downstream molecular and biological analysis.

Results: Significant mean tumor regression or stasis of tumor growth ($P < 0.05$) was seen in OV42, OV150, and OV17 treated with IMGN853 until day 9 with minimal toxicity. For the OV150 model, a second dose of IMGN853 at day 9 maintained tumor stasis and a significant difference in tumor volume compared to control ($P < 0.05$). Western blotting showed no difference in FR α expression between treatment and control groups and showed expression of γ H2AX, cleaved PARP, and cleaved caspase 3 across treatment groups. Candidate biomarkers identified by microarray of tumor profiles that responded to treatment involved receptor binding pathways.

Conclusion: Mirvetuximab soravtansine exhibits promising antitumor activity in high-grade endometrial and serous ovarian cancer PDX models. FR α expression levels do not change with treatment, which correlate with an effective drug mechanism. The compound appears to work through apoptotic pathways and via DNA damage. Putative candidate biomarkers involve a receptor binding pathway and may have the potential to identify patients for treatment with mirvetuximab soravtansine.

117 - Poster Session

Differential microRNA expression in endometrial cancer cells following exposure to aspirin

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Objective: Best studied within the breast and colon cancer literature, NSAIDs are thought to provide a protective effect through inhibition of cellular proliferation and induction of apoptosis; however, the mechanism of chemoprevention remains unclear. Epidemiologic studies have also observed a decreased risk of endometrial cancer in long-term aspirin (ASA) users. We aimed to evaluate the effect of aspirin exposure on microRNA (miRNA) expression in the endometrial endometrioid adenocarcinoma model cell line, Ishikawa H.

Method: Ishikawa H. cells were exposed to ASA dissolved in 100% ethanol at 2 and 4 mM concentrations for 96 hours. Controls were treated with vehicle alone. TaqMan gene expression assays were used to assess changes in miRNA expression at each ASA concentration relative to control cells. All experiments were done in triplicate. Significant differentially expressed miRNAs were introduced in a pathway enrichment analysis by using high-confidence target genes from the miRWalk database in the DAVID Functional Annotation tool.

Results: Twelve microRNAs were identified that showed statistically significant, dose-dependent changes in expression at increasing ASA concentrations when compared to the control cells (Figure 1). Using miRwalk, 140 validated, high-confidence target genes were identified corresponding to the differentially expressed miRNAs. Pathway enrichment analysis showed overexpression of the "miRNAs in cancer" pathway ($P = 4.07 \times 10^{18}$) and "pathways in cancer" ($P = 3.4 \times 10^{16}$). Many of the validated targets contributing to pathway enrichment are oncogenes.

Conclusion: Our study found that exposure of endometrial cancer cells to ASA alters expression of microRNAs within the "miRNAs in cancer" pathway and "pathways in cancer," and does so in a dose-dependent manner. We suggest that part of the potential mechanism contributing to the protective effect of NSAID exposure involves increased miRNA expression that, in turn, suppresses oncogene transcription. Future studies will focus on assessing cellular growth rates and apoptosis associated with ASA exposure.

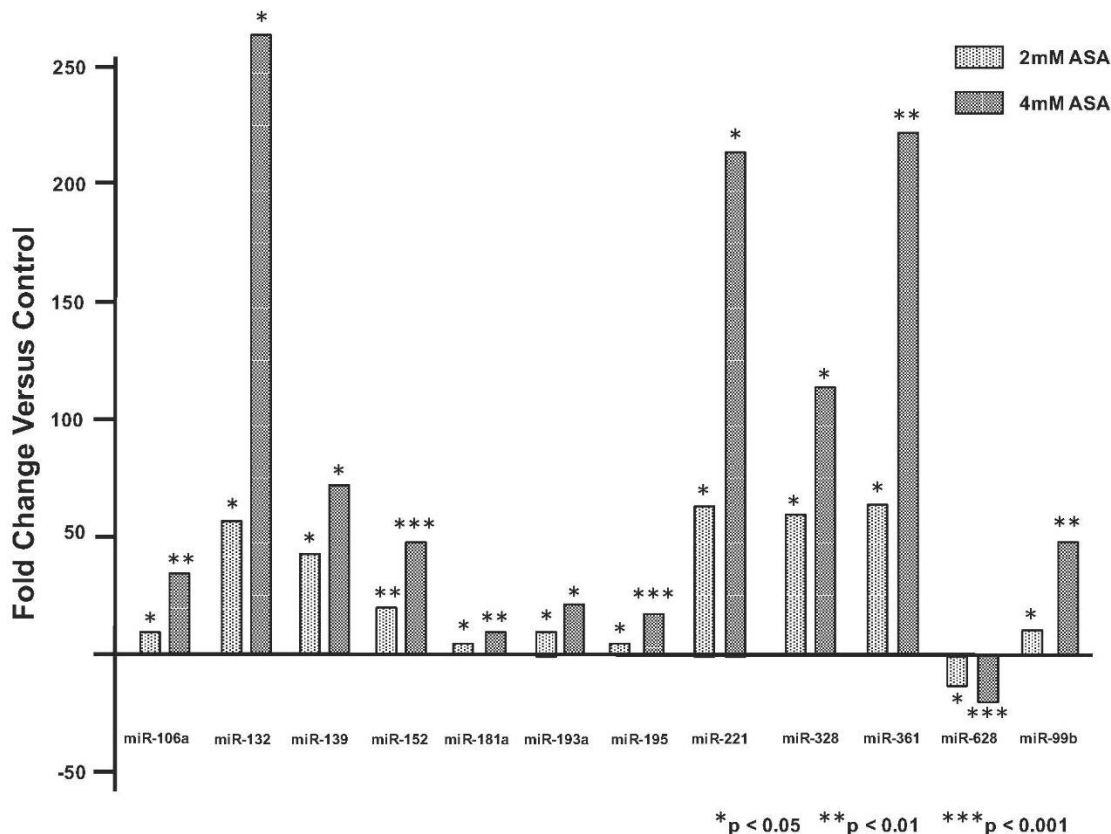


Fig. 1.

118 - Poster Session

A novel long non-coding RNA LNMICC promotes lymph node metastasis in cervical cancer through the reprogramming of fatty acid metabolism

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Objective: The spread of cancer cells from primary tumors to lymph nodes is associated with poor survival in cervical cancer. However, the mechanisms underlying lymph node metastasis remain elusive. Long, noncoding RNAs (lncRNAs) are important epigenetic regulators with critical roles in human cancers. This study aimed to investigate the clinical significance and the potential molecular mechanism of a novel lncRNA associated with lymph node metastasis in cervical cancer (LNMICC).

Method: The clinical relevance of LNMICC was confirmed by in situ hybridization analysis in 211 cervical cancer patients. The χ^2 and Student t tests were used for univariate analysis; the Kaplan-Meier test was used to determine progression-free survival (PFS) and OS. The biological functions of LNMICC in vitro and in vivo were evaluated to support clinical findings. Molecular biology assays were used to determine the underlying mechanisms of LNMICC in lymph node metastasis.

Results: The results revealed that LNMICC was an independent high-risk factor for lymph node metastasis, and its over-expression correlated with poor patient survival ($P < 0.001$). Furthermore, BMI ≥ 25 (kg/cm²) indicated a poorer OS and DFS ($P < 0.001$). LNMICC enhanced cervical cancer cell metastasis and lymphangiogenesis in vitro and in vivo. LNMICC could recruit NPM1 to directly bind to the FABP5 promoter to activate its transcription, which resulted in the reprogramming of fatty acid metabolism. BMI ≥ 25 (kg/cm²) was independently associated with pelvic lymph node metastasis in patients with cervical cancer. Moreover, LNMICC promoted lymph node metastasis in a FABP5-mediated manner. Finally, LNMICC was also a direct target of miR190, and its biological effect could be suppressed by miR190.

Conclusion: This study reveals new mechanisms of lymph node metastasis from the perspective of fatty acid metabolism reprogramming mediated by LNMICC. LNMICC is a promising prognostic predictor for cervical cancer and may serve as a valuable therapeutic target for preventing the lymph node metastasis of cervical cancer.

119 - Poster Session

Docosahexaenoic acid, an omega-3 fatty acid, exhibits anti-tumorigenic effects in endometrial cancer

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Objective: Obesity has been associated with increased risk and mortality of endometrial cancer. Previous studies have shown that omega-3 polyunsaturated fatty acid (PUFA) supplementation may counteract the detrimental effects of obesity-driven cancers, but this has yet to be fully explored in endometrial cancer. Thus, our goal was to assess the effects of omega-3 PUFAs on endometrial cancer cell growth.

Method: The human endometrioid endometrial cancer cell lines ECC-1 and KLE were exposed to varying concentrations of the omega-3 PUFA, docosahexaenoic acid (DHA). Cell proliferation was assessed by MTT assay. Apoptosis was assessed by Annexin V-FITC assay. Reactive oxygen species (ROS) were measured using the dichloro-dihydro-fluorescein diacetate (DCFH-DA) assay. Western immunoblotting was performed to determine the effects of DHA on the antiapoptotic proteins, BCL-2 and MCL-1, and the cellular stress proteins, PERK, Bip, and PDI. Cellular adhesion was assessed with the laminin adhesion assay.

Result: DHA potently inhibited growth in a dose-dependent manner in both cell lines (ECC-1 IC₅₀ of 60 μ M; KLE IC₅₀ of 35 μ M). DHA increased the expression of annexin V (17% at 100 μ M, $P < 0.05$) as well as decreased BCL-2 and MCL-1 expression. Treatment with DHA (50 μ M) significantly increased ROS production (ECC-1 194%, $P < 0.01$; KLE 29%, $P < 0.01$) and induced PERK, Bip, and PDI expression in both cell lines. Cellular adhesion was decreased by 6% in both cell lines ($P < 0.01$).

Conclusion: We find that the omega-3 PUFA, DHA, significantly suppresses cell proliferation through inducing cellular stress and apoptosis in endometrial cancer cell lines. These results suggest that omega-3 PUFA supplementation may be a promising dietary strategy for endometrial cancer prevention and treatment.

120 - Poster Session

Anti-tumor effect of adiponectin receptor agonist in serous ovarian cancer

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Objective: Obesity is one of the few modifiable risk factors for epithelial ovarian cancer. Adiponectin is an obesity-related cytokine that activates the receptors AdipoR1 and AdipoR2 and has been demonstrated to have an anticarcinogenic effect in other disease sites. Increasing levels of obesity are associated with low circulating levels of adiponectin. Prior studies have shown serum adiponectin levels to be lower in patients with ovarian cancer versus controls, suggesting that adiponectin may contribute to the link between obesity and ovarian cancer. We tested the hypothesis that the AdipoR1 and AdipoR2 agonist AdipoRon inhibits proliferation in human high-grade serous ovarian tumor cell lines.

Method: We examined the antitumor activity of AdipoRon in human high-grade serous ovarian tumor cells lines (OVCAR-3, OVCAR-4, and A2780) using the CyQuant proliferation assay. Flow cytometry with propidium iodide was utilized to study the effect of AdipoRon on cell cycle progression. Acridine orange staining was done to determine cellular death. Western blotting was performed to examine changes in cellular signaling induced by AdipoRon. Standard statistical tests were performed.

Results: Treatment of ovarian cancer cell lines with AdipoRon (50 μ M) resulted in a significant decrease in cell number versus vehicle (DMSO) after 48 hours in OVCAR-3 (-61.2%, $P < 0.001$), OVCAR-4 (-79%, $P < 0.001$), and A2780 (-56.9%, $P < 0.001$). AdipoRon induced G1 cell cycle arrest in OVCAR-3 (+12.1%, $P = 0.03$), OVCAR-4 (+4.8%, $P = 0.07$), and A2780 (+12.0%, $P = 0.002$). Microscopic study of tumor cells after acridine orange staining demonstrated induced cell death. AdipoRon treatment promoted phosphorylation of AMPK (OVCAR-3 $P = 0.01$; OVCAR-4 $P = 0.06$; A2780 $P = 0.02$) and decreased the activity of the pro-proliferative mTORC1 pathway (OVCAR-3 $P = 0.03$; OVCAR-4 $P = 0.01$; A2780 $P = 0.001$).

Conclusion: The adiponectin receptor agonist AdipoRon induces activation of AMPK and inhibition of the mTORC1 pathway and exhibits an antitumor effect in serous ovarian cancer. Given the inverse relationship between adiponectin levels and adiposity, this may represent an effective pathway to target in obese patients with ovarian cancer. Further study to evaluate the potential of AdipoRon as a therapeutic in ovarian cancer is warranted.

121 - Poster Session

MUC16 targeted Meso64TR3 overcomes TRAIL resistance by inhibiting AKT activation

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Objective: TNF-related apoptosis-inducing ligand (TRAIL) binds to death receptors (DR) 4 and 5 to activate the extrinsic apoptosis pathway. TRAIL activation of AKT and its antiapoptotic effects has been shown to cause resistance. Meso64-TR3 is a genetically engineered TRAIL trimer, modified to interact with high affinity to CA125 via incorporation of a 64 amino acid sequence derived from mesothelin, and has previously demonstrated superior killing efficacy compared to TR3. Our aim was to evaluate the cell signalling responsible for the improved killing efficacy of Meso64-TR3.

Method: CA125-positive OVCAR3 cells were assessed for sensitivity to TR3 and Meso64TR3 using cell viability assays. Dependency of the CA125/mesothelin interaction was interrogated in the presence of soluble mesothelin during cell viability assays. DR signaling was evaluated using apoptosis arrays. Specific activation of pAKT was assessed by ELISA. The impact of the MUC16/mesothelin on AKT activation induced by Meso64TR3 was probed in the presence of soluble mesothelin. Because AKT activation requires lipid rafts, its membrane insertion capacity was prevented by adding cholesterol-depleting reagents nystatin or methyl beta cyclodextrin (MBCD) to the cultures prior to TR3 treatment.

Results: Meso64-TR3 demonstrated improved killing efficacy over TR3 (EC_{50} of 86 pM vs 1,323 pM). The apoptosis array revealed a 2.8-fold upregulation of pAKT in TR3-treated cells compared to Meso64-TR3. An ELISA format confirmed the strong AKT-activating activity of TR3 relative to Meso64-TR3 or controls (abs = 0.927, 0.647, and 0.454 units, respectively). Cells pretreated with nystatin or MBCD responded with increased susceptibility to TR3 treatment, likely because of diminished AKT activation. Similar pretreatments had no impact on Meso64-TR3-mediated cell killing, suggesting the mesothelin/MUC16 interaction prevents AKT activation. Cells were then exposed to mesothelin prior to Meso64-TR3. By blocking its MUC16 binding sites, AKT phosphorylation was restored to similar levels of nontargeted TR3 (abs = 0.90).

Conclusion: Activation of AKT by TR3 explains its lack of killing efficacy. In contrast, Meso64-TR3 prevents activation of AKT, leading to an increase in apoptotic cell death. Further exploration of additional downstream signalling effects in vitro and in patient-derived xenografts are currently underway.

122 - Poster Session

TP53 domains' mutations alter glycolysis in epithelial ovarian carcinoma: Ex vivo and in vitro study

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Objective: To investigate the effect of TP53 different domain mutations on its transcriptional activity and its ability to induce apoptosis and to regulate glucose consumption and lactate production in epithelial ovarian cancer.

Method: A total of 30 ovarian cancer biopsies were characterized. Immunohistochemistry for p53 expression and PCR for exons 2 to 11 were performed, followed by the Single Strand Conformation Polymorphism technique and sequencing. The transcriptional activity of p53 was studied by a qPCR for its target genes p21 and MDM2. Viability and Annexin V tests were performed to study the ability of mutant p53 to induce apoptosis. The expression of the glycolytic enzymes regulated by p53 was quantified by qPCR. SK-OV-3 cell line was transfected by different p53 mutated plasmids, and the same experiments performed on the biopsies were done on transfected cells.

Results: Of the 22 ovarian cancer cases, 17 were characterized as high-grade serous carcinoma. Out of these 17, mutations were detected in 9 of the cases. Eight patients showed mutations affecting the apoptosis domain of the gene (exons 2, 3, and 4). The immunohistochemistry and qPCR showed an approximately twofold increase in p53 expression between wild type and mutated cases. The expression of p21 and MDM2 decreased only in DNA binding domain mutated cases and transfected cells, which indicates a decreased transcriptional activity with this type of mutation. The highest increase in apoptosis induction was clear in Sk-Ov-3 cells transfected with WT p53, and p53 proline rich domain mutations decreased the protein's apoptotic function. Glucose consumption and lactate production increased by mutated cells compared to wild type.

Conclusion: Mutant p53 is overexpressed in ovarian cancer cells. DNA binding domain mutations modify the protein's transcriptional activity, whereas proline rich domain mutations decrease the protein's apoptotic activity. Glycolysis is affected differently in both types.

123 - Poster Session

Grabbing the Grb2/GAB2 complex in ovarian cancer

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Objective: Given the biological significance of the GRB2/GAB2 complex in high-grade serous carcinoma (HGSC), we aim to assess the effect of prexigebersen (liposome-incorporated nuclease resistant antisense oligonucleotides specific for Grb2; in phase I clinical testing) in preclinical models.

Method: A series of in vitro (Western blot, MTT) and in vivo (orthotopic mouse models) experiments were carried out to test the biological effects of prexigebersen in HGSC models. We also tested the clinical significance of the GRB2/GAB2 complex using publicly available high-throughput data.

Results: We first examined the GRB2/GAB2 complex using TCGA and GISTIC data and found alterations (including shallow deletions and amplifications) in 25% of HGSC cases. These alterations in GAB2 were related to decreased patient survival ($P = 0.01$), suggesting it may be an attractive therapeutic target. GRB2 was expressed in most ovarian cancer cell lines tested (HEYA8, OVCAR5, SKOV3, and OVCAR3). The impact of prexigebersen was evaluated in HGSC orthotopic mouse models (OVCAR5). There was a significant decrease in tumor burden ($P = 0.01$) and multinodular burden ($P = 0.002$) in the combination prexigebersen/paclitaxel group compared to the control group. There was no apparent toxicity; mice on combination therapy lost less weight than the paclitaxel-only group ($P = 0.005$).

Conclusion: Prexigebersen-based therapy demonstrated robust efficacy in preclinical models. Our findings establish the GRB2/GAB2 complex as an important target for clinical development.

124 - Poster Session

Landscape of somatic genetic alterations in endometrioid endometrial cancers with germline and somatic *PTEN* mutations

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Objective: Germline *PTEN* mutations result in a spectrum of autosomal dominant hamartomatous tumor syndromes, most notably Cowden syndrome. Here we sought to determine the repertoire of somatic genetic alterations of an endometrioid endometrial cancer from a germline *PTEN* mutation carrier with Cowden syndrome, and to compare its genomic profile to that of endometrial cancers arising in patients with somatic *PTEN* mutations.

Method: Whole-exome sequencing data of an endometrioid endometrial carcinoma and matched normal tissue from a *PTEN* germline mutation carrier were analyzed to define the somatic mutations, copy number alterations, and mutational signatures. Whole-exome sequencing data of sporadic microsatellite stable endometrioid endometrial cancers with somatic *PTEN* mutations ($n = 82$) were obtained from The Cancer Genome Atlas (TCGA) for comparison.

Results: In the *PTEN* germline mutation carrier, bi-allelic inactivation of *PTEN* was observed in the form of a germline p.Q110fs*5 *PTEN* mutation and somatic loss of the *PTEN* wild-type allele. The resulting endometrioid carcinoma was microsatellite stable and harbored 78 mutations, a mutation rate similar to that of somatic *PTEN*-mutant microsatellite-stable endometrioid carcinomas from TCGA (median 56 mutations, range 28–1,142). Microsatellite-stable endometrioid carcinomas with somatic *PTEN* mutations displayed a heterogeneous repertoire of mutations, including somatic mutations affecting *PIK3CA* (55%), *CTNNB1* (49%), *PIK3R1* (39%), and *ARID1A* (38%) and a limited number of amplifications/homozygous deletions. The mutational landscape of the endometrioid endometrial cancer from the *PTEN* germline mutation carrier seemed to be similar, harboring a *PIK3R1* in-frame-insertion and a hotspot *CTNNB1* mutation. Furthermore, the *PTEN* germline-mutant endometrioid cancer displayed the mutational signature 1 associated with ageing, akin to the vast majority (91%) of microsatellite-stable endometrioid tumors with somatic *PTEN* mutations.

Conclusion: Microsatellite-stable endometrioid endometrial cancers with germline and somatic *PTEN* mutations are similar at the genetic level.

125 - Poster Session

NOTCH2 expression is significantly associated with FIGO stage at diagnosis in endometrioid endometrial cancer

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Objective: Notch receptors play an important role in cell differentiation, proliferation, and apoptosis. Evidence is available to suggest that notch signaling is essential for the endometrial changes necessary during the menstrual cycle. It has also been implicated in pathogenesis in the endometrium and dysregulation of notch has been observed in various neoplastic processes. The aim of this study is to establish an association between NOTCH2 expression and clinical outcomes in endometrioid endometrial cancer (EEC).

Method: EEC tissues from 41 patients were obtained after approval by our institutional review board. Clinical data were extracted from patient charts. Total cellular RNA was purified from all 41 tumors. After RNA yield and purity were evaluated, NOTCH2 gene expression was assessed via SYBR Green qPCR using previously validated primers. Survival and recurrence analyses were performed with the Cox proportional hazard method. Univariate and multivariate analyses with linear regression were performed to identify clinical variables associated with NOTCH2 expression. Significance level was considered a P value <0.05 .

Results: Univariate analysis revealed a statistically significant association between 2009 FIGO stage ($P = 0.003$) and adjuvant treatment after surgery ($P = 0.041$) with NOTCH2 expression. Positive peritoneal cytology ($P = 0.069$) and presence of progesterone receptors by immunohistochemistry ($P = 0.084$) showed a trend for significance in the univariate analysis. In the multivariate analysis only 2009 FIGO stage was confirmed as significantly associated with NOTCH2 expression; see Figure 1.

Conclusion: The findings of this study raise the possibility of utilizing NOTCH2 as a molecular marker to assess risk of advanced-stage disease at time of diagnosis. These findings also add to the growing body of evidence to suggest that the

NOTCH signaling pathway shows promise as a therapeutic target in endometrial cancer.

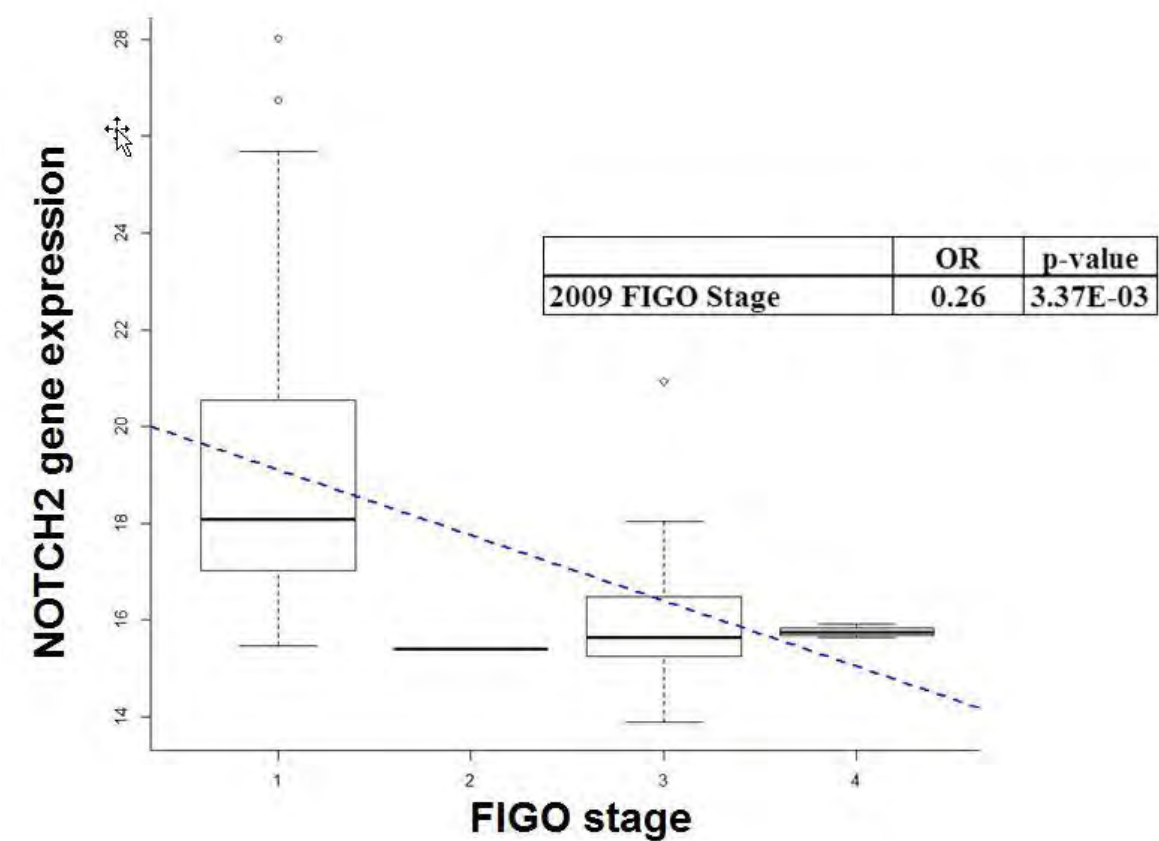


Fig. 1.

126 - Poster Session
The role of L1CAM in early-stage endometrial cancer recurrence

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Objective: Expression of L1 cell adhesion molecule (L1CAM), a glycoprotein involved in cell motility, is suggested to be an independent prognosticator of poor prognosis in early-stage endometrial cancer. This study aims to determine the prevalence of L1CAM, validate it as a prognostic marker, and analyze the pathway associations of L1CAM in endometrial cancer.

Method: Tumors from a cohort of women with primary endometrial cancer of any stage ($n = 159$) were stained by immunohistochemistry (IHC) for L1CAM expression. Samples were positive when >10% of L1CAM-positive cancer cells were present in the stained sections. Agilent gene expression arrays and pathway analysis were performed on 151 of these patients. A second cohort of early-stage recurrent endometrial cancer patients ($n = 20$) was also stained by IHC for L1CAM expression. Recurrent cases were stratified based on GOG risk criteria.

Results: Average age at the time of primary surgery was 61 years; 83.7% were of endometrioid histology; and 65.2% were stage I. Comparison of IHC-positive L1CAM to mRNA expression of L1CAM was highly correlated ($r = 0.5842$, $P < 0.0001$). A total of 137 genes were found to be differentially expressed between IHC L1CAM-positive and L1CAM-negative tumors. Of the 137 genes, pathway analysis identified the KRAS pathway as a dominant pathway for L1CAM-positive cases. Of the 20 stage I recurrent endometrial cancers, average age was 67 years and 18 (90%) had endometrioid-type tumors. Twelve of these recurrent cases (60%) were L1CAM-positive. Using the GOG criteria to risk-stratify these recurrent cases, 71.4% of high-risk patients, 42.9% of high to intermediate risk, and 66.7% of low risk were L1CAM-positive.

Conclusions: This study confirms the prognostic relevance of L1CAM in recurrent stage I endometrial cancers and identifies additional patients at high risk for recurrence despite low clinicopathologic risk. The KRAS pathway may offer additional therapeutic targets in this high-risk patient population.

127 - Poster Session

Endometrial cancers are successfully targeted with a new pan-tyrosine kinase inhibitor in an orthotopic mouse model

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Objective: AL3818 (Anlotinib) is a receptor tyrosine kinase inhibitor targeting vascular endothelial growth factor receptors (VEGFR1, VEGFR2/KDR, and VEGFR3), stem cell factor receptor (C-kit), platelet-derived growth factor (PDGFA), and fibroblast growth factor receptors (FGFR1, FGFR2, and FGFR3). This study evaluates the efficacy of AL3818 studying tumor regression in an orthotopic murine endometrial cancer model.

Method: We tested the cytotoxicity of AL3818 on a panel of 7 human endometrial cancer cell lines expressing either wild-type or mutant FGFR2 and also assessed the in vivo antitumor efficacy in a murine, orthotopic AN3CA endometrial cancer model. AL3818 was administered daily per os either alone or in combination with carboplatin and paclitaxel, which represents the current standard of adjuvant care for endometrial cancer.

Results: AL3818 significantly reduces AN3CA cell number in vitro, characterized by high expression of a mutated FGFR2 protein. Daily oral administration of AL3818 (5 mg/kg) resulted in a complete response in 55% of animals treated and in a reduced tumor volume, as well as decreased tumor weights of AN3CA tumors by 94% and 96%, respectively, following a 29-day treatment cycle. Whereas carboplatin and paclitaxel failed to alter tumor growth, the combination with AL3818 did not seem to exhibit a superior effect when compared with AL3818 treatment alone.

Conclusion: AL3818 shows superior efficacy for the treatment of endometrial cancer irrespective to conventional carboplatin and paclitaxel combination and warrants further investigation.

128 - Poster Session

Galectin-3 induces protein ezrin phosphorylation via integrin $\alpha 3 \beta 1$ /c-src/PI3K/AKT cascade and promotes cervical cancer metastasis

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Objective: Cervical cancer (CC) is one of the most common malignant tumors in women. The exact mechanisms contributing to its development and progression remain unclear, and galectin-3 was reported to be upregulated in cervical cancer. Therefore, we explore the role of galectin-3 in CC metastasis.

Method: In this study, the effect of galectin-3 on actin cytoskeleton remodeling, cell migration, and invasion was confirmed by immunofluorescence and Real Time Cellular Analysis in Siha cell. The activation of actin-regulatory protein ezrin and c-Src/PI3K/AKT signaling pathway in this action was detected by Western blot and the use of specific inhibitor, transfection of corresponding plasmids, and siRNAs. Co-immunoprecipitation was adopted to identify the binding of galectin-3 and integrin $\alpha 3 \beta 1$, which was identified as the source trigger of this signal cascade. In vivo, nude mice and zebrafish migration and metastasis model were performed to further verify the role of galectin-3 in cervical cancer metastasis.

Results: Exposure of galectin-3 triggered actin cytoskeleton remodeling and promoted cervical cancer cell invasion and migration in vitro. These actions were dependent on increased expression and phosphorylation of the actin-regulatory protein ezrin, and specific ezrin siRNA significantly impaired galectin-3 stimulated-cell migration and invasion. The c-Src/PI3K/AKT signaling cascade mediated the increased ezrin phosphorylation. Furthermore, the secretion and expression of galectin-3 and its binding to integrin $\alpha 3 \beta 1$ was upregulated by VEGF-C. In vivo, the knockdown expression of galectin-3 was proved to decrease the migration and metastasis of cervical cancer in nude mice and zebrafish model. At last, the expression of galectin-3, integrin $\alpha 3 \beta 1$, and p-ezrin was upregulated in 110 CC tissues compared to 20 normal cervical tissues and related to several clinical characteristics including lymph node metastasis.

Conclusion: VEGF-C-induced galectin-3 active protein ezrin phosphorylation through integrin $\alpha 3\beta 1$ /c-Src/PI3K/AKT cascade and promotes cervical cancer metastasis. Our findings offer new insight into the role of galectin-3 on cervical cancer progression and may provide potential targets for cervical cancer therapy.

129 - Poster Session

Single cell sequencing: A descriptive subgroup analysis of individual tumor cells from 4 patients with ovarian cancer

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Objective: The purpose of this study was to determine patterns of cell populations and gene expression among 4 patients with ovarian cancer using single-cell sequencing of individual tumor cells.

Method: Using the 10x Genomics platform, transcriptomic data were collected from tumor samples of 4 patients diagnosed with ovarian cancer. Using various clustering techniques, including graph-based clustering, principal component analysis (PCA), t-Distributed Stochastic Neighbor Embedding (tSNE), and clustering through imputation and dimensionality reduction (CIDR), groups of cells were defined based on similar gene expression patterns. Multiple bioinformatics tools were used to define the cell subsets based on differentially expressed genes and expression of genes considered cell-type specific markers.

Results: Transcript expression was characterized for an average of 3,425 (range 1,802–4,638) cells per patient with a mean of 92,662 (range 51,252–138,199) reads per cell in the 4 patients. The median unique molecular identifier (UMI) counts ranged from 607 to 22,632 counts per cell. Different clustering algorithms produced a range of cell subsets, dependent on various clustering parameters. Based on marker genes and gene set analysis, stromal subsets, cancer epithelial subsets, and immune cell subsets were able to be identified in all 4 patients. Using less stringent clustering parameters, these groups were able to be subdivided, indicating extensive subgroup heterogeneity, with the cancer epithelial subset being the most heterogeneous.

Conclusion: Subpopulations of cancer cells in individual patients can be detected using single-cell sequencing, allowing for the analysis of gene expression on a level that was not previously possible given the limitations of bulk sequencing. Single-cell sequencing can provide a means of identifying de novo biomarkers or therapeutic targets for ovarian cancer, and will aid in the understanding of the heterogeneity within the cancer, including cells that have stem-like properties and cells that have gene expression patterns that correlate with drug resistant cells.

130 - Poster Session

Clinical utility of ubiquitin-specific protease 14 as a prognostic biomarker for endometrial cancer

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Objective: Ubiquitin-Specific Protease 14 (USP14) is a proteasome-associated deubiquitinating enzyme (DUB) that cleaves ubiquitin chains from proteins to regulate proteasome degradation. The purpose of this study was to validate the prognostic value of USP14 as a biomarker in endometrial cancer.

Method: Patients diagnosed with endometrial adenocarcinoma between May 1996 and February 2005 were identified. Demographics and clinical data were extracted from the medical record. Immunohistochemistry was performed to determine the level of USP14 expression in these primary tumors. The samples were assigned an H-score based on percent staining and intensity, with a median score of 170 or higher considered positive USP14 expression. USP14 intensity, patient demographics, and clinical data were compared. OS was calculated from the date of diagnosis to the date of last follow-up and was summarized using Kaplan-Meier methods and log rank tests.

Results: A consecutive cohort of 157 patients with endometrial adenocarcinoma was identified. The average age at time of diagnosis was 61 years. Of the 157 patients, 65% had stage 1 adenocarcinoma; 7.8%, stage II; 16%, stage III; and 11.4%, stage IV disease. Endometrioid-type was the most common histology (83%), and 41.5% of these tumors were grade 2. Of all patients, 77 (49%) had a H-score of less than 170, and 51% had a score equal to or greater than 170. Patients with high

expression of USP14 (H-score of 170 or higher) had significantly decreased OS compared to patients with low USP14 expression (H-score less than 170, $P = 0.04$); see Figure 1.

Conclusion: Patients with higher expression of USP14 had significantly decreased OS. H-score based USP14 protein expression may be a potential prognostic biomarker, adding in further molecular risk stratification of patients with endometrial cancer.

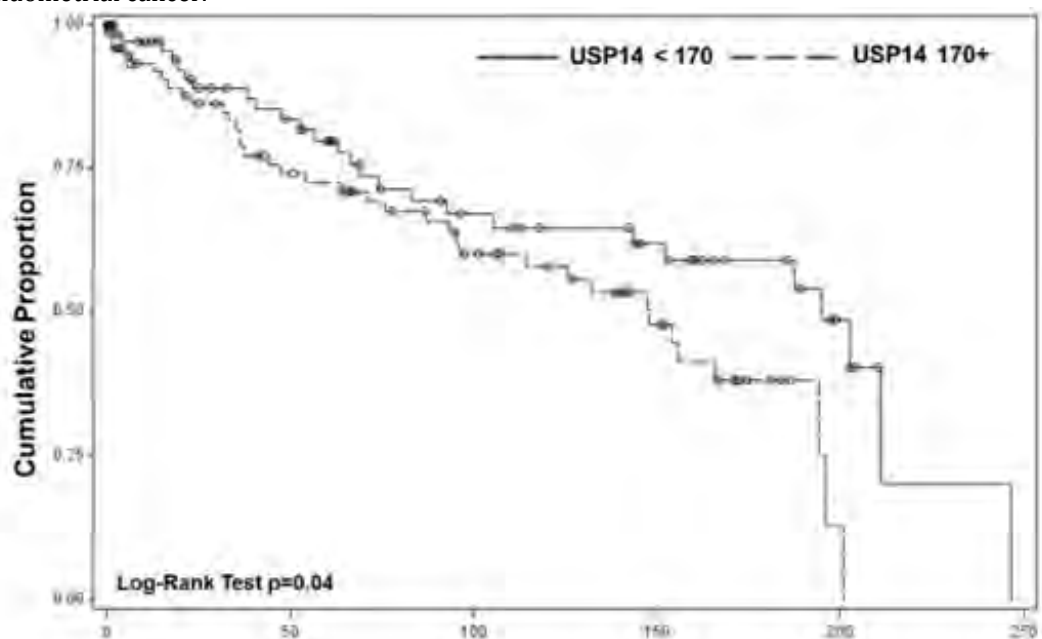


Fig. 1. Overall survival by USP14 status (split at median score of 170).

131 - Poster Session

Prognostic significance of normal pretreatment serum CA-125 levels in women with serous ovarian carcinoma

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Objective: To investigate the prognostic significance of normal pretreatment serum CA-125 levels in women with serous ovarian carcinoma (SOC).

Method: The National Cancer Database was accessed, and a cohort of women diagnosed between 2004 and 2014 with an SOC and known tumor grade was evaluated. Based on available information, two groups were formed: women with elevated pretreatment serum CA-125 levels (CA-125 +ve), and those with levels within the normal limit (CA-125 -ve). Demographic and clinicopathological characteristics were compared using the Mann-Whitney and χ^2 tests. Overall survival (OS) was assessed for patients who had cancer-directed surgery (CDS) with more than 1 month of follow-up. Median and 5-year OS rates were calculated after generation of Kaplan-Meier curves and compared with the log rank test. A Cox proportional hazard model was constructed to evaluate overall mortality after controlling for known confounders.

Results: A total of 51,459 patients were identified; 3,415 (6.6%) were CA-125 -ve. Women in the CA-125 -ve group were younger (median 62 vs 63 years, $P = 0.002$) and less likely to present with bilateral tumors (32.9% vs 57.8%, $P < 0.001$). Patients with grade 1 tumors were more likely to be CA-125 -ve (18.3%) compared to those with grade 2 (9.7%) and grade 3 (5.5%) ($P < 0.001$). Also, women in the CA-125 -ve group were more likely to be diagnosed with early-stage (I-II) disease (52% vs 13.8%, $P < 0.001$). Following stratification by disease stage, women with early-stage disease (I-II) and CA-125 -ve ($n = 1,500$) had better OS compared to those with CA-125 +ve ($n = 5,474$) ($P < 0.001$); 5-year OS was 79.8% vs 74.5%, respectively. Similarly, women with stage III disease and CA-125 -ve ($n = 1,096$) had better OS (median 64.56 vs 47.01 months, $P < 0.001$) compared to those with CA-125 +ve ($n = 25,063$). Better OS for CA-125 -ve ($n = 229$) compared to CA-125 +ve ($n = 8,481$) women was also noted among those with stage IV disease (median 49.15 vs 34.69 months, $P < 0.001$). By multivariate analysis, after controlling for patient age and race, insurance status, tumor grade, disease stage, presence of medical comorbid conditions, and the administration of chemotherapy, CA-125 -ve women had a lower mortality (HR = 0.72, 95% CI 0.67–0.77).

Conclusions: Normal pretreatment serum CA-125 levels may be associated with a favorable prognosis for women with SOC regardless of disease stage.

132 - Poster Session

Docosahexaenoic acid (DHA), an omega-3 fatty acid, inhibits ovarian cancer growth and adhesion

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Objective: Omega-3 polyunsaturated fatty acids (PUFAs), such as those found in fish oil, are thought to have antitumorigenic effects and may be beneficial in the treatment and prevention of cancer, including ovarian cancer. Thus, our goal was to better understand the potential effects of omega-3 PUFAs on ovarian cancer cell growth and adhesion.

Method: The human ovarian cancer cell lines, IGROV-1 and Hey, were exposed to varying concentrations (0.1 to 500 μ M) of the omega-3 PUFA, docosahexaenoic acid (DHA). Cell proliferation was assessed by MTT assay. Cell cycle progression was determined by Cellometer. Cellular stress was measured by the 2'-7'-dichloro-dihydro-fluorescein diacetate assay. Adhesion was assessed by a Laminin Cell Adhesion assay. Western immunoblotting was performed to assess the effect of DHA on relevant proteins involved with cell growth and apoptosis.

Results: DHA potently inhibited growth in a dose-dependent manner in both cell lines after 72 hours of treatment (IC_{50} = 40 μ M). Treatment with DHA resulted in G1 arrest in the IGROV-1 cell line after 24 hours of exposure, but not in the Hey cell line. Following 6 hours of exposure, DHA (50 μ M) increased ROS production in both the IGROV-1 and Hey cell lines relative to control by 47% and 61%, respectively ($P < 0.05$). Western immunoblotting revealed downregulation of the cell cycle proteins, CDK4, CDK6, and cyclin D1, and the antiapoptotic protein Mcl-1 in both cell lines. Treatment with DHA (50 μ M) reduced adhesion by 24% and 8% in the IGROV-1 and Hey cell lines, respectively ($P < 0.05$).

Conclusion: DHA inhibited proliferation in ovarian cancer cell lines via G1 cell cycle arrest and induction of apoptosis and cellular stress. In addition, DHA impaired ovarian cancer cell adhesion, a critical step in the metastatic spread of disease. Thus, PUFAs may be a novel dietary intervention and therapeutic adjunct in the treatment of ovarian cancer.

133 - Poster Session

Overexpression of MYB is associated with growth and malignant behavior of ovarian cancer cells

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Objective: MYB/c-MYB, a cellular progenitor of v-MYB oncogenes, encodes for a transcription factor protein to confer its oncogenic activity through regulation of gene expression. The purpose of this research was to investigate the pathobiological significance of MYB overexpression in ovarian cancer (OC).

Method: Immunohistochemical and immunoblot analyses were performed to examine the expression of MYB in clinical specimens of OC and established cell lines. MYB levels were altered (stable overexpression or knockdown) in OC cells by genetic engineering to assess its pathological functions in growth, survival, and malignant behavior of OC cells.

Results: An intense staining of MYB was reported in all histologic subtypes of OC, while it was detected in normal ovarian tissues. MYB was also expressed at varying levels in all the OC cell lines examined. Stable silencing and forced overexpression of MYB was achieved in 2 high (SKOV3-ip and A2780-cip) and low (SKOV3 and A2780) MYB-expressing OC cell lines, respectively. Stable silencing of MYB led to decrease in growth (37% and 41%) and clonogenic ability (~3.2- and 2.8-fold) in SKOV3-ip and A2780-cip cells, respectively, compared to their scrambled sequence-transfected (Scr) control cells. MYB-silenced SKOV3-ip and A2780-cip cells also exhibited reduced motility (~4.1- and 3.7-fold) and invasion (~7 and 6.2, respectively). Accordingly, forced overexpression of MYB in SKOV3 and A2780 cells promoted their growth (44% and 29%), clonogenicity (~2.6- and 3-fold), motility (~3.5- and 3.9-fold) and invasion (~5.1- and 4.3-fold, respectively), compared to vector only-transfected cells. MYB expression in OC cells also correlated with mesenchymal features and reduced sensitivity to cisplatin cytotoxicity.

Conclusions: A direct association of MYB was seen with oncogenic and chemoresistance potential of OC cells. This suggests that MYB could serve as a novel target for diagnosis, prognosis, and therapy.

134 - Poster Session

Gain-of-function and loss-of-function *TP53* mutations in ovarian carcinomas with and without concurrent *BRCA1* or *BRCA2* mutations

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Objective: Most high-grade ovarian carcinomas (OC) have mutations in the *TP53* tumor suppressor gene. A subset of missense mutations confer oncogenic properties and have been termed gain-of-function (GOF) mutations. We assessed the distribution and impact of GOF versus loss-of-function (LOF) *TP53* mutations in OC with and without concurrent *BRCA* mutations.

Method: We performed BROCA sequencing on 375 unselected OC prospectively followed for survival. For patients with stage II–IV, high-grade, non-clear-cell OC, overall survival was compared using Kaplan-Meier curves and log rank testing, with multivariate Cox regression analysis examining the contribution of *BRCA* and *TP53* mutations. Logistic regression was used to analyze the effects of *TP53* mutation type on platinum resistance.

Results: Of 375 total OC evaluated, 248 (66.1%) had *TP53* mutations, 98 (26.1%) GOF, and 150 (40%) LOF. Of 272 high-grade serous cancers, GOF and LOF *TP53* mutations were present in 82 (30.1%) and 122 (44.9%), respectively. *TP53* mutations were more common in grade 2–3 OC versus grade 1 (69.3% vs 11.8%, $P < 0.001$), and stage III–IV disease versus stage I–II (72.2% vs 32.7%, $P < 0.001$), but the ratio of LOF to GOF mutation did not differ. *BRCA*-mutated OC had a higher total *TP53* mutation rate (70/86, 81.4%, vs 178/289, 61.6%, $P = 0.001$), which was entirely explained by a higher rate of LOF mutations (55.8% vs 35.3%, $P = 0.001$). Median survival was 43 months (95% CI 27–53) for women without *TP53* mutations, 54 months (95% CI 42–60) for LOF, and 43 months (95% CI 33–54) for GOF (log rank $P = 0.51$). Survival curves did not statistically diverge when further stratified by both *TP53* mutation type and *BRCA* mutation status (log rank $P = 0.28$). After adjusting for clinicopathologic factors and *BRCA* status, neither GOF (HR = 1.17, $P = 0.49$) nor LOF (HR = 1.23, $P = 0.39$) mutations affected overall survival. *TP53* LOF and GOF mutations trended toward an association with platinum resistance, but the results were not statistically significant (HR = 0.51, $P = 0.12$, and HR = 0.57, $P = 0.23$, respectively).

Conclusion: OC with *BRCA* mutations have a higher frequency of *TP53* mutations relative to *BRCA* wildtype cases, secondary to an increased frequency of LOF mutations and a similar fraction of GOF mutations. The presence of a LOF versus a GOF *TP53* mutation did not have an impact on overall survival after controlling for *BRCA* mutation status.

135 - Poster Session

Atorvastatin antagonizes carboplatin, synergizes with the glycolytic inhibitor PFK158 and induces lipid laden multilamellar bodies in ovarian cancer

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Objective: To investigate the antitumor potential of the widely used anticholesterol drug Atorvastatin (ATV) alone, in combination with carboplatin (CBPT) and with the glycolytic inhibitor PFK158 (PFKi) in ovarian cancer (OC).

Method: MTT assay and the Chou-Talalay methodology were used to test anticancer activity in vitro; half maximal inhibitory concentration (IC₅₀) and combination index (CI) were calculated. Cellular changes were studied with transmission electron microscopy (TEM). ATV was combined with PFKi as we previously showed that PFKi, in addition to glycolysis, inhibits lipid metabolism by targeting PLA2G3. PLA2G3 expression was studied by Western blot; we have found that its downregulation induces autophagy, a prodeath condition in OC, and is associated with chemosensitization compared to nontargeted controls. PLA2G3 was downregulated using two shRNAs (sh33, sh35). A random sample of 10 patient-derived OC xenografts (PDX) was studied by TEM.

Results: OVCAR8 exhibited a dose-dependent proliferation inhibition when treated with ATV (IC₅₀ 8 μM). PFKi and CBPT IC₅₀ were 4 μM and 78 μM, respectively. PFKi treatment combined with ATV 4 and 8 μM resulted in sensitization to PFKi by shifting its IC₅₀ down to 2.7 and 0.4 μM, respectively. When ATV was combined in constant ratio with CBPT, CIs were >1.0 indicating antagonism. Combination of ATV 4 μM with PFKi 2 μM resulted in greater decrease in PLA2G3 and p62 and greater increase in cleaved PARP compared to PFKi alone, suggesting higher levels of autophagy and apoptosis. ATV and combination treatment resulted in increased caveolin-1 levels, shown to be associated with apoptotic cell death. TEM analysis of ATV- and PFKi-treated cells showed greater number of lipid-rich multilamellar bodies (MLB) compared to controls. PLA2G3 knockouts exhibited higher MBL formation and lower p62, and when treated with statin and with PFKi, cleaved PARP was significantly

higher compared to NTCs. TEM showed that PDXs clustered in low- and high-MLB groups suggesting a distinct novel phenotype. See Figure 1.

Conclusion: ATV could enhance PFKi antitumor activity by jointly targeting PLA2G3 leading to metabolic reprogramming of OC. Importantly, ATV antagonized CBPT. Additional studies are in progress to explore the mechanistic pathway of ATV and characterize the significance of MLB in OC as a prodeath phenotype and biomarker of response.

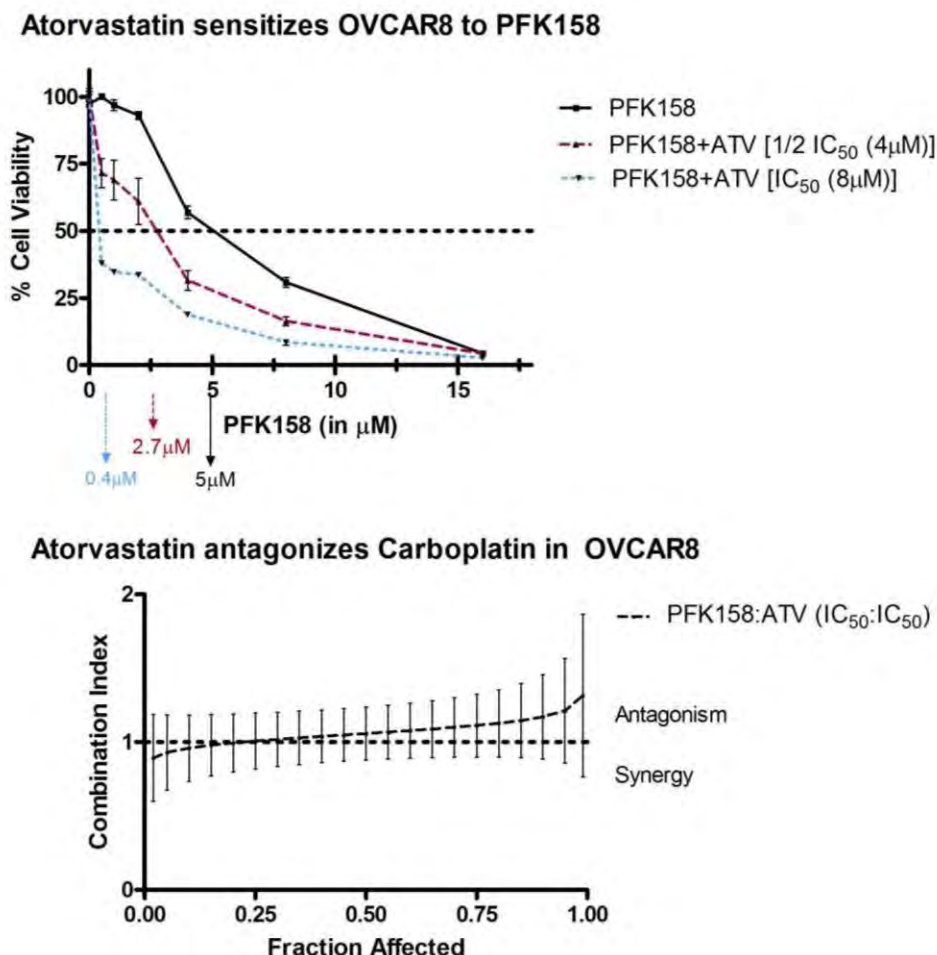


Fig. 1.

136 - Poster Session

HER2 and p95HER2 protein expression varies in primary versus metastatic serous endometrial cancer tumors

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Objective: The purpose of this study was to further characterize HER2 and p95HER2 expression in uterine serous carcinomas and to determine whether HER2 and p95HER2 expression differs in primary versus metastatic tumor samples.

Method: A prospectively maintained database was queried for eligible cases that included patients who underwent surgery for treatment of uterine serous carcinoma between 2004 and 2014 and for whom there were both primary and metastatic tumor samples available. Thirteen cases (26 tumor samples including 13 primary tumor samples and 13 metastatic tumor samples) were identified that met inclusion criteria. HER2 and p95HER2 protein expression was quantified using the VeraTag assay from Monogram Biosciences. The Spearman correlation coefficient was used to assess the association between metastatic and primary samples with respect to HER2, p95, and the p95:HER2 ratio. Wilcoxon signed-rank test was used to determine whether the distributions of HER2, p95, and the p95:HER2 ratio differed between the paired primary and metastatic samples.

Results: Serous endometrial cancers express higher levels of p95HER2 than those previously reported for breast cancers. For paired tumor samples, there was a direct positive correlation between primary and metastatic samples for both p95HER2 protein expression ($P = 0.03$) and the p95HER2:HER2 protein expression ratio ($P = 0.02$). The p95HER2:HER2 protein expression ratio is significantly increased in metastatic tumor samples compared to primary tumor samples ($P = 0.01$). p95HER2 protein expression is unchanged in metastatic tumor samples compared to primary tumor samples ($P = 1.00$). There was a trend towards HER2 protein expression being decreased in metastatic serous endometrial cancer tumor samples compared to primary tumor samples ($P = 0.24$).

Conclusion: Previous studies have shown higher levels of p95HER2 expression in high-grade endometrial cancers than in breast cancers. This observation is corroborated by our data and may provide some rationale for the trastuzumab resistance observed in high-grade endometrial cancers. The decreased HER2 expression and the increased ratio of p95HER2:HER2 expression observed in this study when metastatic tumor samples are compared to primary tumor samples may give additional insight into the pathophysiology of this resistance.

137 - Poster Session

Aberrant TMEM205-CD1B signaling promotes platinum resistance in ovarian cancer

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Objective: TMEM205 is a novel transmembrane protein that may be associated with platinum resistance (PR) in high-grade serous ovarian cancer (HGSOC), but the specific mechanism associated with this resistance is still unknown. The goals of this study are to show that TMEM205 expression is linked with platinum-resistant HGSOC compared to platinum-sensitive and benign disease and to investigate the role of the TMEM205-CD1B (an exosome-related protein) axis in mediating this PR.

Method: TMEM205 expression was analyzed in patient samples by Western blots (WB) and real-time qPCR. Based on the computational data obtained from BIOGRID 3.4, we predicted an interaction between TMEM205 and CD1B (an exosome-related protein) to mediate PR. In an effort to confirm and validate this, we performed a series of coimmunoprecipitations, far-Western blots, immunocytochemistry, and in situ proximity ligation assays. TMEM205 knockdown experiments in vitro will address the correlation to PR, which will be further extended to orthotopic mouse models.

Results: Our initial studies show variable expression of TMEM205 and CD1B in the immortalized ovarian cancer cell lines TR127, TR182, JHOC, A2708CR, A2780CS, A2780CDDP, OVCAR4, OVCAR8, OVTOKO, and SKOV3. In comparison of 4 benign, 4 stage I, and 4 stage IV HGSOC samples, we observed high expression of both TMEM205 and CD1B in advanced-stage HGSOC with little to no expression in the benign setting. There is ubiquitous expression of TMEM205 in PR cell lines and patient serum and tissues samples. These results confirm that TMEM205 is associated with PR. Further, we observed a strong interaction between TMEM205 and CD1B, and this proves that TMEM205 interacts with CD1B to mediate PR via the exosomal pathway.

Conclusion: TMEM 205 over-expression is seen in both serum and tissue of patients with HGSOC compared to benign disease along with an elevated CD1B expression in serum samples. We believe that TMEM205 knockdown will increase platinum sensitivity and improve response to chemotherapy and that TMEM205 can act as a serum marker for platinum-resistant HGSOC. Going forward we are planning in vivo analysis of cisplatin treatment in TMEM205 over-expression and knockdown models, which should support our current results.

138 - Poster Session

Verteporfin sensitizes endometrial cancer cells to radiation or chemo treatment

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Objective: Verteporfin (VP, Visudyne™) is a benzoporphyrin derivative used in the treatment of adult macular degeneration. We investigated the therapeutic efficacy of Verteporfin (VP) alone or in combination with radiation, cisplatin, or paclitaxel on type 1 and 2 endometrial cancer (EMCA) cell lines.

Method: HEC-1-B (type 1) and ARK-1 (type 2) EMCA cell lines were used in clonogenic assay and cell viability experiments. EMCA cell lines were sensitized with 2 nM VP for 15 minutes prior to radiation treatment at 2, 4, and 6 Gy, and clonogenic assay was performed. Cell viability assays were performed with VP, cisplatin, or paclitaxel alone or in combination for 3 hours. For combination treatments, cells were initially sensitized with VP for 30 minutes, then added along with either cisplatin or paclitaxel. RNA was extracted using the Illumina RNA sample prep kit, and RNA-seq data were analyzed with MultiQC and DESeq.

Results: The plating efficiency (PE) of ARK-1 cells without irradiation was 0.239 ± 0.06 and for HEC-1-B cells, 0.194 ± 0.05 . VP sensitization alone (2 nM, 15 minutes) decreased PE of ARK-1 cells to 23.01%, and with radiation treatment (6 Gy), PE further decreased to 0.33%. Similarly, VP sensitization of HEC-1-B cells decreased PE to 14.43%, and with radiation (6 Gy), PE decreased to 0.31%. These results demonstrate VP as a potential radiation sensitizer in both type 1 and type 2 EMCA cells. VP and cisplatin or VP and paclitaxel exhibited synergetic effects when inhibiting viability of EMCA cells. RNA-seq analysis of each cell line showed that type 1 (HEC-1-B) EMCA had more global transcriptomic downregulation after VP treatment than type 2, with 3,316 genes upregulated and 5,266 downregulated (FDR $P < 0.05$); in type 2 (ARK-1), 1,935 genes were upregulated and 1,677 downregulated after VP treatment. Functional enrichment analysis of downregulated genes in type 1 cells after VP revealed that the extracellular matrix (ECM) organization Gene Ontology was most significant (FDR $P = 2.88e-15$).

Conclusion: Chemosensitization of EMCA cells with VP promotes sensitivity to either radiation or chemotherapy. Moreover, the underlying transcriptional response to VP treatment indicates that VP-treated type 1 cells have significantly downregulated ECM pathways, possibly reducing interstitial resistance to therapeutic agents.

139 - Poster Session

Preclinical assessment of SPR965, a dual PI3K/mTOR1/2 inhibitor, in ovarian cancer

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Objective: The PI3K/mTOR pathway is thought to be critical in ovarian cancer (OC) growth and metastasis. First-generation mTORC1 inhibitors, however, have had only modest effects in OC clinical trials. SPR965 (Sphaera), a dual PI3K/mTOR inhibitor, targets PI3K as well as both mTORC1 and mTORC2, potentially improving on the efficacy of first-generation mTOR inhibitors. Thus, we assessed SPR965's potential as an antitumorigenic agent in OC using cell lines and a genetically engineered mouse model (K18-gT₁₂₁^{+/-};p53^{fl/fl};Brca1^{fl/fl}; KpB) of high-grade serous OC.

Method: Cell proliferation was assessed by MTT assay after exposure to SPR965 in the Hey, OVCAR5, OVCAR433, and SKOV3 OC cell lines. Two representative lines, Hey and OVCAR5, were used for further studies. Cell cycle progression and apoptosis were evaluated by Celigo Image Cytometry. Cellular stress was determined by DCFH-DA assay. Western immunoblotting was performed to assess downstream targets of the PI3K/mTOR pathway as well proteins related to cellular stress. AdCre was injected at 6 weeks of age to induce invasive OC in the KpB mice. Mice were treated with placebo or SPR965 (3 mg/kg/day, IM) following tumor onset for 4 weeks ($n = 10$ mice/group).

Results: SPR965 inhibited cell proliferation in a dose-dependent manner in all 4 OC cell lines after 72 hours of exposure (IC₅₀ range 100–500 nM). Treatment with SPR965 resulted in G1 arrest and reduced CDK4 and CDK6 expression in both the Hey and OVCAR5 cell lines ($P < 0.05$); however, apoptosis was not induced with SPR965 treatment. SPR965 induced cellular stress with parallel increases in PERK and BiP expression in both cell lines (100–500 nM, $P < 0.05$). Western immunoblotting demonstrated reduced phosphorylation of Akt and S6 within 24 hours of exposure. SPR965 significantly inhibited tumor weight in the KpB mice by 78% after 4 weeks of treatment ($P < 0.05$).

Conclusion: SPR965 potently inhibited cell proliferation and tumor growth in OC cell lines and an OC mouse model. SPR965 should be considered for ongoing investigation in clinical trials for OC.

140 - Poster Session

N-acetylation as an important metabolite in the ovarian cancer pathways: A study of ovarian cancer metabolome

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Objective: To explore novel pathways integral to ovarian cancer growth and proliferation through comprehensive metabolomic profiling of ovarian tissues with both benign and malignant pathologies.

Method: Fasting systemic arterial blood samples were collected from patients undergoing oophorectomy for benign and malignant disease. Venous blood samples were collected from the ovarian vein intraoperatively. A portion of each ovarian tumor or benign ovarian tissue was also collected to confirm metabolomic differences observed in tumor-associated plasma. Finally, pathologic diagnosis and demographic data were identified from the electronic medical record. Global metabolomic analysis was performed using liquid and gas mass spectrometry to identify differential metabolite expression between benign and malignant tumors of the ovary. Statistically relevant differences were ascertained by employing one-way ANOVA, Welch's two-sample t test, and Matched Pairs t tests.

Results: A total of 37 women were included in the analysis, 16 patients with benign ovarian pathology (median age 63 years) and 21 patients with malignant pathology (median age 55 years). Patients with malignant pathologies had the following ovarian cancer subtypes: 66.7% ($n = 14$) high-grade serous, 9.5% ($n = 2$) endometrioid, 9.5% ($n = 2$) clear cell, and 14.3% ($n = 3$) mixed histology. Of the total, 66.6% (16) of patients presented with stage III or IV disease. The comprehensive metabolomic analysis yielded a statistically significant change in N-acetylated metabolites in ovaries with malignant pathology in comparison to ovaries from patients with benign pathology. Most significantly, aromatic amino acids such as tryptophan were increased >20-fold, and tyrosine was noted to be elevated >11-fold. N-acetylation of polyamines such as N-acetyl putrescine were also elevated in comparison to benign counterparts in a statistically significant fashion ($P < 0.01$).

Conclusion: In the metabolome identified in venous gonadal blood and ovarian tissue from patients with ovarian malignancies, there is evidence of increased global N-acetylation as indicated by increased levels of N-acetyl putrescine, N-acetyl tryptophan, and N-acetyl tyrosine. N-acetyl tryptophan believed to be an antiapoptotic agent in neurons and may have a similar function in malignant ovarian tissues. N-acetyl putrescine is involved in cell growth and differentiation in other cell lines and may have a similar function in ovarian cancer.

141 - Poster Session

Can ARID1A be a predictive marker of detecting endometrial carcinoma from endometrial samplings?

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Objective: Inactivating somatic mutations of ARID1A, a chromatin remodeling gene, are common in endometrioid endometrial carcinoma (EEC) but rare in complex atypical hyperplasia (CAH). Loss of ARID1A expression is a surrogate marker for its mutation. Our objective is to determine the clinical significance of ARID1A loss in the tumor progression from CAH to EEC and to assess its potential clinical application as a cancer predictive tissue biomarker.

Method: Cohort A consisted of 54 women who were diagnosed with CAH in endometrial sampling specimens (biopsy/curettage) and subsequently underwent hysterectomy. Cohort B consisted of 44 patients whose hysterectomy specimens contained concurrent CAH and EEC. ARID1A expression was evaluated on tissue sections.

Results: In cohort A, loss of ARID1A expression was identified in 16 (29.6 %) of 54 endometrial sampling specimens containing CAH. EEC was identified at time of subsequent hysterectomy in 15 of 16 (93.8%) patients with loss of ARID1A expression in their endometrial sampling specimens versus 7 of 38 (18.4%) patients with retained ARID1A expression ($P < 0.0001$). No significant associations were identified between ARID1A expression in endometrial samplings and age, BMI, or length of time from biopsy to hysterectomy. The ARID1A expression pattern was concordant between biopsy and hysterectomy specimen in selected representative cases. In cohort B, 13 (29.5%) of 44 EEC cases showed ARID1A loss in the EEC component. Seven (53.8%) of the adjacent CAH components also lost ARID1A immunoreactivity. In contrast, none of the EEC cases without ARID1A loss in the carcinoma component showed loss of ARID1A expression in the CAH component.

Conclusion: Loss of ARID1A expression, presumably due to somatic inactivating mutations, is associated with tumor progression from CAH to EEC. The ARID1A immunostaining pattern warrants further investigation to determine its potential applicability as a biomarker to predict the presence of underlying EEC in the uterus when only CAH is detected by limited endometrial sampling.

142 - Poster Session

Preclinical trial of targeted agents using NGS, HTS and PDX models in gynecologic cancer

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Objective: Patient-derived tumor xenografts (PDXs) can provide more reliable information about tumor biology than cell line models. We developed PDXs for gynecologic cancer that have histopathologic and genetic similarities to the primary patient tissues and evaluated their cancer genome profiling using targeted next-generation sequencing (NGS) for preclinical tests of the PDX model. We also performed personalized high-throughput sequencing (HTS) for drug screening of target therapeutic agents using primary patient tissues. The aim of this study is to investigate the concordance of the results obtained through NGS and HTS and to evaluate the preclinical efficacy of these drugs using the PDX model.

Method: We successfully established PDXs by subrenal capsule implantation of primary gynecologic cancer tissues into female BALB/C-nude mice. The rate of successful PDX engraftment was 57.5% (115/200 cases). Hematoxylin and eosin staining and short tandem repeat analysis showed histopathological and genetic similarity between the PDX and primary patient tissues. With 93 PDXs, we identified the target gene through NGS. Furthermore, drug screening HTS was performed with 61 primary patient tissues, and the available target agents of the patients were confirmed using z score.

Results: To date, a total of 213 primary patient tissues have been sampled, and 200 samples have been transplanted into mice. Of the 200 PDXs, 52 have been completed, and 148 are being processed. Of these, 63 final PDXs have been formed, and we are waiting for results on 85. We identified the target gene and its pathway through NGS within 93 PDXs. In addition, drug screening HTS was performed in 61 primary patient tissues to detect target therapeutic agent, and HTS results were consistent with the target pathway identified by NGS in some patients.

Conclusion: PDXs for gynecologic cancer with histopathological and genetic stability can be efficiently developed by subrenal capsule implantation and have the potential to provide a promising platform for future translational research and precision medicine for gynecologic cancer using NGS and HTS. Based on these results, precision medicine for gynecologic cancer patients will be possible in the future.

143 - Poster Session

The utility of additional ovarian cancer biomarkers to the dual marker combination of HE4 and CA-125 for the detection of cancer

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Objective: Each year more than 250,000 women in the United States are diagnosed with a pelvic mass, and approximately 10% of these will be an epithelial ovarian cancer (EOC). Management of a woman with a pelvic mass is complicated by difficulty in discriminating between malignant and benign disease when using commonly available diagnostic tests. Many serum biomarkers have been examined to determine their sensitivity for detecting malignancy. This study was designed to evaluate whether the addition of biomarkers to HE4 and CA-125 can improve the detection of EOC.

Method: This was an institutional review board-approved clinical trial examining serum obtained from women diagnosed with a pelvic mass who subsequently underwent surgery. Patients were enrolled through the Program in Women's Cancer at Women and Infants Hospital. Serum biomarker levels for CA-125, HE4, YKL-40, transthyretin, ApoA1, Beta-2-microglobulin, transferrin, and LPA were measured. Logistic regression analysis were performed for various marker combinations and ROC-AUC curves were generated.

Results: A total of 184 patients met inclusion criteria (121 postmenopausal and 63 premenopausal) with a median age of 56 years (range 20–91 years). Final pathology revealed there were 103 (56%) benign tumors, 61 (33.1%) EOC, 2 (1%) non-EOC ovarian cancers, 6 (3.2%) gynecologic cancers with metastasis to the ovary, and 8 (4.3%) nongynecologic cancers with metastasis to the ovary. The combination of HE4 and CA-125 achieved an AUC of 91.9% (95% CI 86.9–96.8) for the detection of EOC versus benign disease. The combination of CA-125, HE4, YKL-40, transthyretin, ApoA1, Beta 2 microglobulin, transferrin, and LPA achieved the highest AUC of 93.8% (95% CI 88.8–98.7), but this combination was not significantly better than the HE4 and CA-125 combination alone ($P = 0.177$). The detection of all cancers + LMP versus benign tumors with HE4 and CA-125 achieved an AUC of 83.5% (95% CI 77.0–90.0). The biomarker combination of CA-125, HE4, YKL-40, transthyretin, ApoA1, Beta 2 microglobulin, transferrin, and LPA achieved the highest AUC at 86.9 (95% CI 80.8–93.0); this was not significantly better than HE4 and CA-125 alone ($P = 0.105$).

Conclusion: The addition of further serum biomarkers to the combination of HE4 and CA-125 does not add to the performance of the dual marker combination for the detection of ovarian cancer.

144 - Poster Session

Proton pump inhibitor use during chemotherapy for platinum-resistant or platinum-refractory ovarian cancer improves overall survival

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Objective: Proton pump inhibitors (PPIs) interfere with tumor cell adaptive strategies in nutrient-poor environments; thus they can improve outcomes in patients undergoing chemotherapy. Our objective was to investigate whether the use of PPIs during chemotherapy administration improves survival in patients with recurrent, platinum-resistant, or platinum-refractory ovarian cancer.

Method: All patients with stage III–IV platinum-resistant or platinum-refractory ovarian cancer treated at our institute between 2003 and 2014 were reviewed to identify patients who were taking a PPI for the duration of at least 1 course of chemotherapy. The median follow-up for all patients was 24.7 months (29.6 months for PPI users vs 23.9 months for nonusers). Kaplan-Meier plots and log rank tests were used to compare overall survival (OS) and survival after first recurrence of PPI user versus nonuser patients.

Results: We identified 157 patients with 56 being PPI users and 101 nonusers. There were no significant differences in baseline characteristics, such as stage, histology, and rate of optimal debulking. The most commonly used PPI was omeprazole (39 patients). Patients who took a PPI during their chemotherapy had an overall survival of 35.0 months versus 25.4 months for nonusers ($P < 0.001$). Survival after first recurrence for PPI users was 33.3 months, compared with 13.9 months for nonusers ($P < 0.001$). See Figure 1.

Conclusion: Use of a PPI during chemotherapy administration for recurrent platinum-resistant or platinum-refractory ovarian cancer significantly improved OS and survival after first recurrence, and should be further evaluated in prospective studies.

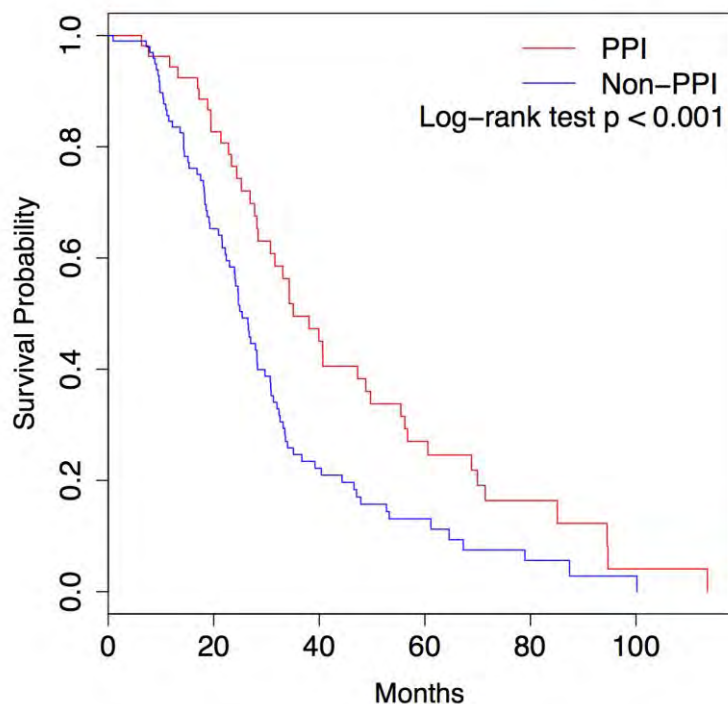


Fig. 1.

145 - Poster Session

REV3L, a promising target in regulating chemosensitivity and stemness of ovarian cancer

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Objective: REV3L, the catalytic subunit of DNA Polymerase ζ (Pol ζ), plays an essential role in the DNA damage tolerance mechanism of translesion synthesis (TLS), which contributes to chemoresistance and tumor progression in a variety of cancers. However, the underlying mechanism is not fully understood, and the role of REV3L in ovarian cancer remains unknown. In the current study, we aimed at exploring roles of REV3L in ovarian cancer to find potential targets in chemotherapies.

Method: Immunohistochemistry of a paraffin-embedded tissue microarray was performed to evaluate the protein expression level of REV3L and its relationship with prognosis. Then we established ovarian cancer cell lines with REV3L suppression or over-expression to examine the effects on biological characteristics of tumor cells in vitro and in vivo, including proliferative ability, chemosensitivity, and stem-ness. We further sorted ALDH (acetaldehyde dehydrogenase)-high and ALDH-low ovarian cancer cells by using flow cytometry to analyze the effects of REV3L suppression in ovarian stem-like cancer cells.

Results: Expression of REV3L was upregulated in ovarian carcinoma compared with normal ovary tissues and related to platinum resistance and poor prognosis. Depletion of REV3L inhibited proliferative ability in vitro, suppressed tumorigenicity in vivo, and restored chemosensitivity to cisplatin and PARP (poly ADP-ribose polymerase) inhibitor of ovarian cancer cells as well as ALDH-high cancer stem-like cells. Moreover, downregulation of REV3L also suppressed sphere formation ability and expression level of stem-ness transcription factors (sox2, oct3/4, nanog) in ovarian cancer cells and blocked cisplatin-induced cancer stem-like cell enrichment.

Conclusion: Taken together, our results suggest that REV3L plays an important role in regulating chemosensitivity and stem-ness characteristics of ovarian cancer cells. Thus, targeting REV3L might be a promising way to improve the prognosis of ovarian cancer patients.

146 - Poster Session

Single nucleotide polymorphism and associated gene expression related with Japanese ovarian clear cell adenocarcinoma: eQTL analysis using HapMap3 and survival analysis with TCGA data

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Objective: Epithelial ovarian cancer (EOC) is the ninth most common malignancy in American women with poor prognosis. Ovarian clear cell carcinoma (OCCC), which accounts for 5%-10% of EOC, has platinum-resistant characteristics and therefore shows worse prognosis than serous carcinoma. OCCC is significantly higher in Japanese than in Western women, which is about 15% to 25% of population. This difference of incidence suggests that a genetic difference in OCCC occurs. The purpose of this study is to investigate the single nucleotide polymorphism (SNP) of Japanese OCCC and specific genetic expression by HapMap data analysis and to estimate overall survival of OCCC using TCGA data.

Method: We performed e-QTL analysis using HapMap Data to discover the SNPs that differ in Japanese compared to Europeans and Chinese women. Then we identified 7 genetic expressions associated with 4 SNPs using the Genevar tool. To investigate the expression of these genetic mutation and survival of OCCC, we analyzed renal clear cell carcinoma (RCCC) and compared it with ovarian serous carcinoma using TCGA data.

Results: Through e-QTL analysis, we found 4 different SNPs (rs4873815, rs11136002, rs13259097, and rs12976454) in Japanese compared with in Chinese and European women. Based on this result, we also used the Genevar tool to identify 7 gene expressions (*ZNF707*, *NAPRT1*, *C8orf58*, *RHOBTB2*, *TNFRSF10B*, *RHOBTB2*, and *APBA3*) associated with four SNPs. To investigate clinical significance, TCGA data analysis was done even if there is a limit to the use of RCCC data. It showed that there were significant differences in 7 genetic expressions in RCCC compared with ovarian serous carcinoma. Moreover, overall survival was significantly decreased in the *ZNF 707* and *TNFRSF10B* and increased in *RHOBTB2* genetic mutation groups than ovarian serous carcinoma.

Conclusion: This study showed that there is a difference in genetic expression of 7 genes in Japanese OCCC compared with others. Although the RCCC data were used, TCGA analysis suggested differences in genetic expression and overall survival

according to ovarian cancer histologic subtype. By identifying the differences of these genetic expressions, we could predict the prognosis of OCCC patients and ultimately provide the basis for the development of the target therapeutic agent for OCCC patients.

147 - Poster Session

Transforming growth factor downregulates homologous recombination repair genes and increases PARP inhibitor sensitivity in *BRCA2* wild-type epithelial ovarian cancer cells

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Objective: Transforming growth factor b (TGFb) is a ubiquitous cytokine named for its ability to transform normal fibroblasts in culture. TGFb has been shown to induce tumor growth and proliferation. High levels of TGFb at tumor sites correlate with high grade, increased risk of metastasis, and poor prognosis. TGFb is implicated in resistance to chemotherapies for various cancers. Paradoxically, TGFb has also been shown to inhibit growth of normal epithelial cells. The role of TGFb in the development and progression of ovarian cancer is yet to be fully elucidated. This study aims to investigate the link between TGFb signaling and progression of *BRCA2*-mutated and wildtype epithelial ovarian cancer (EOC) cells.

Method: *BRCA2*-mutated PEO1 and *BRCA2* wildtype PEO4 EOC cell lines were derived from the same patient at first and second relapse, respectively, following platinum-based chemotherapy. Western blot analysis was performed to determine expression of mesenchymal markers snail and fibronectin and the epithelial marker, E-cadherin, at baseline and in response to TGFb and LY2109761, a small molecule inhibitor of the TGFb type I/II receptors. Western blot analysis was also performed to determine expression of homologous recombination (HR) repair genes: *BRCA1*, *BRCA2*, and *Rad51*. Scratch wound assays were conducted to determine cells' migratory ability. Clonogenic assay was carried out to determine cell survival in response to various concentrations of olaparib and cisplatin with or without TGFb and LY2109761.

Results: TGFb increased expression of mesenchymal markers in PEO1 and PEO4 cells. LY2109761 decreased TGFb-induced expression of mesenchymal markers in both PEO1 and PEO4 cells. TGFb changed the morphology of PEO4 cells, making them resemble PEO1. In addition, TGFb downregulated the HR repair genes *BRCA1*, *BRCA2*, and *Rad51*. PEO4 cells treated with TGFb showed heightened sensitivity to the PARP inhibitor olaparib.

Conclusions: The model of PEO1 and PEO4 cell lines represents the progression of EOC at stages of initial chemosensitive and late chemoresistant diseases. TGFb changed the morphology of *BRCA2* wildtype chemoresistant PEO4 cells, downregulated the HR repair genes, and increased sensitivity to the PARP inhibitor olaparib. Comprehensive assessment of the link between TGFb signaling and HR repair pathways is needed to help identify molecular targets for treatments of late-stage and chemoresistant EOC.

148 - Poster Session

Omega-3 lipid metabolites inhibit the growth of ovarian cancer cells

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Objective: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), 2 omega-3 lipids that are the end products of linolenic and α -linolenic acid, have shown promising in vitro results inhibiting the growth of breast, colon, and prostate cancer cells. Metformin is known to alter lipid metabolism in cancer cells. We explored (1) the effects of EPA and DHA on ovarian cancer cells and (2) the impact of metformin on lipid metabolism in those cell lines.

Method: Three human ovarian cancer cell lines (*A2780*, *C200*, and *SKOV3IP*) treated with metformin (10 mM) for 48 hours were subjected to untargeted global metabolomics by ultra-high- performance liquid chromatography and gas chromatography mass spectroscopy. Five human ovarian cancer cell lines (*A2780*, *C200*, *SKOV3IP*, *ID8*, and *OVCAR5*) with different genetic makeups and characteristics were treated with varying doses of EPA/DHA (12.5–400 μ M) with or without metformin or cisplatin. Cell survival was assayed by MTT and clonogenic assay (12.5–100 μ M). The expression of SREBP-1, a transcription factor that controls lipid metabolism, was measured by Western blot.

Results: Under metformin treatment, enrichment analysis of the commonly upregulated metabolites indicated a universal increase of α -linolenic and linoleic acid metabolism ($P < 0.001$). EPA or DHA treatments alone or in combination with metformin resulted in a significant dose-dependent inhibition of proliferation in all 5 cell lines ($P < 0.001$). Furthermore, EPA

and DHA potentiated cisplatin cytotoxicity in all cell lines ($P < 0.05$). Significant inhibition of colony formation was noted with the lowest doses of EPA and DHA ($P < 0.01$). Protein expression of SREBP-1 (in A2780, SKOV3, ID8, and patient ascites cells) was significantly decreased by EPA.

Conclusion: Both EPA and DHA inhibited ovarian cancer cell proliferation alone and in combination with cisplatin. The cytotoxic effect of metformin may be partially mediated through upregulation of omega-3 lipids. Further work is being conducted to explore the therapeutic potential of these combinations and their mechanism of action.

149 - Poster Session

A novel nanoparticle platform, p5RHH-siAXL, inhibits metastasis in gynecologic serous cancers

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Objective: The receptor tyrosine kinase, AXL, has been shown to be critical in uterine serous and ovarian cancer metastasis. The objective was to evaluate the specificity and ability of p5RHH-siAXL nanoparticles (NPs) to inhibit the steps of metastasis.

Method: P5RHH, a peptide carrier of siRNA, aids in endosomal escape within cells, thus facilitating siRNA knockdown of target mRNA. P5RHH-siRNA NPs were created with siAXL (silencing RNA to AXL). Western blot analysis and Matrigel invasion assays were performed with a uterine serous cancer cell line, *ARK1*, or ovarian cancer cell line, *OVCAR8*, treated with p5RHH-siControl or p5RHH-siAXL NPs. Two in vivo intraperitoneal (IP) models were used. Mice were treated with IP-injected p5RHH-siAXL NPs or control for 2 weeks, and blood was drawn for assessment of toxicities. NP localization was determined after IP injection of fluorescently (eGFP or cy5.5)-labeled NPs at 24 hours postinjection.

Results: p5RHH-siAXL NPs successfully inhibited 90% of AXL expression compared to both p5RHH-siControl and untreated *ARK1* and *OVCAR8* cells after treatment for 72 hours. P5RHH-siAXL NP therapy prevented tumor cell invasion compared to control-treated cells (152 vs 390 for *OVCAR8*, $P = <0.0001$; 106 vs 186 for *ARK1*, $P = <0.0001$), or p5RHH-siControl-treated cells (152 vs 359 for *OVCAR8*, $P = <0.0009$; 106 vs 186 for *ARK1*, $P = <0.0001$), respectively. Fluorescently tagged NPs were found to preferentially target tumors after either IV or IP injection at 24 hours. Furthermore, p5RHH-siAXL NP therapy decreased tumor weight (58 mg vs 34 mg, $P = 0.018$) and decreased the number of tumor implants (32 vs 17, $P = 0.006$) in an *OVCAR8* murine xenograft model. *ARK1*-injected mice treated with p5RHH-siAXL NPs demonstrated decreased tumor implants (21 vs 10, $P = 0.006$) with no statistical difference in platelets, white blood cells, hemoglobin, alanine aminotransferase, or blood urea nitrogen compared to control.

Conclusion: P5RHH-siAXL NPs successfully inhibited tumor cell invasion, migration, and metastasis. P5RHH-siAXL NPs preferentially target tumor tissue with no significant toxicities. P5RHH-siAXL NPs show potential as a novel therapeutic for metastatic serous cancers, and this nanoparticle platform could be adapted to inhibit other critical pathways in gynecologic cancers.

150 - Poster Session

Remarkable *in vitro* and *in vivo* activity of IMG853, an antibody-drug conjugate targeting folate receptor alpha linked to the tubulin-disrupting maytansinoid DM4, in biologically aggressive (type II) endometrial cancers

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Objective: Grade 3 endometrioid and uterine serous carcinomas (USC) account for the vast majority of endometrial cancer deaths. The purpose of this study was to determine folate receptor alpha (FR α) expression in biologically aggressive (type II) endometrial cancers and to evaluate FR α as a targetable receptor for IMG853.

Methods: The expression of FR α was evaluated by immunohistochemistry (IHC) and flow cytometry in 91 endometrioid and uterine serous carcinoma samples. The *in vitro* cytotoxic activity and bystander effect of IMG853 were studied in primary uterine cancer cell lines expressing differential levels of FR α . *In vivo* antitumor efficacy of IMG853 was evaluated using endometrioid and serous cancer xenograft/patient-derived xenograft (PDX) models.

Results: Semiquantitative IHC analysis indicated that 41% of the USC patients over-expressed FR α . Further, over-expression of FR α (i.e., 2+) was detected via flow cytometry in 22% (2/9) of primary endometrioid and in 27% (3/11) of primary USC cell lines. Increased cytotoxicity was seen with IMGN853 treatment compared to control in 2+ expressing uterine tumor cell lines. In contrast, tumor cell lines with low FR α showed no difference when exposed to IMGN853 versus control. IMGN853 induced bystander killing of FR α = 0 tumor cells. The aggressive endometrioid xenograft model with 2+ FR α treated with IMGN853 had complete resolution of tumors compared to control (P = 0.0005); see Figures 1A and 1B. IMGN853, in the USC PDX model with 2+ FR α , induced a 2-fold increase in median survival (P = 0.0006); see Figures 1C and 1D.

Conclusions: IMGN853 shows remarkable specific antitumor activity in biologically aggressive FR α 2+ uterine cancers. These preclinical data suggest that patients with chemotherapy resistant/recurrent endometrial cancer over-expressing FR α may benefit from treatment with IMGN853.

FIGURE 1A: Antitumor activity of IMGN853 was compared to PBS CTRL, ADC ISO type, M9345A in endometrial endometrioid xenograft tumor models with END(K)265 (FR α =2+). Mice were treated intravenously with two doses administered once a week as described in Materials Methods. A significant difference in tumor growth inhibition was detected on day 24 (p =0.00179) in IMGN853-treated group when compared to the other control groups.

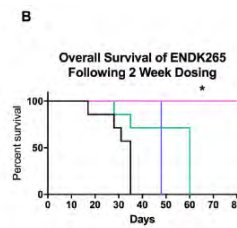
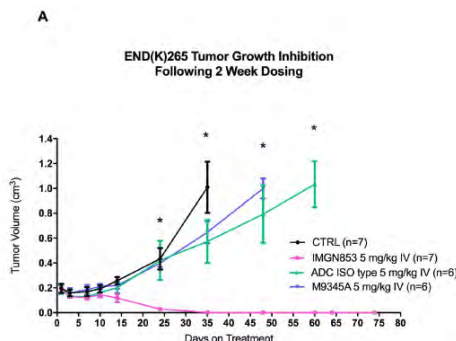


FIGURE 1B: Overall survival of IMGN853 was compared to PBS CTRL, ADC ISO type, M9345A in the endometrial endometrioid xenograft tumor models with END(K)265 (FR α =2+). A significant overall survival (0.0005) advantage was seen with IMGN853 when compared to the controls. At the time of analysis (80 days) no tumor recurrence or death occurred in the IMGN853 treated group.

FIGURE 1C: Antitumor activity of IMGN853 was compared to PBS CTRL, ADC ISO type, M9345A in uterine serous cancer xenograft tumor models of BIO(K)1 (FR α =2+). Mice were treated intravenously with two doses administered once a week as described in Materials Methods. A significant difference in tumor growth inhibition was detected on day 7 (p =0.00049) in IMGN853-treated group when compared to the other control groups.

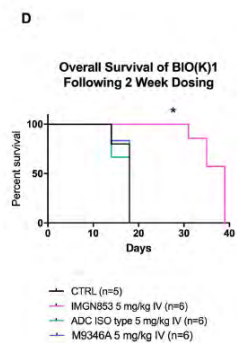
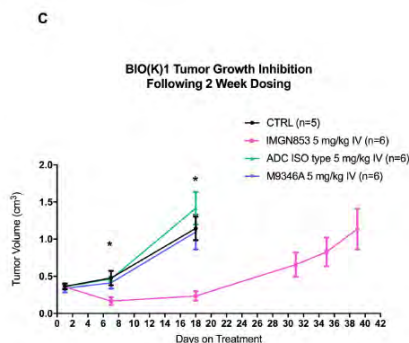


FIGURE 1D: Overall survival of IMGN853 treated xenograft model of the uterine serous cancer, BIO(K)1. A significant overall survival (p =0.0006) advantage was seen with IMGN853. Median survival for IMGN853 was 39 days compared to 18 days for ADC ISO type, M9345A and PBS CTRL, respectively.

151 - Poster Session

PI3K/AKT/mTOR pathway inhibition sensitizes ovarian cancer cells to anti-estrogen therapy

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Objective: Antiestrogen therapy is a clinically appealing treatment option for epithelial ovarian cancer because of its low side-effect profile. Yet estrogen receptor (ER) expression is not a strong predictor of response, suggesting modifiers. Recent data suggest that active PI3K/AKT/mTOR signaling is correlated with a lower response to antiestrogen therapy in ovarian cancer. We therefore sought to determine whether PI3K/AKT/mTOR inhibition improves response to antiestrogen therapy.

Method: Epithelial ovarian cancer cell lines *OVCAR3*, *OVCAR8* and *IGROV1* were treated with drugs targeting the PI3K/AKT/mTOR pathway and antiestrogen therapy either alone or in combination. PI3K/AKT/mTOR pathway inhibitors included the AKT inhibitor MK2206, and MTX-216, a novel PIK3CA/EGFR inhibitor. MTX-216 was designed and later shown to selectively inhibit members of the HER and PI3K families and exhibits low nanomolar inhibitory potency against purified PIK3CA and EGFR. Antiestrogen treatments included the selective estrogen receptor degrader fulvestrant, the aromatase inhibitor letrozole, and the selective estrogen receptor modulator tamoxifen. IC₅₀ and target dose range for each drug were determined by MTT assay. Synergy was calculated by the Chou-Talalay Method using Compusyn software. Following treatment combinations, cell lysates were prepared, and expression of total AKT, phosphorylated AKT, total mTOR,

phosphorylated mTOR, PTEN, ERK 1/2, ER α , and ER β proteins determined by immunoblotting. A FOXO reporter assay was utilized to assess ER signaling-mediated transcriptional activity following treatments.

Results: MTX-216 and MK2206 sensitized ovarian cancer cell lines to antiestrogen therapy, based on synergistic cell killing compared to either treatment alone. Both MTX-216 and MK2206 treatment results in decreased phosphorylated AKT levels, consistent with on-target effects. Treatment with MK-2206 also decreased PTEN levels. Further molecular characterization of the molecular crosstalk between the PI3K/AKT/mTOR and estrogen-signaling pathways is under way, and animal tumor xenograft treatment studies are planned.

Conclusion: Inhibition of the PI3K/AKT/mTOR pathway with concurrent antiestrogen therapy results in synergistic ovarian cancer cell killing. Thus, targeting this pathway may be a new treatment strategy to improve antiestrogen response in patients. MTX-216 is a novel inhibitor that warrants further study.

152 - Poster Session

Neurotensin signaling pathway as a potential therapeutic target in high-grade serous ovarian cancer

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Objective: The presence of serous tubal intraepithelial carcinoma (STIC) in the fallopian tube (FT) is used to designate FT rather than ovary as the site of tumor origin in high-grade serous ovarian carcinomas (HGSOC). Based on gene profiling, we have identified neurotensin (NTS) as significantly over-expressed in HGSOC associated with STIC, but the role of NTS in HGSOC remains unclear. The objective of this study was to investigate the expression of NTS and its receptors in HGSOC and to test whether the neurotensin (NTS)-signaling pathway could be used as a therapeutic target.

Method: Expression of NTS and its receptors (NTSR1, NTSR2, NTSR3) was compared by RNA sequencing in normal FT and HGSOC patient samples and by qPCR in immortalized FT epithelial (FTE) and ovarian cancer (OvCa) cell lines. The selective NTSR1 inhibitor SR48692 was used to test the role of NTS/NTSR1 signaling on cell proliferation, apoptosis, and reactive oxygen species (ROS) generation.

Results: NTS expression was significantly higher in HGSOC associated with STIC compared to normal FT and HGSOC without STIC. While NTSR1 and NTSR3 were expressed in HGSOC, no differences were observed. NTS expression differed among OvCa cell lines with some expressing higher levels than FTE cells and some lower. OvCa cell lines demonstrated decreased expression of NTSR3 and increased expression of NTSR1 compared to FTE cells. To test the role of NTS/NTSR1 signaling in OvCa cells, PE01 and OVCAR5 cells (which express different levels of NTS, but similar levels of NTS receptors) were treated with SR48692. SR48692 inhibited cell proliferation in both lines, which was associated with an increase in apoptosis. Interestingly, PE01 cells, which express low levels of NTS, were more sensitive to the growth-inhibitory effects of SR48692. Further, a differential effect of SR48692 was observed on ROS generation where treatment increased ROS in PE01 cells and decreased ROS in OVCAR5 cells. Taken together, the results suggest that the role of NTS signaling in OvCa cells may be dependent on the cellular context.

Conclusion: Components of the NTS signaling pathway are expressed in HGSOC. OvCa cells are sensitive to NTS pathway inhibition suggesting that NTS may represent a potential therapeutic target. However, given the differential effects observed, the role of NTS in HGSOC needs further study.

153 - Poster Session

Evaluating exosome proteins as biomarkers for the early detection of high-grade serous ovarian cancer

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Objective: The main objective of the study is to evaluate the unique signature of exosome-derived proteins as biomarkers for early detection of high-grade serous ovarian cancer (HGSOC).

Methods: In the current study exosomes were isolated using a microfluidic chip developed at our institution for the economic and rapid isolation of serum exosomes from large numbers of samples. Exosome lysates were subjected to mass spectrometry (1D-LC-MS/MS) for label-free quantification of protein profiles to identify the differentially expressed proteins in the isolated exosomes from normal ovarian epithelial cells, cancer cell lines, and patient serum samples. To discover changes in the proteins across study groups, Limma (Linear Models for Microarray Analysis) and DESeq2 R packages from the Bioconductor project were used. A combination of *P* value and fold change was used for selecting top differentially expressed protein candidates. Absolute quantification of the prioritized candidate proteins was further validated in human serum exosome samples by parallel reaction monitoring (PRM) a more direct and targeted proteomics approach.

Results: Our preliminary studies using mass spectrometry have identified over 25 proteins that are differentially expressed in HGSOC cell lines when compared to normal cells (OSE and FTSEC). The top proteins were identified based on their fold change and statistical significance between groups. Also, IPA identified STAT3 as the top regulator effect network. Some of the candidate protein expressions, including STAT3, IL6, VEGF-A and CXCL, were also confirmed in serum exosomes of both early- and late-stage HGSOC patients making them potential candidates for early detection of HGSOC.

Conclusion: Overall this study has identified potential candidates that can serve as specific biomarkers for early detection of HGSOC when successful in a large clinical validation study.

154 - Poster Session

Prognostic impact of loss of heterozygosity in uterine serous carcinoma

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Objective: While uterine serous carcinomas (USCs) are morphologically and immunophenotypically indistinguishable from their ovarian counterparts, questions remain on whether these tumors share similar molecular profiles and could benefit from similar therapies. Somatic and germline defects in the homologous recombinant (HR) pathway genes (*BRCA1*, *BRCA2*, and others) have been implicated in ovarian cancer predisposition and are associated with high sensitivity to platinum-based and targeted therapies (PARP inhibitors). HR deficiency impairs normal DNA repair resulting in loss or duplication of chromosomal regions, termed genomic loss of heterozygosity (LOH). Whether this phenomenon applies to USCs is yet to be determined. In this study, we analyzed genome-wide LOH in USCs and correlated clinicopathologic parameters and outcomes.

Method: A total of 69 platinum-treated USC patients diagnosed between 1998 and 2015 were included. DNA was isolated, and LOH analysis was performed querying over 220,000 SNPs using the Affymetrix OncoScan. Selecting the top quartile of LOH distribution as a cutoff to separate patients into LOH “high” and LOH “low” groups, data were analyzed using the Kaplan-Meier method.

Results: Patient age ranged from 45 to 89 (median 68) years. Stage distribution was I, 11.5%; II, 1.5%; III, 62%; and IV, 25%. Lymphadenectomy was performed in 74% and omentectomy in 62% of patients. Eighty percent of patients received adjuvant radiotherapy. Median LOH was 1.4% (range 0–30.1%), and the top quartile threshold was 9.9%. Fifty-two tumors showed LOH lower than the top quartile. In the top quartile of LOH, tumors were more common in African-Americans (83% vs 56%) and advanced-stage disease (100% vs 82%) and more commonly associated with outer half MI (76.5% vs 47%) and LVI (88% vs 65%) when compared to tumors with LOH lower than the top quartile. In general, LOH did not significantly correlate with age (*P* = 0.41), race (*P* = 0.43), tumor size (*P* = 0.72), stage (*P* = 0.36), MI (*P* = 0.52), LVI (*P* = 0.40), LN metastases (*P* = 0.43), or recurrence (*P* = 0.34). Kaplan-Meier analysis showed no survival benefit or prolonged DFI for platinum-treated patients with LOH in the top quartile compared to LOH lower than that.

Conclusion: In our cohort of USCs, median LOH was 1.4%, with 25% of tumors showing genomic LOH higher than 9.9%. In contrast to their ovarian counterparts, a high degree of genomic LOH does not correlate with survival benefit for platinum-treated USC patients, suggesting that these tumors have distinct biology and genomic profiles.

155 - Poster Session

Fallopian tube cells from high-risk women have altered adipokine signaling

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Objective: Recent evidence has implicated the fallopian tube epithelium (FTE) as the major site of origin for high-grade serous ovarian cancer (HGSC). Adipose tissue secretes inflammatory cytokines, fatty acids, glucose, and hormones, creating an environment that promotes cancer invasion and metastasis. The objective was to understand the role of adipokines in DNA damage in ovarian cancer pathogenesis.

Method: Fallopian tubes were obtained from women undergoing bilateral salpingo-oophorectomy. Microarray data were analyzed to compare the *BRCA* versus non-*BRCA* FTE and normal versus HGSC. FTE and HGSC cell cultures were assayed for DNA damage repair, adipokine production, and signaling by quantitative PCR (qPCR) and Western blot analyses.

Results: Nicotinamide phosphoribosyl transferase (NAMPT, $P < 0.0001$), ceruloplasmin (CP, $P < 0.05$), CXCL1 ($P = 0.014$), and CXCL2 ($P = 0.011$) were upregulated in primary FTE-*BRCA1* ($n = 4$) and FTE-*BRCA2* ($n = 4$) cultured cells. FTE-*BRCA1* cells showed increased phosphoSTAT and increased DNA damage. Gene expression data associated with metabolic response pathways, such as acyl-CoA synthetases (ACSL4, $P = 0.05$, and ACSL6, $P = 0.04$), glucose transporter 1 ($P = 0.0005$), phosphoenolpyruvate carboxykinase 1 and 2 (PCK1, $P = 0.011$, and PCK2, $P = 0.03$) were also upregulated in FTE-*BRCA1* cells. Notably, HGSC cells showed 3-fold increase in PCK1/2 and GLUT1 expression compared to FTE, indicating a shift in metabolic adaptation from glycolysis to gluconeogenesis.

Conclusion: Our data support the hypothesis that the FTE in *BRCA* mutation carriers exhibit a chronic pro-inflammatory profile because of both intrinsic and extrinsic environmental factors in the peritoneal cavity. These extrinsic factors secreted by adipocytes stimulate nutrient sensing and cellular metabolic pathways that drive metabolic rewiring and reduced DNA damage repair response. Understanding the impact of the local microenvironment on FTE is critical for further development of risk-reducing and early detection strategies.

156 - Poster Session

Heat shock protein 60 (HSP60) serves as a potential target for the sensitization of chemoresistant ovarian cancer cells

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Objective: HSP60 is a mitochondrial chaperone protein that has been shown to promote cell survival and to be associated with decreased overall survival of ovarian cancer patients. We determined whether targeting HSP60 with its monoclonal antibody induces cytotoxicity in sensitive and chemo-resistant ovarian cancer cells and whether it is synergistic when combined with chemotherapeutic drugs.

Method: Epithelial ovarian cancer (EOC) cell lines (MDAH-2774, SKOV-3, A2780) and their docetaxel- or cisplatin-resistant counterparts were utilized. HSP60 mRNA levels were determined by real-time RT-PCR. Cytotoxicity of HSP60 and isotype control antibodies (0.5 or 1.5 $\mu\text{g/mL}$) and in combination with chemotherapy (0.0075, 0.01, 0.025 μM docetaxel or 0.1, 0.5, 1.0 μM cisplatin) were assessed by MTT Cell Proliferation Assay. Unpaired t tests were used to compare groups for real-time RT-PCR, while a one-way ANOVA followed by Tukey's post hoc tests with Bonferroni correction was performed for cytotoxicity comparisons. Significant synergistic effects of the antibody combined with chemotherapy were determined by CompuSyn Software.

Results: HSP60 mRNA levels were $21.5\% \pm 4.0$ and $27.8\% \pm 3.4$ higher in cisplatin- and docetaxel-resistant EOC cell lines compared to their sensitive counterparts, respectively ($P < 0.05$). Treatment with the HSP60 antibody (0.5 or 1.5 $\mu\text{g/mL}$) resulted in a significant cytotoxic effect in sensitive ($32.8\% \pm 14.2$ and $44.9\% \pm 12.1$), in docetaxel ($40.1\% \pm 12.4$ and $50.3\% \pm 10.2$), and in cisplatin ($32.4\% \pm 13.4$ and $44.8\% \pm 15.0$) resistant EOC cells compared to respective controls ($P < 0.05$). There was no significant difference in cytotoxicity between cell types or between doses of the antibody. Combination of the HSP60 antibody with either docetaxel or cisplatin was significantly synergistic in both sensitive and chemo-resistant EOC cell lines.

Conclusions: Here we identify a novel target that may serve as a treatment not only for killing ovarian cancer cells but also, more importantly, for the sensitization of patients to chemotherapy.

157 - Poster Session

Targeting myeloperoxidase enhances apoptosis in chemoresistant epithelial ovarian cancer cells by reversing s-nitrosylation of caspase-3

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Objective: Lower apoptosis, a hallmark of epithelial ovarian cancer (EOC) cells, was shown to be attributed to myeloperoxidase (MPO)-mediated S-nitrosylation of caspase-3. Here we investigated whether inhibiting/silencing MPO expression reduced the S-nitrosylation of caspase-3 and thus increases apoptosis in chemo-resistant EOC cells.

Method: S-nitrosylation of caspase-3 and its activity were evaluated in sensitive and chemo-resistant (docetaxel or cisplatin) EOC cell lines (*MDAH-2774* and *SKOV-3*). MPO gene expression was silenced with specific siRNA or MPO activity inhibited with melatonin (400 μ M) for 24 hours. Scrambled siRNA or dimethylformamide served as controls. MPO mRNA, caspase-3 activity, and S-nitrosylation of caspase-3 were measured utilizing real-time RT-PCR, ELISA, and Western blot, respectively. Data were analyzed with unpaired t-tests.

Results: There was an increase in the level of S-nitrosylation of caspase-3 in docetaxel ($26.7\% \pm 0.07$ and $3.2\% \pm 1.2$) and cisplatin ($8\% \pm 0.7$ and $4.6\% \pm 0.2$) compared to sensitive *MDAH-2774* and *SKOV-3* EOC cell lines, respectively ($P < 0.05$). There was a decrease in caspase-3 activity in docetaxel ($49.2\% \pm 1.0$ and $20.6\% \pm 1.5$) and cisplatin ($32.9\% \pm 2.9$ and $36.4\% \pm 1.0$) resistant *MDAH-2774* and *SKOV-3* EOC cell lines, respectively, compared to sensitive counterparts ($P < 0.05$). Silencing of MPO or inhibiting MPO led to a reduction in MPO mRNA levels in sensitive ($32.7\% \pm 0.1$ or $66.0\% \pm 0.01$), docetaxel ($59.9\% \pm 0.1$ or $43.6\% \pm 0.1$), and cisplatin ($53.7\% \pm 19.3$ or $74.2\% \pm 1.9$) resistant *MDAH-2774* EOC cells compared to controls ($P < 0.05$). Silencing MPO or inhibiting MPO resulted in increased caspase-3 activity in sensitive ($19.1\% \pm 1.5$ or $16.2\% \pm 0.01$), docetaxel ($48.2\% \pm 1.3$ or $32.1\% \pm 0.003$), and cisplatin ($52.8\% \pm 0.7$ or $53.2\% \pm 0.001$) resistant *MDAH-2774* EOC cells, compared to controls ($P < 0.05$).

Conclusion: Similar to our previous finding with sensitive EOC cells, targeting MPO reversed the S-nitrosylation of caspase-3 and enhanced apoptosis in chemo-resistant EOC cells, a finding that has important potential clinical implications.

158 - Poster Session

Promising TRAIL-based cancer therapy using genetically engineered human mesenchymal stem cells as drug delivery vehicles

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Objective: To further enhance the therapeutic efficacy of TRAIL-based cancer drugs, we devised a strategy utilizing tumor-homing mesenchymal stem cells (MSCs) to secrete the biomarker-targeted agents. Using a specifically identified and highly efficient adenovirus modification, we show that we can “arm” MSCs with novel TRAIL variants via infection with adenovirus and assess bioactivity both in vitro and in vivo.

Method: Transduction efficiency of MSCs was assessed by fluorescent protein expression using modified adenovirus vectors. MSCs were isolated from adipose tissue of gynecologic oncology patients and phenotypically identified by flow cytometry using established surface markers. Drug-producing capability of novel TR3-based therapeutics (TR3 and Meso64-TR3) was evaluated both by using functional cell viability assays in vitro and by employing preclinical mouse models of ovarian cancer in vivo. Treatment efficacy following intraperitoneal injection of drug-secreting MSCs was assessed by caliper measurements in tumor-bearing SCID mice. Mock infected MSCs were used as a control.

Results: Stable MSC lines from patient-derived adipose tissue were established. Adenovirus vectors encoding TR3 and Meso64-TR3 showed transduction efficiency approaching 100%. Secreted TR3 and Meso64 from infected MSCs showed equivalent cell death on MUC16-deficient cancer cells, indicating equivalent drug production levels. Meso64-TR3 demonstrated greater killing capacity with MUC16-positive OVCAR-3 cells, as previously shown. A single intraperitoneal injection of drug-producing MSCs resulted in a substantial reduction in tumor growth relative to controls. Drug-specific activity profiles between TR3 and Meso64-TR3 were noted, consistent with their in vitro drug characteristics, with Meso64-TR3 being much more potent. See Figure 1.

Conclusion: Genetically engineered MSCs can produce targeted TRAIL-based therapeutics and demonstrate significant killing activity in vitro and, more importantly, in vivo for the treatment of ovarian cancer.

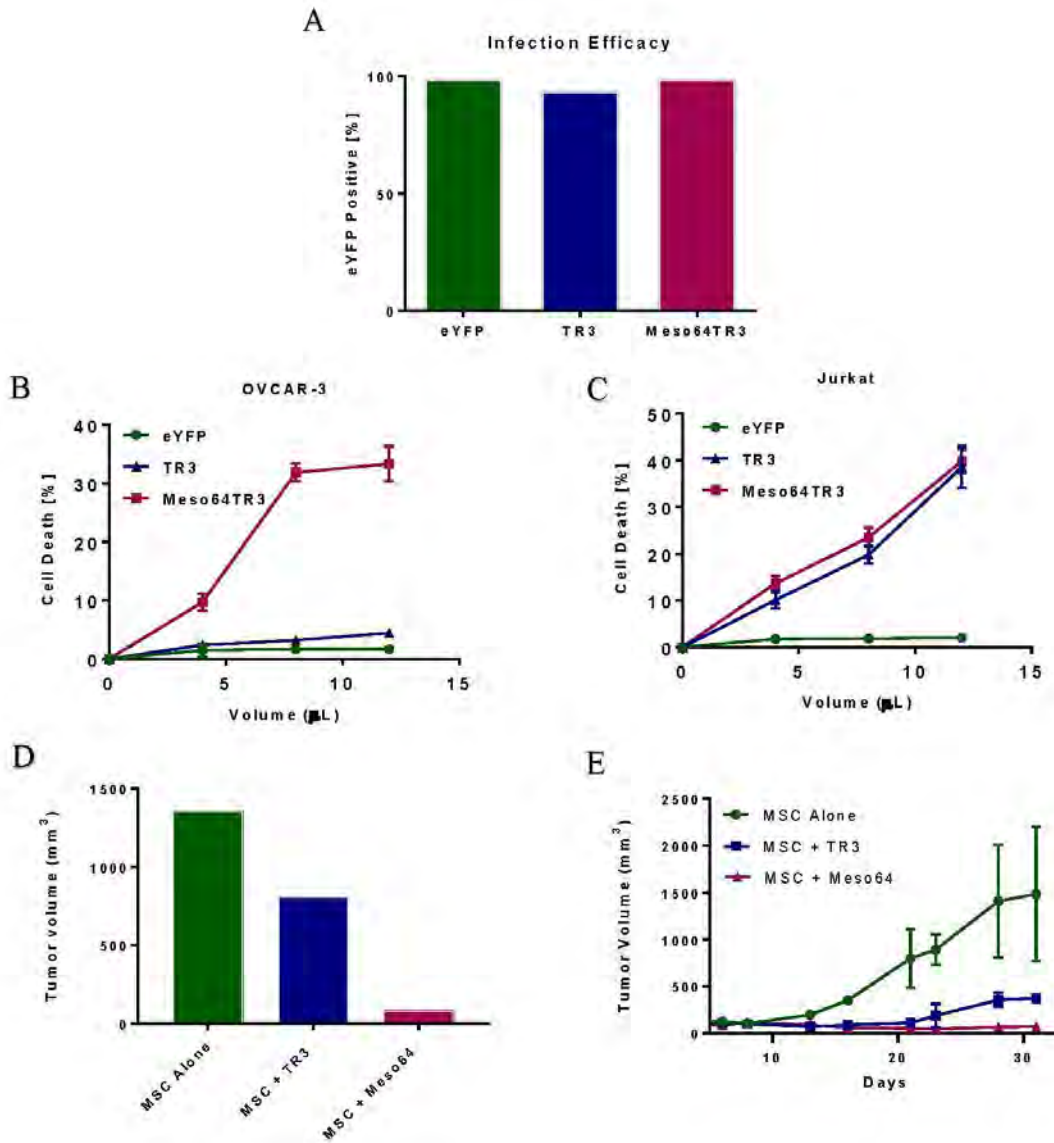


Fig. 1. (A) The eYFP signal was used as an indicator of expression level of the respective MSC. Control (eYFP alone), and both TR3- producing groups show that nearly 100% of the infected cells display eYFP activity, indicating adequate transduction in nearly all cells tested. (B) Cell killing profiles of TR3 and Meso64-TR3 at increasing drug volumes were established on MUC16-deficient T-cell leukemia cell line, Jurkat. Both drug activity profiles are nearly identical, as expected, which suggests that the eYFP infection marker is a valid surrogate for the amount of drug production. (C) Cell death determination using MUC16-positive OVCAR3 cells performed at increasing volumes. There is an enhanced activity profile of MUC16-targeted Meso64-TR3, which is consistent with our previously published data. (D and E) SCID mice bearing established subcutaneous ovarian tumors were given intraperitoneal injections of MSCs that underwent Ad transduction to produce the indicated TR3 drugs. Tumor sizes were measured regularly via caliper. Note the impressive retardation of tumor growth of MSCs secreting Meso64-TR3.

159 - Poster Session

Triapine-olaparib combination therapy deters peritoneal progression of PARP inhibitor-resistant epithelial ovarian cancer

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Objective: PARP inhibitors exploit synthetic lethality to target killing of epithelial ovarian cancer (EOC) with hereditary *BRCA* mutations and defective homologous recombination repair (HRR). However, a considerable portion of EOC cases with intrinsic and acquired HRR proficiency are resistant to PARP inhibitor therapy. Triapine is a small molecule inhibitor of ribonucleotide

reductase previously demonstrated to impair HRR and sensitize cancer cells to DNA-damaging therapeutic modalities. The objective of this study was to evaluate the effectiveness of the triapine-olaparib combination regimen to deter peritoneal progression of *BRCA* wildtype and HRR-proficient EOC cells in xenograft mouse models.

Method: PEO4 is a *BRCA* wildtype and PARP inhibitor-resistant EOC cell line derived from a patient who developed platinum-resistant disease. PEO4 cells were injected intraperitoneally (IP) into SCID-Beige mice, followed by daily IP administration with olaparib, cediranib, triapine, and various double or triple combinations. The abdominal circumference of SCID-Beige mice was measured to determine the ability of drug treatment to impede ascitic distension and to extend the survival time of mice. The toxicity of treatment, as determined by body weight and body condition score, was also monitored throughout the treatment period.

Results: Addition of triapine to the combination of olaparib and cediranib resulted in marked deterrence of peritoneal progression of PEO4 cells and significant prolongation of the survival time of mice. The drug combination with varied triapine to olaparib-cediranib ratios and dosing schedules was tolerable to mice.

Conclusion: The combination of triapine, olaparib, and cediranib is demonstrated to be highly effective against *BRCA* wildtype EOC over the combination of olaparib and cediranib, with minimal or no toxicity in mice. This combination regimen holds promise in the treatment of *BRCA* wildtype and PARP inhibitor-resistant EOC in patients.

160 - Poster Session

Comprehensive molecular profiling of 19 perivascular epithelioid cell tumors (PEComas): Implications for novel therapy

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Objective: We aim to evaluate molecular, genomic, and protein expression patterns in a cohort of malignant perivascular epithelioid cell tumors (PEComas) to identify potential biomarkers for triaging adjuvant treatment options for this group of rare mesenchymal tumors that exhibit wide variations in clinical behavior.

Method: A total of 19 malignant PEComas from all tumor sites were submitted to Caris Life Sciences from 2009 to 2015, of which 8 were from the gynecologic tract. Testing included a combination of sequencing (Sanger or next generation sequencing), protein expression (immunohistochemistry), and/or gene amplification (FISH/CISH).

Results: Of the 19 tumors, the majority (13/19, 68.4%) were from female patients. Table 1 depicts the molecular aberrations of 19 PEComa cases. Of the samples evaluated by sequencing, the most common genetic mutations were *BRCA 1* (50%) and *TP53* (37.5%). Along the STK/AMPK pathway, STK11 mutation was only seen in PEComa of pelvic origin (25%). Loss of PTEN was observed in approximately 40% of tumors. High levels of PD-1 and PD-L1 expression (80% and 40%, respectively) were noted among all PEComas. PD-1 and PD-L1 expressions are absent in *TP53* mutated tumors and predominant in *TP53* wild type cases (100% and 67%, respectively). Increased TOPO2A expression (62.5%) and low levels of PGP expression (20%) were also observed. Loss of RRM1, a DNA synthesis protein known to determine efficacy of gemcitabine, was seen in 81% of cases. MRP1 was expressed in 66.7% of PEComas. Low expression of TUBB3 (25%) was also noted, suggesting potential sensitivity to taxanes. The overall expression of hormone receptors was low: ER, 16.7%; PR, 16.7%; and AR, 11.1%. Pelvic PEComas were more likely to express estrogen receptors compared to nonpelvic PEComas ($P = 0.06$).

Conclusion: Given the rarity of PEComas diagnosis, optimal treatment strategies have not been established. We did not find a significant difference in selected molecular profiles between pelvic and nonpelvic PEComas. For a subset of patients with malignant PEComas, mTOR inhibitors, anthracyclines, and inhibitors of PD-L1 and EGFR may present potential therapeutic options. In pelvic PEComas, hormonal therapy may be considered.

Table 1. Summary of molecular and genomic alterations in PEComa.

Molecular Marker	All PEComas (n = 19)	Pelvic (n = 8)	Non-Pelvic (n = 11)
IHC-PD-1	80.0%	100.0%	66.7%
IHC-MRP1	66.7%	50.0%	75.0%

IHC-TOP2A	62.5%	66.7%	60.0%
IHC-PTEN	61.1%	62.5%	60.0%
IHC-EGFR	60.0%	50.0%	66.7%
IHC-ERCC1	45.5%	50.0%	42.9%
IHC-TS	41.2%	42.9%	40.0%
IHC-PD-L1	40.0%	50.0%	33.3%
IHC-TOP01	37.5%	28.6%	44.4%
ISH-EGFR	33.3%	0.0%	50.0%
IHC-TUBB3	25.0%	25.0%	25.0%
IHC-MGMT	23.5%	12.5%	33.3%
IHC-PGP	20.0%	16.7%	22.2%
IHC-TLE3	20.0%	33.3%	0.0%
IHC-RRM1	18.8%	16.7%	20.0%
IHC-ER	16.7%	37.5%	0.0%
IHC-PR	16.7%	25.0%	10.0%
IHC-AR	11.1%	0.0%	20.0%
IHC-SPARC-Monoclonal	6.7%	0.0%	12.5%
SEQ-BRCA1	50.0%	100.0%	0.0%
SEQ-TP53	37.5%	25.0%	50.0%
SEQ-STK11	14.3%	25.0%	0.0%

161 - Poster Session

Differentiated vulvar intraepithelial neoplasia (dVIN): Establishing the most helpful morphological parameters and evaluating the diagnostic usefulness of cytokeratin 13 and 17

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Objective: Differentiated vulvar intraepithelial neoplasia (dVIN) is a challenging histopathological diagnosis because of its resemblance to vulvar non-neoplastic epithelial disorders (NNED), lichen sclerosus (LS) in particular. In this study the morphological features of dVIN to establish the most specific and reproducible features were quantified. To further add to the objectivity in dVIN diagnosis, combined immunohistochemistry with CK13 and CK17 was assessed.

Method: All the cases of vulvar squamous lesions, that is, high-grade squamous intraepithelial lesions (HSIL), dVIN, NNEDs, and squamous cell carcinoma (SCC), were retrieved from the archives of Erasmus University Medical Center, 2010–2013. Individual morphological features were enumerated from a predetermined checklist, and statistical comparison (dVIN vs LS) was made. Inter-observer agreement between 2 pairs of pathologists for the overall diagnosis and the relevance of each feature for the diagnosis were measured. Immunohistochemistry with p53, CK13, and CK17-MIB1 was carried out on dVIN, LS, and other NNED cases, and expression patterns were compared.

Results: Morphological features of 180 dVIN, 105 LS, and 126 other NNEDs were studied. Nuclear angulation, macronucleoli, disturbed maturation, and architectural changes occurred more frequently in dVIN than in LS ($P < 0.05$). Good inter-observer agreement for the dVIN diagnosis (weighted $\kappa = 0.71$) was found, with macronucleoli, disturbed maturation, and mitotic count $>5/5$ mm having the highest agreement. Expression of p53 did not differ ($P = 0.26$) in dVIN ($n = 24$) and LS ($n = 9$). Cytokeratin 13 loss coupled with CK17 expression was seen in about 70% of cases of dVIN ($n = 32$). LS (and other NNEDs) did not show a similar pattern ($P < 0.01$).

Conclusion: Nuclear angulation, macronucleoli, and disturbed maturation are the most specific and reproducible morphological parameters for dVIN. Paired staining with CK13 and CK17 shows promise as an adjunct to histology for

discriminating dVIN from NNEDs.

162 - Poster Session

Septin-2 as the binding partner of HE4 with a biological role in HE4 secretion

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Objective: Human epididymis protein 4 (HE4) is a small secretory protein that has been identified as a biomarker for epithelial ovarian cancer (EOC) and is also highly expressed in endometrial cancer. Apart from the clinical utility of HE4 as a biomarker, accumulating evidence suggests that it contributes to various biological functions in cancer, such as migration, invasion, interaction with MMPs, and cell proliferation. The present study was conducted to identify proteins that interact with HE4 and to determine their therapeutic potential in the treatment of cancer.

Method: To identify HE4 binding proteins, HE4 and its binding partners were immunoprecipitated from cancer cell lysates with anti-HE4 antibody and subject to mass spectrometry-guided proteomics analysis. The interaction of HE4 and septin-2 proteins was confirmed by coimmunoprecipitation (forward and reverse) using capture antibodies with the respective binding partners being analyzed by Western blot. Stable HE4 expression clones were established by transfection with human HE4 open reading frame DNA plasmid, followed by antibiotic-mediated clonal selection. The depletion of septin-2 was performed by transfection with septin-2 specific small interfering RNAs (siRNA) or antisense oligonucleotides. For the detection of HE4 secretion, cells were treated with forchlorfenuron or transfected with septin-2 siRNAs, and supernatant levels of HE4 were measured by enzyme immunoassay.

Results: Immunoprecipitation with anti-HE4 antibody and subsequent proteomics analysis identified septin-2, a GTP-binding cytoskeletal protein, as an HE4 binding partner (12.5-fold increase vs IgG-treated control). Our preliminary data indicate that HE4 overexpression clones, derived from human EOC cell lines SKOV-3 and OVCAR-8, expressed higher levels of septin-2 than their empty-vector transfected counterparts. When the same cell lines were tested, septin-2 protein was found to coimmunoprecipitate with HE4, implicating septin-2 as a novel HE4 binding partner. HE4/septin-2 association was confirmed with reverse coimmunoprecipitation. The knockdown of septin-2 potently inhibited proliferation of EOC cells. We also found that the suppression of septin-2 by siRNA or its inhibition with forchlorfenuron, an antagonist of septin dynamics, markedly reduces the secretion of HE4.

Conclusion: Our study suggests septin-2 as a novel HE4 interacting protein. The disruption of septin-2 function inhibited HE4 secretion.

163 - Poster Session

Polycomb fusion proteins in endometrial stromal sarcomas

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Objective: Endometrial stromal sarcomas (ESS) are characterized by frequent chromosomal translocations involving genes that encode Polycomb group proteins (PcG). PcG proteins occur in 2 main chromatin remodeling complexes, the Polycomb Repressive Complex 1 and 2 (PRC1 and PRC2). Understanding the pathogenic role of these genetic alterations in relevant cellular and animal models will improve our understanding of this tumor with important clinical implications.

Method: Primary human endometrial stromal cells (hEnSC) were derived from hysterectomy specimens and genetically manipulated to express Polycomb fusion proteins generated from previously characterized chromosomal translocations identified in ESS. Cells harboring these alterations were characterized using genome-wide technologies (RNA-sequencing and ChIP-sequencing) along with proteomic approaches to identify potential new chromatin dysfunctions. In addition, primary patient tumor samples were analyzed following a similar approach to confirm the findings in the genetically modified cell lines.

Results: Expression of a prototypical example of an ESS-associated Polycomb fusion protein, JAZF1-SUZ12, in hEnSC resulted in the downregulation of the endogenous SUZ12 protein levels, which is central for the PRC2-dependent methylation of the lysine 27 on histone H3. In vitro and cell culture data demonstrate that JAZF1-SUZ12 is incorporated in the PRC2 without

effect upon the catalytic activity of the complex toward histone H3. This is in agreement with results obtained from 7 primary patient low-grade ESS tumor samples that were positive for trimethyl-lysine 27 histone H3 immunohistochemistry. Preliminary genome-wide analyses suggest specific changes in the transcriptome of hEnSC expressing the JAZF1-SUZ12 fusion protein compared to controls.

Conclusion: hEnSC is a relevant cellular model to recapitulate ESS pathogenesis by expressing fusion proteins associated to common chromosomal translocation found in these tumors. JAZF1-SUZ12, as a prototypical product of these genetic lesions, can induce downregulation of the endogenous SUZ12 levels in hEnSC without affecting the PRC2 catalytic function. Further studies using this model will help clarify the role that Polycomb fusion proteins may have in the malignant transformation that leads to ESS formation.

164 - Poster Session

MEK inhibition in clear cell ovarian cancer with a novel drug candidate

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Objective: To assess the therapeutic potential of MEK inhibition with a novel drug candidate in the treatment of clear cell ovarian cancer.

Method: CCOC cell lines (*OVMANA*, *ES-2*, *OVAS*, *OVTOKO* and *HCH-1*) were cultured, and their cell viability was assessed after exposure to various concentrations of MTTL1, by both MTS and SRB assays. Cell proliferation was determined by BrdU uptake, and apoptosis was determined by AnnexinV staining. Cell-free inhibition assays and Western blot for MAPK phosphorylation were used to confirm MEK inhibition of MTTL1. In vivo drug efficacy was determined by measuring growth of *OVMANA* xenografts on immunodeficient mice.

Results: MTTL1 performs in vitro and in vivo as a selective MEK1/2 inhibitor that reduces the viability of multiple CCOC cell lines and works in a dose-dependent manner. It has an impact on cell viability by both inhibiting proliferation and inducing apoptosis in tumor cells. When tested in vivo, MTTL1 was able to significantly delay the growth of xenografted clear cell ovarian tumors ($P < 0.01$) and was well tolerated by mice. MTTL1 was also tested in combination with chemotherapy and was found to inhibit chemotherapy-induced prosurvival signaling.

Conclusion: MTTL1 is a novel MEK inhibitor that shows preclinical efficacy against clear cell ovarian cancer. It also holds promise as a combinatorial treatment with chemotherapy.

165 - Poster Session

Correlation of chemotherapy response score to residual tumor at interval debulking surgery in ovarian cancer

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Objective: Chemotherapy response score (CRS) has been shown to correlate to progression-free survival (PFS) with high reproducibility. The aim of the present study was to investigate the correlation of CRS to residual tumor after interval debulking surgery (IDS) as well as to survival data in ovarian cancer.

Method: CRS was retrospectively determined on pathology slides of all pathologically evaluable patients with epithelial ovarian cancer who had IDS between July 2009 and December 2014. CRS 1 was given to slides where tumor was present and infiltrated by inflammatory cells. CRS 2 was assigned when both tumor and regressive chemotherapy changes were present. In CRS 3, scant tumor deposits were seen amid extensive chemotherapy induced regressive changes. Patient data including age, stage, grade, histology, CA-125 levels, residual tumor after IDS, and survival information were also collected. Data were compared among the three CRS groups.

Results: Ovarian tissue pathology slides of 132 patients were reviewed. A total of 49 patients had CRS 1; 65 had CRS 2; and 18 had CRS 3. Age, stage, and residual tumor at the end of IDS were not different across CRS groups. The CRS 3 group showed the most significant CA-125 decrease after NACT (97% decrease, $P = 0.016$). PFS but not OS was significantly longer for patients with CRS 3 (median PFS was 7.5, 12, and 17 months for patients with CRS 1, 2, and 3 respectively, $P = 0.012$).

Conclusion: No correlation was found between rate of optimal debulking and CRS score. Patients with CRS 3 have the longest PFS and the highest CA-125 drop after NACT. These two parameters can be used to assess response to NACT before determining whether to continue with IDS.

166 - Poster Session

Factors associated with completion and physician and patient attitudes towards salpingectomy at the time of cesarean delivery

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Objective: We have demonstrated that salpingectomy (SPG) in lieu of standard tubal ligation (TL) during cesarean delivery (CD) is feasible, safe, and can successfully be performed in two-thirds of patients. We sought to evaluate factors associated with completion of bilateral SPG and to compare physician and patient attitudes toward SPG and TL at time of CD.

Method: We performed a planned secondary analysis of SCORE, an RCT (NCT02374827) of SPG, versus TL in women desiring permanent sterilization at CD. During the trial, a survey was administered to the primary surgeon after each case about their attitudes toward the procedure performed. Subjects were also assessed postpartum (PP) about their concern about developing ovarian cancer (0–10, 0 = no concern). We compared physician level (e.g., fellow, attending) and patient characteristics between the successfully completed (bilateral) SPG and unsuccessful SPG (completed alternate sterilization) groups. We also compared physician attitudes (by intent-to-treat) and patient attitudes (by actual procedure performed) between SPGs and TLs. Groups were compared using the Student t, Wilcoxon rank-sum, χ^2 , and Fisher exact tests as appropriate, evaluated at $\alpha = 0.05$.

Results: Eighty subjects were randomized to TL ($n = 40$) or SPG ($n = 40$) with 27 bilateral SPGs completed (67.5%). While there was no difference in SPG completion based on physician level, patients in whom bilateral SPG was not completed had higher BMI (46.2 ± 12.1 vs. 36.2 ± 7.9 kg/m², $P = 0.012$) and longer operative time from skin incision to start of sterilization procedure (47.6 ± 23.2 vs. 29.2 ± 14.7 minutes, $P = 0.009$). There was no difference in the number of abdominopelvic surgeries/CDs or type of skin incision between groups. When comparing physician attitudes, providers responded that SPG added difficulty and the procedure took longer than expected, and they would not perform SPGs at CD in general practice (Table 1). However, at 6 weeks PP, subjects who had SPGs reported less concern than those with TLs about developing ovarian cancer (0.8 ± 1.7 vs. 2.8 ± 3.0 , $P = 0.005$).

Conclusion: Patients are more reassured about ovarian cancer risk after SPG than after TL. While SPG is feasible and safe, providers are less satisfied performing SPG versus TL. Higher patient BMI and longer operative times were noted in patients in which SPG was not successfully completed.

Table 1. A comparison of physician satisfaction between standard tubal ligation and salpingectomy at the time of cesarean delivery.

	Tubal ligation ($n = 40$)	Salpingectomy ($n = 40$)	P-value
Satisfaction with tubal segment exposure	6.4 ± 1.3	5.9 ± 1.6	0.046
Satisfied	37 (94.9)	29 (85.3)	0.24
Dissatisfied	2 (5.1)	5 (14.7)	0.24
Satisfaction with feasibility of procedure	6.5 ± 1.2	4.8 ± 1.7	<0.001
Satisfied	36 (92.3)	21 (61.8)	0.002
Neutral	1 (2.6)	3 (8.8)	0.33
Dissatisfied	2 (5.1)	10 (29.4)	0.005
Satisfaction with safety of procedure	6.6 ± 1.0	4.5 ± 1.8	<0.001
Satisfied	38 (97.4)	18 (52.9)	<0.001
Neutral	0 (0.0)	7 (20.6)	0.003
Dissatisfied	1 (2.6)	9 (26.5)	0.005
Did procedure require adhesiolysis	7 (18.0)	14 (38.9)	0.044
Did procedure add difficulty to the case	3 (7.7)	25 (71.4)	<0.001
Did procedure take more time than expected	3 (7.7)	20 (57.1)	<0.001
Would you perform this procedure again	39 (100.0)	19 (54.3)	<0.001

Would you perform this procedure as part of general practice	39 (100.0)	12 (35.3)	<0.001
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* Data presented as n (%) or mean \pm standard deviation on Likert scale (1-7, 7= very satisfied)

167 - Poster Session

Analysis of adjuvant therapy for recurrent medium risk factors in young patients with locally advanced cervical cancer after neoadjuvant chemotherapy followed by radical surgery

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Objective: This paper summarizes the clinical and pathological data of patients younger than 45 years with stage IB2 and IIA2 local advanced cervical cancer (LACC) in West China Second Hospital from January 2008 to October 2016, and reports the adjuvant treatment for medium risk factors after neoadjuvant chemotherapy (NACT) followed by radical surgery.

Method: Young patients with stage IB2 and IIA2 LACC underwent 1-3 neoadjuvant chemotherapy followed by III type radical surgery (one or both ovaries retained for squamous cell carcinoma). The postoperative pathological examination showed recurrent medium risk factors (interstitial $>1/2$ or lymphovascular invasion) found in patients with a total of 103 cases. We report their survival outcomes after postoperative treatment.

Results: All the tumors reduced after NACT, including 11 cases of complete remission, accounting for 10.7% (11/103). The clinical response was (94.2%) (97/103). Postoperative pathological examination showed 8 cases for complete remission and 5 cases for slight invasion, all of them without recurrence except 2 cases lost to follow-up. The follow-up time ranged from 7 months to 9 years; 82 cases underwent postoperative chemotherapy and 2 of them relapsed, while 21 cases chose periodic review and 1 of them recurred (pretherapeutic focus was 8+ cm). The ovarian function of 68 patients with squamous cell carcinoma was normal after postoperative chemotherapy.

Conclusion: After full communication and informed consent, patients with stage IB2 and IIA2 who had medium risk factors may choose chemotherapy or periodic review for decreasing the possibility of radiotherapy or chemoradiotherapy after operation to avoid radiotherapeutic adverse reaction and protect their ovarian and vaginal function.

168 - Poster Session

Primary debulking surgery versus neoadjuvant chemotherapy in elderly patients with epithelial ovarian cancer

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Objective: Neoadjuvant chemotherapy (NAC) is increasingly utilized as initial therapy in women with epithelial ovarian cancer (EOC), but the benefits in an elderly population have not been well defined. This analysis evaluates the impact of NAC compared to primary debulking surgery (PDS) among elderly women with EOC.

Method: Women older than 70 years who underwent surgery for stage II–IV EOC from 2006 to 2013 were identified from the New York State Cancer Registry and the Statewide Planning and Research Cooperative System. Demographic factors, comorbidity burden (Charlson comorbidity index, CCI), and oncologic and surgical factors were compared for women treated with PDS versus NAC. The effect of NAC on 5-year overall survival and EOC-specific survival was examined using Cox proportional hazards models.

Results: A total of 1,152 women with ovarian cancer were included in this analysis. Overall, 14.2% of patients received NAC, but the percentage of women receiving NAC during the study period increased from 8.3% in 2006 to 22.5% in 2013 ($P < 0.01$). Race, marital status, and insurance were similar for women treated with NAC compared to PDS. Factors associated with receipt of NAC included advanced-stage disease, serous histology, hospital volume, and surgeon volume and having a gynecologic oncologist as a primary surgeon ($P < 0.01$). No difference in CCI was observed between groups. The extent of surgery was similar whether patients underwent PDS or NAC. After adjustment for patient, hospital, and surgeon characteristics, NAC did not have a significant effect on overall survival ($P = 0.47$) or EOC-specific survival ($P = 0.24$). However, the subgroup of elderly women without comorbid conditions ($CCI = 0$) had 1.67 (1.19, 2.34, $P < 0.01$) times the odds of death when initially treated with NAC compared to PDS. See Table 1.

Conclusion: Among elderly patients with EOC, the impact of NAC on survival differs depending on coexisting medical comorbid conditions. For elderly patients without concurrent medical comorbid conditions, the initial surgical approach should be tailored to disease factors rather than dictated by age. For women older than 70 years with EOC and medical comorbid conditions, there is no survival advantage to PDS.

Table 1. 5 Year Hazards of Death for Women with EOC over 70 years of age (HR, 95%CI).

	Neoadjuvant Therapy when CCI=0	Neoadjuvant Therapy when CCI=1	Neoadjuvant Therapy when CCI=2+
Risk of ovarian cancer specific death	1.67 (1.19, 2.34)*	0.91 (0.55, 1.49)	0.61 (0.33, 1.11)

* $P < 0.05$

169 - Poster Session

A nationwide analysis of salpingectomy rates for sterilization following the 2015 American College of Obstetricians and Gynecologists committee opinion, "Salpingectomy for ovarian cancer prevention"

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Objective: Using a nationwide database, the study objective was to identify the rate of salpingectomy for sterilization before and after the January 2015 American College of Obstetricians and Gynecologists (ACOG) Committee Opinion titled "Salpingectomy for Ovarian Cancer Prevention."

Method: Utilizing the Vizient database (representing primarily academic medical centers, formerly named the University HealthSystem Consortium), female patients between 18 and 50 years old who underwent a sterilization procedure between January 2013 and January 2017 were identified. Patients were included if their medical record included an ICD-9/10 diagnosis code for sterilization (V25.2/Z30.2). Subjects were identified as undergoing a salpingectomy based on ICD-9/10 procedure codes or CPT codes. Change over time in proportion of salpingectomy for sterilization was analyzed using the Cochran-Armitage trend test.

Results: The database identified 211,312 patients across 303 hospitals who underwent a sterilization procedure between January 1, 2013, and January 31, 2017. Of these, 180,665 patients were identified among 160 hospitals that provided data over the entire study period. The top 2 primary diagnoses associated with a sterilization procedure were 654.21/034.21x (previous cesarean delivery NOS/maternal care for scar from previous cesarean delivery) and V25.2/Z30.2 (encounter for sterilization) accounting for 28% and 24% of admissions, respectively. The sterilization procedures were evenly distributed over the study period (monthly mean 2%, SD 0.1%). Overall, 25,882 (14.3%) women in the study subset underwent a salpingectomy for an indication of sterilization. The proportion of salpingectomies was $\leq 1\%$ in 2013 but slowly rose until October 2015 when the proportion climbed to 20%, rising to nearly 60% by January 2017 (Figure 1). This increase over time was statistically significant ($P < 0.0001$).

Conclusion: Following the release of the ACOG Committee Opinion, "Salpingectomy for Ovarian Cancer Prevention," there was an increase in the frequency of salpingectomies done in the setting of sterilization among women seen in predominately academic medical centers.

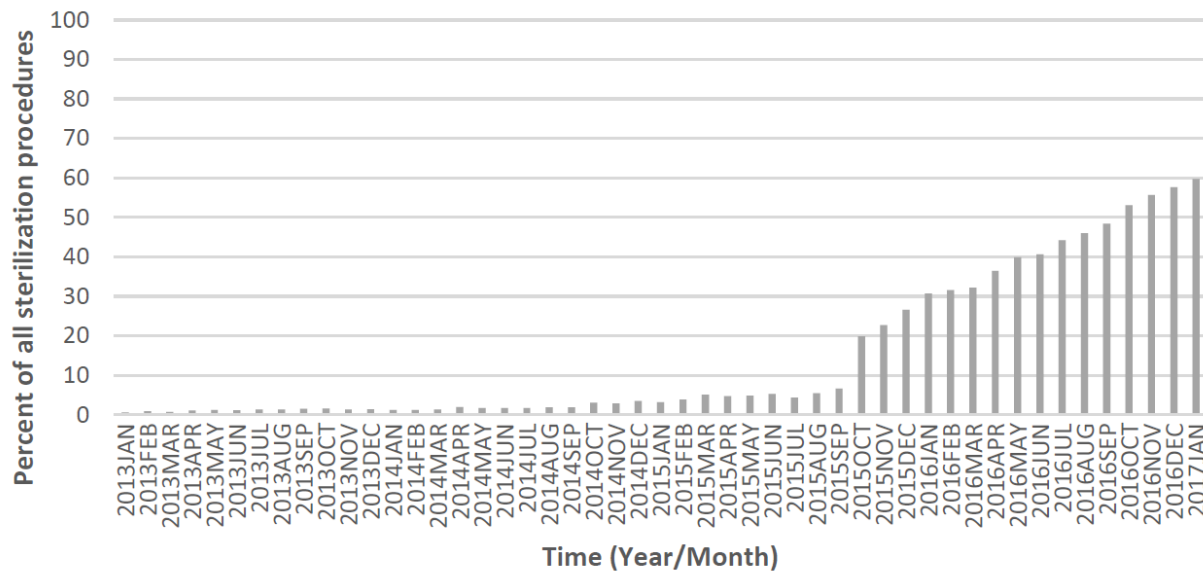


Fig. 1. Percent Salpingectomy for Sterilization between 2013-2017.

170 - Poster Session

Trends in performance of lymphadenectomy for women with early-stage epithelial ovarian cancer between 1988 and 2013

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Objective: To examine the proportion of adequate regional lymphadenectomy during surgical treatment for women with early-stage epithelial ovarian cancer.

Method: This is a retrospective observational study examining a population-based tumor registry, the Surveillance, Epidemiology, End Results Program, for cases of stage I–II epithelial ovarian cancer diagnosed between 1988 and 2013 (serous, $n = 7,838$; clear cell, $n = 7,239$; mucinous, $n = 4,247$; and endometrioid, $n = 3,251$). A time-trend analysis of the proportion of adequate regional lymphadenectomy (≥ 8 sampled lymph nodes per the GOG criteria) and survival estimates associated with adequate regional lymphadenectomy were performed.

Results: There were significant increases in the proportion of women who underwent regional lymphadenectomy for all the histologic types from 1988 until the mid to late 2000s: serous, 26.2% to 68.9% (1988–2009); clear cell, 33.7% to 77.3% (1988–2008); mucinous, 20.4% to 71.6% (1988–2005); and endometrioid, 48.6% to 81.8% (1988–2005) (all, $P < 0.05$). However, there was no significant change thereafter for any of the histology types (all, $P > 0.05$). Across the 4 histologic types, the proportion of adequate lymphadenectomy significantly increased between 1988 and 2008 (6.3% to 50.4%, $P < 0.001$), and then there was no change between 2008 and 2013 (50.4% to 51.5%, $P = 0.58$). Cause-specific survival was significantly higher among women who had adequate lymphadenectomy compared to those who did not after propensity score matching (5-year rate, 91.0% vs 83.7%, adjusted hazard ratio = 0.60, 95% CI 0.55–0.66, $P < 0.001$). See Figure 1.

Conclusion: Our analysis found that the quality of lymphadenectomy during surgical treatment for stage I–II epithelial ovarian cancer significantly improved until the late 2000s but has not changed since. Adequate lymphadenectomy was associated with improved survival.

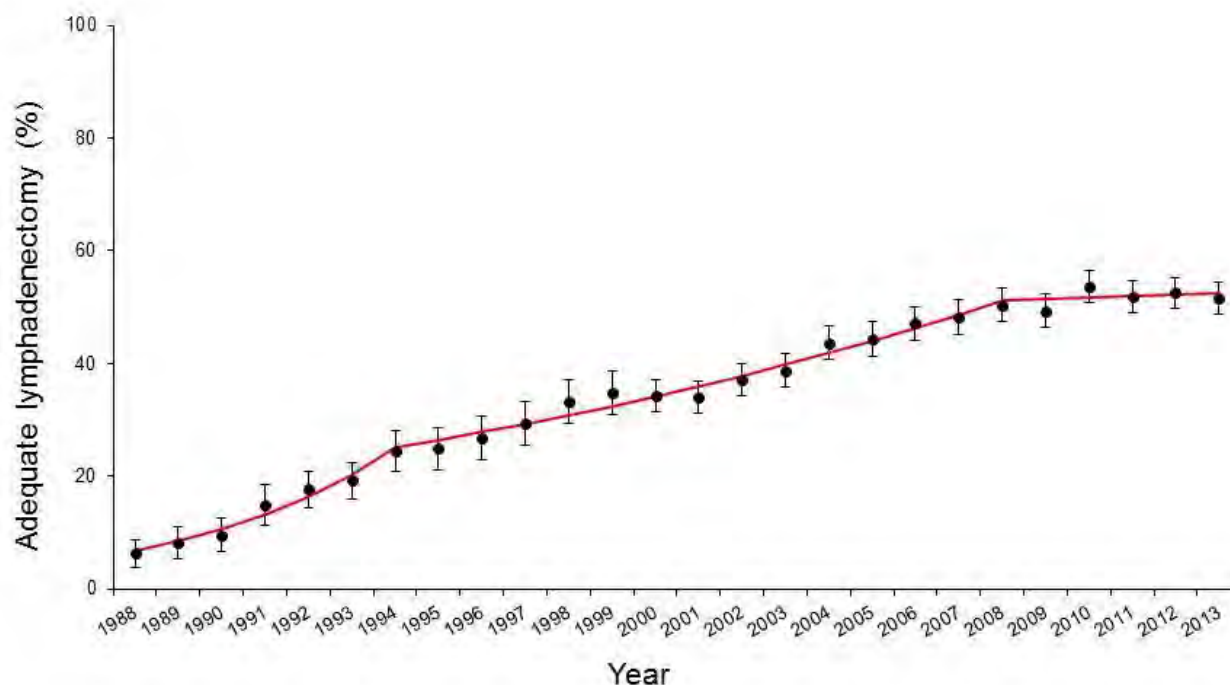


Fig. 1.

171 - Poster Session

Postoperative complication rates are improved with sentinel lymph node biopsy during laparoscopic hysterectomy for women with endometrial cancer

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Objective: The role of routine lymphadenectomy (LND) in the surgical management of early-stage endometrial cancer is controversial due to the low rate of lymph node metastasis and the potential morbidity associated with LND. There is a growing body of literature regarding the feasibility and diagnostic accuracy of sentinel lymph node biopsy (SLN) in lieu of LND. We sought to evaluate the association between type of lymph node assessment and postoperative complications (POC) in patients undergoing laparoscopic hysterectomy (LH) for endometrial cancer.

Method: Patients who underwent LH for endometrial cancer from 2010 to 2015 were identified from the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) database by ICD-9 and CPT codes. Comparative analyses were performed and stratified by type of lymph node assessment to evaluate the rates of POC.

Results: We identified 11,878 patients who underwent LH for endometrial cancer: 4,912 (41.4%) did not undergo lymph node assessment, 6,703 (56.4%) underwent LND, and 263 (2.2%) had SLN. Rates of lymph node assessment remained stable over time. When comparing patients who underwent LND and who did not have LND, LND patients had longer operative times (median 174 vs 138 minutes, $P < 0.0001$). When comparing patients after LND to no LND, there were more conversions to laparotomy with LND (1.5% vs 0.3%, $P < 0.0001$) and fewer same-day discharges (7.7% vs 10.0%, $P < 0.0001$). There were higher rates of POC with LND (8.2% vs 7.0%, $P = 0.04$) and hospital readmissions (1.8% vs 1.1%, $P = 0.005$). There were no differences in reoperations. See Table 1. Patients who had SLN and who did not have any lymph node assessment were evaluated. SLN patients still had longer operative times (median 170 vs 138 minutes, $P < 0.0001$) and higher rates of conversions (3.0% vs 0.3%, $P < 0.0001$). There were no differences in rates of same-day discharge, POC, hospital readmissions or reoperations.

Conclusion: Patients with endometrial cancer who underwent LND with LH had longer hospital stays and higher rates of POC when compared to patients who did not have LND. There was no observed increase in hospital stays or POC between patients who underwent SLN and patients who did not undergo lymph node assessment. SLN allows for lymph node evaluation in patients with EC while reducing hospital admissions and rates of POC.

Table 1. Perioperative outcomes by type of lymph node assessment.

Perioperative Outcome	Routine Lymphadenectomy (n = 6,703)	No Lymph Node Assessment (n = 4,912)	P Value	Sentinel Lymph Node Biopsy (n = 263)	No Lymph Node Assessment (n = 4,912)	P Value
Operative time, median \pm SD (minutes)	174.0 \pm 74.0	138.0 \pm 64.6	< 0.0001	170.0 \pm 66.0	138.0 \pm 64.6	< 0.0001
Anesthesia time, median \pm SD (minutes)	271.0 \pm 101.2	211.0 \pm 89.6	< 0.0001	258.5 \pm 69.5	211.0 \pm 89.6	0.4
Conversions, n (%)	103 (1.5%)	15 (0.3%)	< 0.0001	8 (3.0%)	15 (0.3%)	< 0.0001
Same-day discharge n (%)	519 (7.7%)	492 (10.0%)	< 0.0001	30 (11.4%)	492 (10.0%)	0.5
Any postoperative complication, n (%)	548 (8.2%)	346 (7.0%)	0.03	15 (5.7%)	346 (7.0%)	0.5
Hospital readmission, n (%)	121 (1.8%)	56 (1.1%)	0.005	4 (1.5%)	56 (1.1%)	0.8
Reoperation, n (%)	65 (1.0%)	56 (1.1%)	0.4	2 (0.8%)	56 (1.1%)	0.6

172 - Poster Session

Trends in radical hysterectomy for early-stage cervical cancer: A National Cancer Data Base study

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Objective: Recent studies have indicated that more conservative treatment, such as extrafascial hysterectomy or cold knife cone (CKC), may be appropriate for patients with low-risk, early-stage cancer in lieu of radical hysterectomy. We sought to examine whether these studies have changed patterns of treatment for early-stage cervical cancer in the United States over time or by hospital type and region.

Method: The National Cancer Database (NCDB) was used to compare rates of radical hysterectomies performed at participating institutions from 2004 to 2014 for women with stage I cervical cancer. Regions were geographically grouped into five areas: New England/Mid-Atlantic, South Atlantic, Eastern North Central/Eastern South Central, Western North Central/Western South Central, and Mountain/Pacific. Types of facilities included Community Cancer Centers, Comprehensive Community Cancer Centers, Academic/Research Centers, and Integrated Network Cancer Centers.

Results: A total of 14,310 radical hysterectomies for stage I cervical cancer were performed by NCDB-reporting institutions during the study period; both facility type and region were available for 8,927 of them. The number of radical hysterectomies performed per year ranged from 1,285 in 2004 to 1,187 in 2014 (7.6% decrease), a trend that was statistically significant ($P < 0.001$). Overall, 31% of patients with stage I disease underwent radical hysterectomy, and 69% underwent other treatment (including extrafascial hysterectomy, CKC, and radiation therapy). The rate of radical hysterectomy for stage I cancer was significantly higher in the Mountain/Pacific group compared to other regions (33% vs 28%–29%, $\chi^2 P < 0.001$). There was a lower rate of radical hysterectomy in Community Cancer Programs compared to other facility types (10% vs 16%–18%, $\chi^2 P < 0.001$).

Conclusion: Our study demonstrates that the rate of radical hysterectomy for stage I cervical cancer decreased from 2004 to 2014 by almost 8%. This may be a reflection of new evidence and changing attitudes toward the management of early-stage cervical cancer and warrants further exploration.

173 - Poster Session

Pelvic exenteration for cervical cancer: An endangered skill?

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Objective: Pelvic exenteration (PE) is a radical surgery for cervical cancer that is uncommonly performed and confers substantial risk of morbidity. We sought to identify rates over time and short- and long-term mortality of PE.

Method: The National Cancer Data Base (NCDB) was used to determine numbers of PEs performed for cervical cancer at participating institutions from 2004 to 2014. The NCDB represents an estimated 70% of cancer diagnoses per year. Procedures included in the PE variable were those coded as total pelvic exenteration, anterior or posterior pelvic exenteration, total exenteration, and extended exenteration. Yearly rates of PE, 30- and 90-day mortality and overall survival, facility type, cancer stage, and patient age were evaluated. Types of facilities included Community Cancer Centers, Comprehensive Community Cancer Centers, Academic/Research Centers, and Integrated Network Cancer Centers.

Results: A total of 397 PEs were identified. The total number of PEs performed per year ranged from 29 to 51, with no significant change in rate over the study period (Kendall's tau b, $P > 0.1$). Of patients who underwent PE, 56% had previously undergone radiation, 59% had undergone prior chemotherapy, and 43% had undergone both chemotherapy and radiation. Fifty percent of PEs were performed at academic medical centers. Overall 30- and 90-day mortality was 2.82% and 7.43%, respectively, which did not differ by hospital type in univariate analysis (χ^2 , $P = 0.61$). Median overall noncancer-specific survival was 42.5 months. There was no statistically significant difference in overall survival based on hospital type when adjusted for age and stage at diagnosis in multivariate analysis.

Conclusion: Our data show that PE is a rare procedure and that the frequency of its performance has not changed over time. Ninety-day mortality was high at over 7%. Thirty-day mortality, 90-day mortality, and overall survival were equivalent between different hospital types. Given that evidence has shown that outcomes of complex surgical procedures are better at high-volume centers, consideration should be given to consolidation of PE at academic medical centers. Furthermore, this would have the benefit of providing more training opportunities to gynecologic oncology fellows.

174 - Poster Session

A contemporary evaluation of the current state of sentinel lymph node (SLN) dissection for vulvar cancer in the United States

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Objective: To describe the application of sentinel lymph node dissections in patients with vulvar cancer and to determine individual hospital surgical volume.

Method: All unique patients with ICD-9 or -10 codes for diagnosis of vulvar cancer and procedure code for inguinal lymph node dissection were selected from October 2013 to August 2017 in the Vizient database. Patients with vulvar cancer who underwent inguinal node dissection who received radionuclide dye (technetium sulfur colloid or tc-99m tilmanocept) were identified as having had sentinel lymph node dissections (SLNDs).

Results: A total of 854 patients with vulvar cancer underwent a groin lymph node dissection; 279, distributed among 60 hospitals, had a SLND. Of patients who received a SLND, 90% were white, 4% black, 1% Asian, and 5% unknown race. Age distribution was 36% <65 years, 42% 65–79 years, and 22% >79 years. Twenty-five patients received tilmanocept, and 254 patients received technetium sulfur colloid. Sixty hospitals reported having performed an SLND on at least 1 patient during the 46-month study period; the range was 1 to 25. The mean number of SLNDs was 4.7 patients per hospital or 1.2 patients per hospital per year. Of all SLNDs, 23% were performed at 3 hospitals, and 45% of hospitals performed SLNDs on 2 or fewer patients during the study period (0.5 procedures per year). Ten (17%) hospitals performed SLNDs on more than 2 patients per year, on average. More than half the patients who had SLNDs were treated in 11 (18%) hospitals. There were 114 patients (41%) who had intraoperative pathologic consultation and 38 patients (14%) who had final pathologic specimens with positive inguinal metastases.

Conclusion: Inguinal SLNDs for patients with vulvar cancer are performed infrequently, and most are performed in a few hospitals. It is widely known that SLNDs result in decreased postoperative morbidity without compromising outcomes. The National Comprehensive Cancer Network recommends that SLNDs be performed by high-volume surgeons. Further study should investigate differential outcomes between high- and low-volume settings. Consideration should be given to concentration of these procedures in centers of excellence.

175 - Poster Session

Oncologic outcome of stage IIA1 cervical cancer: Is surgical treatment justified?

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Objective: Data on the outcome of stage IIA cervical cancer are limited, as these tumors account for a small percentage of early tumors. National Comprehensive Cancer Network guidelines suggest consideration of surgical management for small tumors with vaginal involvement. Since stratification of the risk of postoperative radiation is essential to select patients for surgical management, our objective in this study was to assess the risk of adjuvant radiotherapy in stage IIA cervical cancer and to investigate its associated features.

Methods: This was a retrospective cohort study comparing surgically treated cervical cancer patients with stage IB1 and stage IIA disease. Women treated between 2000 and 2015 in 10 Israeli medical centers were included in the study. Data were abstracted from the medical records. Patient and disease features were compared between stages. The relative risk (Fisher exact test) of receiving postoperative radiation was calculated and compared for each risk factor. A general linear model (GLM) was used for multivariate analysis, after confirmation of no collinearity among the risk factors using the variation inflation factor (VI F = 1.04–1.48).

Results: A total of 300 patients were included, of whom 28 patients had stage IIA disease. Patient and disease characteristics were comparable for stage IB1 and stage IIA1 disease, although the rate of close or involved surgical margins was higher for patients with vaginal involvement (23% vs 9.3%, $P = 0.02$). Patients were more likely to receive radiation after surgery for stage IIA disease (75% vs 52%, RR = 1.437, 95% CI 1.13–1.83, $P = 0.027$). The performance of a preoperative MRI was associated with a decreased risk for adjuvant radiotherapy (RR = 1.90, 0.96–3.74, $P = 0.03$). Stage was not an independent predictor of radiation on multivariate general linear modeling, whereas tumor diameter, LVI, and lymph node metastases were. See Table 1.

Conclusion: Cervical cancer patients with vaginal involvement are highly likely (75%) to require postoperative radiation, although this may be mediated by other pathological risk factors. These patients need to be considered for primary chemoradiation, and careful selection should be employed before surgical management may be offered.

Table 1. Relative risk of receiving postoperative radiation.

Parameter	Relative Risk	P Value
Stage IIA (ref, IB1)	1.44 (1.13–1.83)	0.03
MRI omitted (ref, performed)	1.90 (0.96–3.74)	0.03
PET omitted (ref, performed)	1.058 (0.86–1.3)	0.64
Lymph node involvement (ref, none)	2.28 (1.96–2.66)	<0.001
Tumor diameter (ref, <20 mm)		
20–<40	1.36 (0.99–1.86)	0.06
≥40	1.96 (1.44–2.68)	<0.001
Depth of invasion (ref, <5 mm)		
5–9	0.78 (0.48–1.27)	0.33
10–19	1.28 (0.9–1.83)	0.18
≥20	1.95 (1.39–2.76)	<0.001
LVSI (ref, none)	2.28 (1.87–2.77)	<0.001
Parametrial involvement (ref, none)	1.81 (1.48–2.20)	<0.001
Surgical margins close or involved	1.43 (1.12–1.83)	0.03

176 - Poster Session

Tozzi classification of diaphragmatic surgery in patients with stage IIIC-IV ovarian cancer based on surgical complexity and morbidity

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Objective: To introduce a systematic classification of diaphragmatic surgery in patients with ovarian cancer based on the disease spread, the complexity of the procedure, and the complication rate.

Method: For all consecutive patients who underwent diaphragmatic surgery during visceral-peritoneal debulking (VPD) in the period 2009–2017, we extracted the following information: initial surgical finding, extent of liver mobilization, type of procedure performed, and intra- and postoperative specific complication rate. Combining these features, we aimed to define the surgical procedures necessary to tackle different presentation of diaphragmatic disease.

Results: A total of 170 patients were included in this study; 110 (64.7%) had a peritonectomy, while 60 (35.3%) had a full thickness resection with pleurectomy. We identified 3 types of procedures in relation to increasing tumor spread, surgical complexity, and morbidity rate. Type 1 treated 28 out of 170 patients (16.5%) who only had anterior diaphragm disease, needed no liver mobilization, included peritonectomy, and had no morbidity recorded. Type 2 pertained to 105 out of 170 patients (61.7%) who had anterior and posterior disease, needed partial and sometimes full liver mobilization, had a mix of peritonectomy and full thickness resection, and experienced 10% specific morbidity. Type 3 included 37 out of 170 patients (21.7%) who needed full mobilization of the liver, always had full thickness resection, and suffered 30% specific morbidity.

Conclusion: Diaphragmatic surgery can be effectively classified in 3 types based on initial findings, surgical complexity, and morbidity rate. A widespread adoption of this classification can facilitate standardization of the surgery and comparison of data and accurately define the level of expertise required. The latter can in turn assist patient referral to centers where appropriate expertise is available. Finally, this classification can be a benchmark to establish the training required to treat diaphragmatic disease.

177 - Poster Session

Outcomes of secondary cytoreductive surgery for patients with recurrent epithelial ovarian cancer

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Objective: The primary objectives of this study were to describe the clinical characteristics of patients with platinum-sensitive recurrent epithelial ovarian cancer (ROC) who underwent secondary cytoreductive surgery (SCS) versus second-line chemotherapy (CT) and to identify factors associated with overall survival of patients treated with SCS versus CT.

Method: This is a multiinstitutional study of 626 patients with ROC diagnosed between January 1, 2004, and December 31, 2011, from 6 National Cancer Institute-designated cancer centers. We used multivariable logistic regression models including age, BMI, stage, histology, grade, comorbidity index, income, institution, year of treatment, interval to recurrence, and extent of residual disease at primary surgery to examine factors associated with use of SCS versus CT. Survival outcome analyses were conducted in a propensity-score matched sample to balance observed covariates that might confound the effect of treatment approach on survival.

Results: Among 626 women with ROC, 144 (23%) received SCS. The proportion of ROC patients receiving SCS increased from 23% in 2004 to 32% in 2007 and then decreased to 13% by 2012. In adjusted analyses, patients who received SCS were younger ($P = 0.001$), had earlier stage disease at diagnosis ($P = 0.002$), and had longer intervals to disease recurrence ($P < 0.001$), compared with patients receiving only CT. Among women undergoing SCS, 116 (81%) achieved optimal secondary cytoreduction. Compared with those treated with CT alone, patients who underwent SCS were more likely to experience infections (1.4% vs 0.8%), ICU admissions (2.8% vs 0.2%), and thromboembolic events (1.4% vs 0.2%). In a propensity score-matched cohort of 236 patients followed for a median of 25 months, the median overall survival after initiation of secondary treatment was 59 months among patients undergoing SCS and 32 months among patients receiving CT alone (Figure 1; $P < 0.001$).

Conclusion: Patients with ROC who underwent SCS had favorable characteristics for surgical intervention and were likely to have minimal residual disease at the conclusion of SCS. These patients had superior median overall survival compared to patients who were treated with CT alone, although unmeasured confounders may partially explain this observed difference.

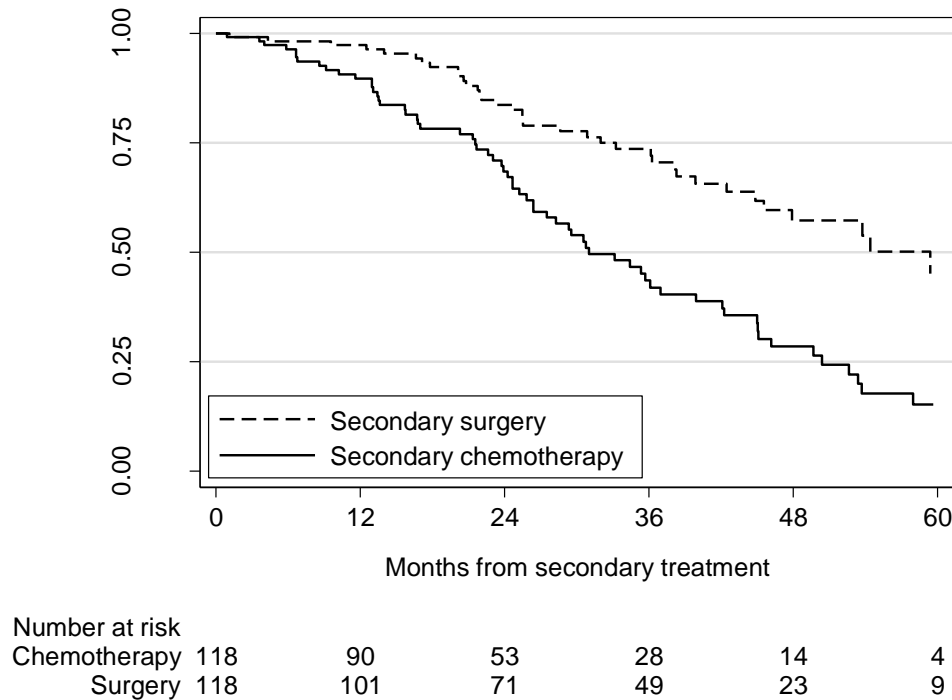


Fig. 1. Propensity score matched sample: overall survival by treatment for recurrence.

178 - Poster Session

Factors that predict optimal debulking at interval cytoreductive surgery after neoadjuvant chemotherapy in epithelial ovarian cancer

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Objective: Optimal debulking to no gross residual disease has been shown to provide significantly improved survival in patients undergoing both primary and interval cytoreductive surgery (CRS) for epithelial ovarian cancer (EOC). However, factors predicting resectability in the neoadjuvant chemotherapy (NACT) population are not well defined. We sought to evaluate variables that may help predict whether optimal debulking is achieved at interval CRS in ovarian cancer patients who have undergone NACT.

Method: We performed a single-institution retrospective chart review to identify women diagnosed with advanced EOC from 2013 to 2017 who received NACT followed by interval CRS. Clinicopathologic characteristics were extracted, and progression-free survival was calculated. SAS version 9.3 was used for descriptive statistics and multivariate analyses

Results: Forty-four patients were included in the analysis; 72% were debulked to no gross residual disease, optimal CRS. A higher laparoscopic Fagotti score prior to NACT was associated with lower odds of optimal interval CRS (OR = 0.30, 95% CI 0.14–0.65, $P = 0.002$). A higher Aletti surgical complexity score was associated with higher odds of optimal debulking (OR = 2.44, 95% CI 1.24–4.82, $p = 0.01$), as was longer surgery time (OR = 1.01, 95% CI 1.00–1.02, $P = 0.02$). Optimal debulking at interval CRS improved outcomes with a median progression-free survival (PFS) of 4.8 months for suboptimal and PFS of 14.6 months for optimal interval CRS ($P = 0.01$).

Conclusion: Cytoreduction to no gross residual disease remains an important predictor of improved PFS in the NACT population undergoing interval CRS. Interestingly, a higher Fagotti score at initial laparoscopy remains associated with a lower likelihood of optimal CRS despite traditional objective signs of partial or complete response to NACT. As expected, higher Aletti surgical complexity scores and longer surgery times indicating a strong attempt to achieve no gross residual disease are also associated with a higher likelihood of optimal CRS. As NACT has become a standard-of-care option in advanced EOC, interval CRS has become more prevalent. Further study into more objective predictive factors for optimal CRS is imperative.

179 - Poster Session

Rates over time and regional variation of radical minimally invasive surgery for cervical cancer: A population-based study

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Objective: To determine the rates of radical minimally invasive surgery (MIS) in women with cervical cancer and whether these rates vary over time and by region. To assess whether changes in the use of MIS have had an impact on length of hospital stay and readmissions.

Method: This retrospective population-based cohort study included women diagnosed with cervical cancer from the provincial cancer registry between April 2002 and March 2016 who had radical surgery (hysterectomy or trachelectomy) as their primary management. Those undergoing radical MIS versus laparotomy were compared. Trends in the rate of MIS over time, length of hospital stay, and readmission within 30 days of surgery were determined using the Cochran-Armitage test. Multivariate logistic regression was used to determine factors associated with MIS approach.

Results: A total of 1,343 women underwent radical surgery for cervical cancer during the study period, 59.9% by laparotomy and 40.1% by MIS. Those with MIS were significantly younger (43.3 vs 46.3 years, $P < 0.001$) and more likely to live in urban centers ($P < 0.001$). There was no significant difference in comorbid conditions between the groups ($P = 0.677$). There was an increase in rate of radical MIS over time, from 17.7% in 2002 to 61.5% in 2015 ($P < 0.0001$). Mean length of hospital stay and readmissions after radical MIS were reduced over the study period ($P < 0.0001$ and $P = 0.0161$, respectively). Rates of radical MIS varied significantly by institution, ranging from 0 to 55.9% of total radical procedures for cervical cancer ($P < 0.001$) among 7 centers with gynecologic oncologists. On multivariate regression, the most significant predictor of MIS approach was institution, with up to a 14-fold difference when compared to the site with the lowest rate of MIS (OR = 14.04, 95% CI 7.92–24.89). To a lesser extent, younger age (OR = 1.02, 95% CI 1.01–1.03) and later year of diagnosis (OR = 1.26, 95% CI 1.22–1.30) were also significant predictors of MIS approach.

Conclusion: Although rates of radical MIS for cervical cancer have increased over time, there remains significant regional variability. These findings can be used to facilitate educational initiatives for institutions with lower rates of MIS in order to help improve access to this approach for women with cervical cancer.

180 - Poster Session

Secondary surgical resection for patients with recurrent uterine leiomyosarcoma

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Objective: To assess outcomes after secondary surgical resection in patients with recurrent uterine leiomyosarcoma (LMS).

Method: We retrospectively identified all patients who had no evidence of disease after initial surgery for uterine LMS and underwent surgical resection for their first recurrence at our institution between January 1991 and October 2013. We excluded patients who received any therapy for recurrence prior to the secondary resection and patients who underwent surgery soon after morcellation and disease encountered. Overall survival (OS) was determined from the time of first recurrence to death or last follow-up.

Results: We identified 62 patients: 29 with abdominopelvic recurrence only, 30 with lung recurrence only, and 3 with both. The median time to first recurrence was 18 months (95% CI 13.3–23.3). The median time to first recurrence was 15.8 months (95% CI 13.0–18.6) for those with abdominopelvic recurrence and 24.1 months (95% CI 14.5–33.7) for those with lung-only recurrence ($P = 0.03$). Median OS was 37.7 months (95% CI 25.9–49.6) for those with abdominopelvic recurrence and 78.1 months (95% CI 44.8–111.4) for those with lung-only recurrence ($P = 0.02$). A complete gross resection (CGR) was achieved in 58 patients (94%), gross residual to ≤ 1 cm in 2 patients (3%), and gross residual to > 1 cm in 2 patients (3%). The median OS based on residual disease was 54.1 months (95% CI 24.9–83.3), 38.7 months (95% CI NE), and 1.7 months (95% CI NE), respectively ($P < 0.001$). In patients who achieved a CGR, the use of adjuvant radiation ($n = 9$), chemotherapy ($n = 8$), and/or hormonal therapy ($n = 10$) was not associated with improved OS.

Conclusion: Secondary surgical resection of recurrent uterine LMS is a reasonable option for patients with a high probability of achieving CGR. Lung-only recurrences seem to have a more favorable outcome. Following complete resection, additional therapy may not offer benefit.

181 - Poster Session

Gamma knife stereotactic radiosurgery for brain metastases of primary gynecologic origin

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Objective: Stereotactic radiosurgery (SRS) is a treatment employed for brain metastases of primary gynecologic origin, but few data exist on outcomes in this population. We report on outcomes of these patients undergoing GammaKnife (GK)-based SRS.

Method: We conducted a retrospective chart review of patients diagnosed with brain metastases of gynecologic origin treated with GK-SRS at our institution from 1998 to 2015. We performed Kaplan-Meier estimates of local control and OS. X² tests were performed to determine whether histology or primary disease site were associated with differences in local control/OS.

Results: In total 25 patients and 49 lesions were analyzed. Median follow-up was 14 months (range 0–79 months). Primary sites included placenta (7 patients), ovary/fallopian tube (7), cervix (4), endometrium (4), and uterine body (3). At initial diagnosis, the majority of patients had stage III–IV disease, and median time to detection of brain metastases was 17 months (range 0–319 months). Nineteen patients (76%) presented with CNS symptoms. At time of brain metastasis detection, 48% of patients had other systemic disease. Fourteen patients (56%) had a single lesion seen on initial imaging; 11 patients (44%) underwent surgical resection prior to radiation. Five patients (20%) received whole brain radiation therapy (WBRT) prior to GK-SRS. Median GK-SRS dose was 18 Gy prescribed to the 50% isodose line (range 10–20 Gy). Of the 19 patients who did not receive upfront WBRT, 6 later required salvage WBRT. Local control at 1 year was 80.4% (95% CI, 55.1%–92.3%) and at 2 years, 71.43% (95% CI 42%–87.8%). Patients with ovarian/fallopian tube primary had better local control than other primary gynecologic disease sites ($P = 0.02$). OS at 1 year was 68.9% (95% CI 45.5%–83.9%) and at 2 years, 46% (95% CI 24.8%–64.8%). Serous and small cell carcinoma histology were associated with better OS ($P = 0.007$). At the time of analysis, 5 patients (20%) were alive; 6 died due to CNS progression (24%); 7 to systemic progression (28%); 2 to simultaneous progression (8%); and 5 from unknown cause (20%).

Conclusion: Brain metastases from gynecologic primary tumors remain rare events. GK-SRS provides good local control of primary gynecologic brain metastases and can spare patients the neurocognitive toxicity of WBRT. Even among the rare gynecologic patient with brain metastases, systemic progression remains the most common mode of cancer-specific mortality.

182 - Poster Session

Immune checkpoint blockade and a neoepitope vaccine in a metastatic ovarian cancer model

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Objective: Immunotherapy offers an opportunity for a personalized approach to ovarian cancer. Therapeutic success currently seen with immune checkpoint blockade (ICB) occurs primarily in immunogenic tumors with high rates of genetic mutations, leading to neoepitope presentations and robust T cell infiltration. Using RNA seq and a murine preclinical ovarian cancer model, we sought to test our ability to boost the immune system's cytotoxic response to tumor cells by combining ICB with a personalized tumor-specific vaccine derived from neoantigens.

Method: We had developed an orthotopic human MUC-1 expressing, murine ovarian cancer model from which we derived a cell line that served as a novel and in vivo model for metastatic ovarian cancer. RNA seq was used to evaluate the mutanome for gene fusions and point mutations, confirmed with PCR and Sanger sequencing. Haplotype-specific in silico analysis of mutations was performed; immunogenic neoantigens were synthesized and used with MUC-1 peptide to create a type one polarized dendritic cell vaccine. Mice were injected with 5×10^6 tumor cells and divided into three treatment groups: RatIgG ($n = 8$), PD-L1 ($n = 15$), and vaccine + PD-L1 ($n = 7$). Mice received three weekly treatments. Tumor burden served as the primary

endpoint; tumors were evaluated with flow cytometry and immunohistochemistry (IHC). A MUC-1 enzyme-linked immunosorbent assay (ELISA) was used to test for the presence of antibodies.

Results: RNA seq analysis of our metastatic murine ovarian cancer cell line revealed a large mutational burden. Sixteen potential peptide binders ($IC_{50} < 500$), 2 with strong and 14 with moderate binding, 1 of which was a gene fusion, were identified. The gene fusion was verified by PCR. The vaccine comprised the top 7 MHC-I restricted, short (9-11 mer) peptide candidates with $IC_{50} < 500$ nM and 1 large (MHC-II, 100 mer) candidate peptide for CD4 T cell responses. A MUC-1 ELISA confirmed the presence of antibodies in experimental mouse sera. No difference in tumor burden was seen between treatment groups (ANOVA $P = 0.35$).

Conclusion: Neoepitopes represent a unique and personalized opportunity in ovarian cancer therapy. Mutanome evaluation and tumor-specific neoantigen synthesis for vaccination is feasible via a standardized pipeline. This concept is employed in melanoma treatment but is novel in ovarian cancer. Improved results may be seen with a longer timeline and an optimized dendritic cell approach.

183 - Poster Session

2-Octyl cyanoacrylate for the prevention of anastomotic leak

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Objective: Optimal primary cytoreductive surgery for patients with advanced ovarian cancer may require bowel resection. Anastomotic leak following colorectal surgery is a significant cause of morbidity and mortality. The aim of this study was to evaluate the impact of a reinforced colo-colonic anastomosis with tissue adhesive, 2-octylcyanoacrylate (2-O), on the integrity of anastomotic healing as measured by anastomotic bursting pressure (ABP).

Method: A total of 68 female Sprague-Dawley rats underwent a rectosigmoid colon transection followed by a sutured end-to-end anastomosis followed by randomization to receive no further intervention or reinforcement with the tissue adhesive, 2-O. After seven postoperative days, a macroscopic assessment of the anastomosis, a mechanical assessment to determine ABP, and a detailed semiquantitative histopathologic healing assessment were performed.

Results: A total of 34 animals were randomized to each group. Study characteristics did not differ between the groups including preoperative weight, number of sutures used, presence of stool at the anastomosis, operative time, arcade ligation, or postoperative day of first bowel movement. There was also no difference in the degree of adhesions present postoperatively. Although there was no difference between the net proximal and distal luminal areas in the two groups (0.37 cm^2 vs 0.55 cm^2 , $P = 0.26$), the 2-O group exhibited evidence of obstruction in 15% of anastomoses compared to 3% in the suture-only group ($P < 0.0001$). Histologically, the presence of only fibroblasts density was statistically more evident in the 2-O group compared to the sutured-only group ($P = 0.0183$). The ABP was increased in the 2-O group, 238.9 mm Hg, compared to the suture-only group, 231.8 mm Hg ($P = \text{NS}$). Bursting pressure failures occurred peri-anastomotically in 29% in the suture-only group compared to none in the 2-O group ($P < 0.0001$). There was no difference in the rate of anastomotic leak in the 2-O group compared to the suture-only group (9.1 vs 8.8%).

Conclusion: Application of 2-octylcyanoacrylate to reinforce a colo-colonic anastomosis nonsignificantly increases its mechanical strength, but to the detriment of a significantly increased rate of obstruction and/or stricture. There appears to be no benefit in the use of 2-octylcyanoacrylate for the prevention of anastomotic leak.

184 - Poster Session

Diverse indications for risk-reducing salpingo-oophorectomy: Experience from a tertiary care center

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Objective: This study seeks to understand the indications for risk-reducing salpingo-oophorectomy (RRSO) and to describe the associated complications, pathologic findings, and additional risk reduction surgeries undertaken.

Method: Using a single-institution retrospective cohort, billing data were utilized to identify subjects who underwent salpingo-oophorectomy between June 2003 and May 2017. Only subjects who underwent surgery for cancer risk reduction, as

defined by operative report, were included. The medical record was reviewed to abstract associated clinicopathologic data. The study was institutional review board approved.

Results: Of the 154 patients who underwent RRSO, 127 (82.5%) had germline genetic testing before surgery, 86 (55.8%) of whom were found to carry a deleterious mutation in *BRCA1* ($n = 44$), *BRCA2* ($n = 37$), *PALB2* ($n = 3$), *MLH1* ($n = 1$), or *MSH2* and *MSH6* ($n = 1$). A total of 27 subjects (17.5%) underwent RRSO without having had germline genetic testing performed, and 41 (26.6%) had no pathologic mutation identified (including 6 variants of unknown significance). Among these patients, 42 had estrogen receptor (ER) positive breast cancer, 17 had ER negative or ER unknown breast cancer with family history of breast or ovarian cancer, 8 had a family history of breast or ovarian cancer, and 1 had a personal history of colon cancer with postradiation menopause. Over the time of the cohort, the proportion of patients undergoing RRSO who had germline genetic testing prior to surgery increased. In this cohort, only 11 (7.1%) also had a prophylactic bilateral mastectomy during the course of their care. Hysterectomy was performed concomitantly in 36 patients (22.4%). Almost all surgeries ($n = 151$, 98.0%) were performed by gynecologic oncologists. Eight subjects (5.2%) had a surgical complication requiring prolonged hospitalization or additional surgery. Review of pathology identified three (1.9%) occult metastatic breast cancers and no occult gynecologic cancers or serous tubal intraepithelial carcinomas (STICS).

Conclusion: In this retrospective cohort, the indications for RRSO were varied and were not limited to high-risk genetic mutations. Given the increasing uptake of genetic testing, prophylactic surgeries including RRSO will continue to be common, but surgeons should be prepared for unanticipated pathology findings and surgical complications.

185 - Poster Session

Utilization of a multimodal preoperative pain regimen prior to gynecologic oncology exploratory laparotomies

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Objective: The aim of this study was to evaluate the use of a combination of nonopioid preoperative pain medications including Tylenol, Lyrica, and Celecoxib (TLC) in patients undergoing gynecologic oncologic exploratory laparotomies. We evaluated postoperative narcotic use in morphine equivalents (ME) and pain scores.

Method: A retrospective cohort study was performed of all gynecologic oncologic patients who underwent exploratory laparotomies from February 2011 to April 2013 by one surgeon at a tertiary care center and who either received TLC or did not. The primary outcome was postoperative narcotic use in ME during the first 24 hours after surgery. Secondary outcomes included postoperative pain scores and total ME during the hospital stay. Data were analyzed using STATA Version 12 with a combination of Kruskal-Wallis test, Student t test, χ^2 , and ANOVA analysis.

Results: Patients who received preoperative TLC had a statistically significant difference in total IV and PO median morphine equivalent (ME) use over the total postoperative period, at 90.6 ME with TLC, compared to 123.8 ME without TLC ($P = 0.0008$). Total IV ME over the postoperative course was also statistically significant, with a median of 71.7 ME with TLC and 106.8 ME without TLC ($P = 0.0003$). Within the first 24 hours after surgery, there was a statistically significant difference in total IV morphine equivalents used with a median ME with 40.2 for TLC and 66 without TLC ($P = 0.001$). Mean pain scores in the first 24 hours after surgery were reduced in the TLC group with a mean of 3.4, compared to a mean of 4.6 without TLC ($P = 0.009$). In the first 24 hours after surgery, the maximum pain score was higher without TLC at 7.1 compared to 5.8 with TLC ($P = 0.004$), and the minimum pain score was significantly lower with TLC at 1.2 compared to 2.3 without TLC ($P = 0.002$).

Conclusion: Using a multimodal approach to pain control preoperatively can help reduce patients' IV narcotic usage in the first 24 hours after surgery. The mean pain score in the 24 hours after surgery was significantly less in the group that received TLC. In addition, both the maximum and minimum pain scores in the first 24 hours after surgery were significantly less in the group that received TLC. The total combined PO and IV MEs, as well as the total IV ME, were also reduced over the entire postoperative period in the group that received TLC. Using ANOVA analysis, statistical significance was retained, although minimal pain scores had a weak association.

186 - Poster Session

An electrical scalpel conization versus shimodaira-taniguchi conization procedure for cervical intraepithelial neoplasia

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Objective: The incidence of cervical intraepithelial neoplasia among women of reproductive age has increased in Japan. Conization is commonly applied for local cervical treatment to preserve fertility. The Shimodaira–Taniguchi conization (S–T) procedure using a high-frequency current and a triangular probe with a linear excision electrode to remove cervical tissue as a single informative specimen has been widely adopted in Japan. On the other hand, an electrosurgical scalpel (ES) has the advantage of allowing adjustment of the surgical margin to the transformation zone to preserve adequate healthy cervical tissue with good hemostasis. The aim of this study was to retrospectively analyze data, including surgical margin status, cervical stenosis, and perinatal outcomes, to compare between S–T and ES.

Method: Between January 2009 and December 2014, the medical records of 1,155 patients who were diagnosed as having cervical intraepithelial neoplasia II or III, or stage 1a1 cervical cancer, and treated with conization in seven hospitals in Gunma prefecture, Japan, were enrolled in this retrospective study. Their clinicopathological data (Table 1) were analyzed to statistically compare between S–T and ES by using the χ^2 test, and odds ratios and 95% CI were calculated. All analyses were performed using SAS V.9.4.

Results: No significant differences in age and postoperative follow-up period were found between ES and S–T. However, a positive surgical margin significantly less frequently occurred in the patients who underwent operation with S–T (OR 0.39, 95% CI 0.26–0.57) and resulted in a lower retreatment rate than that in the patients who underwent ES (OR 0.31, 95% CI 0.12–0.76). The incidence rates of preterm delivery and cervical stenosis were not statistically significantly different between the two groups.

Conclusions: We demonstrated that the S–T conization procedure was an alternative method with a low risk of recurrence and acceptable low rate of adverse events. The results drawn from this study provide useful information for future studies on patient management with cervical intraepithelial neoplasia.

Table 1. Patient characteristics.

	Electrosurgical scalpel	Shimodaira- Taniguchi	P value
age (years)	32.01 (19-39)*	32.26 (19-40)*	0.355**
post operative follow-up period (months)	36.36 (0-94)*	36.81 (0-107)*	0.759**
smoking status			
no	351	342	<0.0001***
yes	100	65	
unknown	26	282	
delivery history before operation			
no	201	270	0.79***
yes	276	383	
unknown	0	36	
delivery history after operation			
no	308	456	0.0206***
yes	102	107	
unknown	67	126	

* Average (range), ** t-test or ***Chi-squared test was used, respectively.

Table 2. The odds ratio and 95% confidence for clinical outcomes after conization by Shimodaira-Taniguchi method to conization by electrosurgical scalpel.

	electrosurgical scalpel	Shimodaira- Taniguchi	Odds ratio	95% CI	P value*
Surgical margin status					
positive					
negative	377	627	0.384	0.273- 0.542	<0.001
positive	97	62			
Recurrence after conization					
No	452	667	0.596	0.332- 1.071	0.083
Yes	25	22			
Preterm delivery					
No	81	81	1.3636	0.591- 3.129	0.5297
Yes	11	15			
Cervical stenosis					
No	465	654	1.495	0.698- 3.205	0.291
Yes	10	21			

* Logistic regression was used.

187 - Poster Session

Heterogeneity of operative approach in long-term survivors of high-grade serous carcinoma

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Objective: Little is known about the precise surgical procedures performed on long-term survivors (LTS) of high-grade serous carcinoma (HGSC). The objective of this retrospective review is to determine whether particular features of surgery are associated with LTS.

Method: Patients with HGSC of the ovary, fallopian tube, or peritoneum who survived more than 7 years were identified from our academic institution's database of ovarian neoplasms treated since 1992. Patients with nonserous histology and low-grade and low-malignant potential tumors were excluded. Descriptive statistics are reported.

Results: Fifty-three of 450 consecutive patients were analyzed. Median age was 61 years. Progressive disease was the cause of death in 19 women (36%), and their mean survival was 126.6 months. Mean time to last contact was 132.1 months for the 34 LTS alive or dead of other causes. Disease stages were FIGO I (4%), II (11%), III (72%), and IV (13%). Neoadjuvant chemotherapy was administered to 11% of LTS. At initial debulking, LTS had gross or pathologic involvement of the following organs: uterus (32%), fallopian tube (74%), ovary (90%), omentum (57%), small bowel (38%), large bowel (47%), appendix (14%), spleen (10%), liver (25%), diaphragm (45%), palpable lymph nodes (14%), pleural effusion (8%), and ascites >500 cc (31%). High-volume disease, defined as involvement of diaphragm, liver, or spleen, was present in 46% of LTS. Surgical procedures performed during initial debulking were hysterectomy/BSO completed or previously performed (100%), omentectomy (94%), pelvic lymph node dissection (55%), paraaortic lymph node dissection (47%), pelvic peritonectomy (39%), abdominal peritonectomy (14%), appendectomy (43%), small bowel resection (6%), large bowel resection (21%),

splenectomy (4%), liver resection (6%), diaphragm stripping (14%). Cytoreductive outcomes were no visible disease (43%), <1 cm (39%), >1 cm (18%) with 33% of suboptimally debulked patients undergoing secondary cytoreduction.

Conclusion: Less than half of LTS were debulked to no visible disease, and nine women were LTS despite suboptimal debulking. LTS underwent a wide variety of procedures with the goal of maximal debulking. The variety of surgeries associated with LTS suggests that other determinants, such as tumor biology, sensitivity to chemotherapy, or patient factors, play a significant role in LTS.

188 - Poster Session

Salpingectomy for ovarian cancer prevention at the time of cesarean delivery: Comparison of outcomes of surgical technique

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Objective: To evaluate the surgical outcomes of prophylactic salpingectomy during sterilization at time of cesarean delivery by surgical technique with bipolar electrocautery versus suture ligation.

Method: This is a retrospective cohort study using electronic medical records at Kaiser Permanente Northern California (KPNC) of women age 18 years and older, undergoing sterilization by salpingectomy at time of cesarean delivery. The study includes all eligible women from 2011 to 2016 at time of elective surgical sterilization. The primary objective is to compare surgical outcomes using electrosurgical bipolar (LigaSure, Metronic, MD USA) versus suture ligation, including estimated blood loss (EBL), major or minor intraoperative complications, blood transfusions, operative time, length of hospital stay, postoperative readmission and emergency department visits.

Results: There were 190 patients with salpingectomies for sterilization at time of cesarean delivery identified. There were 96 salpingectomies by bipolar electrocautery device and 94 by suture ligation. The primary indication for cesarean was repeat cesarean delivery. Cesarean deliveries with salpingectomies performed by bipolar electrocautery compared to suture was associated with lower EBL with an average 600 ml versus 762 ml ($P = 0.03$), respectively (Table 1). Surgery time and operating room time were longer for suture ligation than for electrocautery (66 versus 60 minutes, $P = 0.03$, and 104 versus 100 minutes, $P = 0.04$, respectively) There were two major and eight minor intraoperative complications during cesarean delivery with salpingectomy, but only two minor complications specifically related to salpingectomy. There was one postoperative blood transfusion. There were no emergency room visits within 7 days of discharge in either group and no observed difference in readmission rates. The length of stay postoperatively did not differ.

Conclusion: Salpingectomy instead of tubal ligation at the time of cesarean delivery for sterilization performed with a bipolar device is faster and associated with less blood loss than suture ligation. However, there is no difference in postoperative care complication rates. The balance of cost of the instrument and time saved may vary in different health care systems.

Table 1. Surgical outcomes of salpingectomies at cesarean delivery by method.

Characteristic	Bipolar Cautery Device ^a (n = 96)	Suture Ligation (n = 94) ^a	P ^b
Length of stay (hours)	54 (49–720)	52 (48–71]	0.31
Surgery time (min)	60 (46–71)	66 (52–80)	0.04
Operating room time (min)	100 (82–112)	104 (89–120)	0.04
Estimated blood loss (mL)	600 (445–800)	762 (500–882)	0.03
Readmission within 30 days – N (%)	10 (10.4)	10 (10.6)	0.96
Emergency room visit within 7 days – N (%)	0	0	

^a Data are median (Q1, Q3) unless otherwise specified. Percentages are percent with outcome, where percent without outcome not shown.

^b Statistical tests were nonparametric Kruskal-Wallis for continuous variables and χ^2 test for categorical variables among cesarean and interval procedure and Fisher exact test for 30-day readmission among postpartum procedures.

189 - Poster Session

Impact of surgical volume on complete gross resection rates for women with advanced stage epithelial ovarian carcinoma

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Objective: To investigate the impact of hospital surgical volume on the rate of complete gross resection (R0) for patients with advanced-stage epithelial ovarian carcinoma (EOC) undergoing primary surgery.

Method: The National Cancer Data Base was accessed and a cohort of women diagnosed between 2010 and 2014 with an advanced-stage (III–IV) serous, endometrioid, mucinous, or clear cell ovarian carcinoma, who underwent cancer-directed surgery at the reporting facility, were selected for further analysis. Average surgical volume for each institution was calculated by dividing the number of reported cases who met the inclusion criteria by the number of reporting years. For analysis, surgical volume was divided into tertiles (high, intermediate, and low). The interval between definite surgical treatment and administration of chemotherapy was calculated to identify patients who received neoadjuvant chemotherapy. Univariate analysis was performed with the χ^2 test and multivariate analysis with binary logistic regression.

Results: A total of 26,022 patients with advanced-stage EOC who underwent cancer-directed surgery at the reporting facility were initially identified. After excluding women who had neoadjuvant chemotherapy, residual disease could be assessed for 11,990 patients; 49% had R0. Rates of R0 for women diagnosed in 2010 and 2011 were 39.8% and 48.5% compared to 50.5%, 52.4% and 56.9% for those diagnosed in 2012, 2013, 2014, respectively ($P < 0.001$). By univariate analysis, higher rates of R0 were noted for women younger than 65 years ($P < 0.001$), without medical comorbid conditions ($P = 0.001$), with stage III ($P < 0.001$) nonserous ($P < 0.001$) tumors, private insurance ($P < 0.001$), and high income ($P = 0.001$) managed in the Midwest ($P = 0.018$). Rates of R0 for patients managed in low-, intermediate-, and high-volume centers were 49.4%, 48.3%, and 49.7% respectively ($P = 0.39$). Based on site-specific surgery codes, high- and intermediate-volume centers performed more complex surgical procedures (67.3% and 62.7%) than low-volume centers (56.3%, $P < 0.001$). However, according to multivariate analysis, surgical volume was not associated with the likelihood of achieving R0.

Conclusion: Results of the present study demonstrate that hospital surgical volume may not be associated with the likelihood of achieving complete gross resection following primary surgery.

190 - Poster Session

From unresectable to cancer-free at interval surgery: An evaluation of complete pathologic responders

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Objective: To determine preoperative factors and survival outcomes associated with complete pathologic response at interval tumor reductive surgery (TRS) following neoadjuvant chemotherapy (NACT).

Method: Patients with suspected advanced-stage ovarian cancer who received NACT followed by interval TRS between February 2013 and September 2017 were identified. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier product-limit estimator. Prognostic factors of interest were compared by response using χ^2 , Fisher exact, or Wilcoxon rank sum tests, depending on the normality assumption testing.

Results: A total of 291 patients were identified and included in the study. The median age at diagnosis was 64 years. The majority of patients were white (86%), not Hispanic or Latino (89%), and had either stage IIIC (41%) or IVB (46%) ovarian cancer. Most patients underwent R0 resection at interval TRS (79%). The primary reason for NACT was surgically unresectable disease (74%), as evaluated by preoperative imaging or laparoscopic triage. Sixteen patients (5.5%) had a complete pathologic response (cPR) at interval TRS. The median PFS for the cPR group was 24.2 months, while for the non-cPR group it was 11.6 months ($P = 0.020$, Figure 1). Overall survival was similar between the cPR and non-cPR groups ($P = 0.253$). No association was observed between age and cPR (OR 1.0, $P = 0.856$). Patients with a *BRCA1/2* mutation, or those

identified as having their platelets “normalize” (<400,000/mm³) over the course of NACT, were slightly less likely to achieve a cPR (OR 0.86, *P* = 0.846; OR 0.80, *P* = 0.692, respectively). The odds of achieving a cPR for those who underwent more than four cycles of dose-dense chemotherapy were two times larger, compared to those who underwent less than four cycles (OR 2.09, *P* = 0.373).

Conclusion: Patients who achieve a complete pathologic response after NACT have a significantly longer PFS. These findings have potential implications for the design of clinical trials, and further work is needed to elucidate related mechanisms.

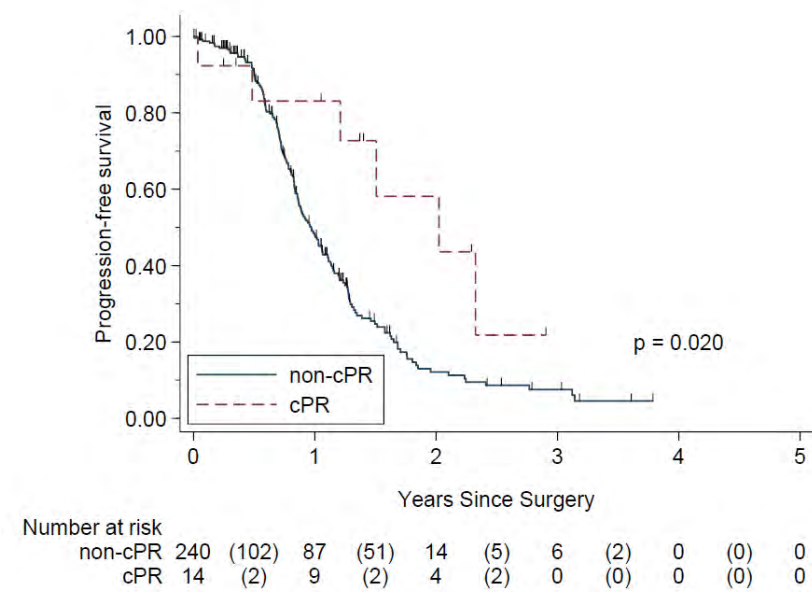


Fig. 1. Kaplan-Meier curve of PFS.

191 - Poster Session

Sentinel lymph node mapping in endometrial and cervical cancer: A survey of practices and attitudes in gynecologic oncologists

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Objective: To determine practice patterns in use of sentinel lymph node mapping (SLNM) in endometrial cancer (EC) and cervical cancer (CC) staging.

Method: A 24-question online survey assessing the current practice of SLNM, including incidence, patterns of usage, and reasons for nonuse was distributed to SGO candidates and full members in August 2017. Descriptive statistics were performed.

Results: A total of 1,117 members were surveyed, and 197 responses (17.6%) were received. Of the 70% currently performing SLNM, the majority reported use for both CC and EC (63.7%) or EC alone (33.3%). In those using SLNM in EC, the majority (86.6%) performed SLNM in more than 50% of cases, for all patients regardless of histology (56.0%) or FIGO grade 1 (44.0%) and 2 (41.8%). SLNM was utilized less frequently in patients with complex atypical hyperplasia (20.8%), FIGO grade 3 (22.4%), and high-risk histologies (17.9%). Benefits of SLNM in EC were reported to include reduced surgical morbidity (89.6%), lymphedema (85.1%), and operative time (63.4%). Among those using SLNM for CC, the majority (72.8%) did so in more than 50% of cases. Respondents reported use of SLNM for Stage IA1 in 46.7%, IA2 in 92.4%, IB1 in 92.4%, and IB2 in 32.6%. In EC, 77.2% and 21.3% reported that micrometastatic disease (0.2–2.0 cm) and isolated tumor cells (ITCs) should be treated as node positive, respectively. Similarly, in CC, 71.1% and 34.5% reported that micrometastatic disease and ITCs should be treated as node positive, respectively. In those not using SLNM for EC (*n* = 64) and CC (*n* = 105), concerns were efficacy of SLNM and lack of training (Table 1). While 75.6% thought that data supported use in low-risk EC histology, only 45.2% agreed that data supported use of SLNM for all histologies. When queried regarding fellows training, 73.6% thought that SLNM would have an impact on skill in full lymphadenectomy. Among those not using SLNM in their practice, 76.7% reported that they would be interested in further training through surgical videos, case proctoring, and observation.

Conclusion: SLNM is utilized frequently among gynecologic oncologists for endometrial and cervical cancer staging. Common reasons for non-uptake include uncertainty of current data, lack of training, and technology. The majority of those not using SLNM would like more training in this technique.

Table 1. Reasons for non-uptake of SLNM.

Reason	EC (n = 64) Number (%)	CC (n = 105) Number (%)
Uncertain of data	29 (45.3%)	62 (59.0%)
Did not receive training in fellowship	23 (35.9%)	22 (21.0%)
Lack of access to technology	22 (34.4%)	19 (18.1%)
Concerns regarding efficacy of mapping	20 (31.3%)	25 (23.8%)
Concerns regarding the impact of ultrastaging on patient outcomes	20 (31.3%)	20 (19.0%)
Concern for missing node positive disease	18 (28.1%)	34 (32.4%)
To aid in training of full lymphadenectomy in fellowship	8 (12.5%)	8 (7.6%)
Pathology department uncertain on how to process specimens for ultrastaging	11 (17.2%)	10 (9.5%)

192 - Poster Session

Surgical consultants during cytoreduction for advanced ovarian cancer

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Objective: To examine associations between surgical consultation and outcomes among women undergoing cytoreductive surgery for advanced ovarian cancer with a gynecologic oncologist.

Method: This was a retrospective chart review at two referral centers with distinct gynecologic oncology divisions. All patients undergoing cytoreductive surgery between January 2010 and July 2015 with a gynecologic oncologist for stage IIIC–IV high-grade epithelial malignancy of the ovary, fallopian tube, or peritoneum were reviewed. Patients who underwent any procedure beyond hysterectomy, salpingo-oophorectomy, omentectomy, pelvic lymphadenectomy, or appendectomy were included for analysis. Outcomes of surgeries involving a surgical consultant were compared to surgeries performed entirely by the gynecologic oncologist.

Results: A total of 556 cytoreductive surgeries were identified; 251 of these (45.1%) included procedures beyond hysterectomy, salpingo-oophorectomy, omentectomy, pelvic lymphadenectomy, or appendectomy and were included for analysis. Of these 251 surgeries, 186 (74.1%) were performed exclusively by gynecologic oncologists and 65 (25.9%) cases involved surgical consultants. Patients who had surgical consultants were more likely to have stage IV disease and receive neoadjuvant chemotherapy. The most common surgical consultants were colorectal surgeons and general surgical oncologists. Cytoreductions involving surgical consultants were more likely to result in no gross residual disease (58.5 vs 40.3%, $P = 0.03$); however, this effect was limited to patients undergoing interval cytoreduction after neoadjuvant chemotherapy (Table 1). There were no significant differences between groups in estimated blood loss, transfusion rate, length of stay, 30-day complications, readmissions, reoperations, or time to chemotherapy. Gynecologic oncologists performed 167 of 194 (86.1%) distinct gastrointestinal (GI) procedures, and there were no significant differences in GI-specific complication rates with GI surgery performed by gynecologic oncologists or surgical consultants (35.3 vs 28.6%, respectively, $P = 0.55$).

Conclusion: Gynecologic oncologists can safely perform most GI and upper abdominal procedures at the time of cytoreductive surgery for advanced ovarian cancer. The inclusion of surgical consultants may be of value in achieving no gross residual disease after neoadjuvant chemotherapy.

Table 1: Clinical outcomes with and without a surgical consultant.

Characteristic	Total cohort (N = 556)	GO only (N = 186)	GO + SC* (N = 65)	P-value**
Residual disease:				0.031
NED	278 (50.0%)	75 (40.3%)	38 (58.5%)	
Optimal	219 (39.4%)	97 (52.2%)	22 (33.8%)	
Suboptimal	59 (10.6%)	14 (7.5%)	5 (7.7%)	
Not stated	1 (0.2%)			
If primary cytoreduction				0.621
Residual Disease:				
NED	101 (38.5%)	49 (39.8%)	11 (42.3%)	
Optimal	121 (46.2%)	62 (50.4%)	11 (42.3%)	
Suboptimal	40 (15.3%)	12 (9.8%)	4 (15.4%)	
If interval cytoreduction				0.022
Residual Disease:				
NED	177 (60.0%)	26 (41.3%)	27 (69.2%)	
Optimal	98 (33.2%)	35 (55.6%)	11 (28.2%)	
Suboptimal	19 (6.4%)	2 (3.2%)	1 (2.6%)	
Not stated	1 (0.3%)			
EBL (mL)				0.156
Mean (SD)	581 (689)	771 (774)	949 (1097)	
Median (range)	400 (0-7000)	500 (0-4850)	650 (0-7000)	
Intra-op transfusion	123 (22.1%)	60 (32.3%)	23 (35.4%)	0.645
Post-op transfusion	222 (39.9%)	101 (54.3%)	37 (56.9%)	0.715
Length of stay, days				0.943
Mean (SD)	7.3 (4.6)	9.3 (5.1)	9.3 (5.8)	
Median (range)	6 (1-37)	8 (2-37)	8 (3-35)	
ICU admission post-op	41 (7.4%)	19 (10.2%)	14 (21.5%)	0.020
Complications <30 days				0.613
PE/DVT	27 (4.9%)	11 (5.9%)	5 (7.7%)	
Pneumonia	25 (4.5%)	11 (5.9%)	2 (3.1%)	0.374
Ileus	67 (12.1%)	36 (19.4%)	8 (12.3%)	0.198
SBO	11 (2.0%)	3 (1.6%)	4 (6.2%)	0.057
Bowel perforation	2 (0.4%)	2 (1.1%)	0	0.401
MI	0	0	0	n/a
Intra-abdominal infection	27 (4.9%)	16 (8.6%)	3 (4.6%)	0.296
Wound complication	76 (13.7%)	27 (15.1%)	12 (18.5%)	0.450
Re-admission <30 days	73 (13.1%)	35 (18.8%)	11 (16.9%)	0.734
Re-operation <30 days	17 (3.1%)	12 (6.5%)	3 (4.6%)	0.591
Unable to receive chemo	3 (0.5%)	1 (0.5%)	1 (1.5%)	0.435
Death < 30 days	0	0	0	n/a
Days to post-op chemo, mean (SD)	28.1 (21.6)	27.6 (14.0)	30.4 (14.5)	0.190

*GO = gynecologic oncologist; SC = surgical consultant.

**P-value from t-test or chi-square test where applicable. P-value ONLY comparing GO surgeon vs GO + SC, not total cohort.

193 - Poster Session

When less is more: Minimally invasive surgery compared to laparotomy for interval debulking after neoadjuvant chemotherapy in women with advanced ovarian cancer

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Objective: To compare minimally invasive surgery (MIS) to laparotomy for interval cytoreduction in patients with advanced ovarian cancer treated with neoadjuvant chemotherapy (NACT).

Method: We conducted an institutional review board-approved retrospective review of all consecutive patients with ovarian cancer seen from April 2006 to July 2017 at a single institution. Patients had stage III–IV epithelial ovarian, tubal, or peritoneal

cancer and underwent either MIS or laparotomy for interval cytoreduction by 1 of 7 gynecologic oncologists following at least 1 cycle of NACT. Patient-related and surgical end points were compared by Fisher exact test; survival was estimated by the Kaplan-Meier method and compared with the log rank test.

Results: A total of 157 evaluable patients underwent NACT followed by interval cytoreductive surgery. There were no differences between MIS ($n = 53$) and laparotomy groups ($n = 104$) with regard to age, race, socioeconomic status, histology, stage, *BRCA* status, number of chemotherapy cycles, or response to chemotherapy. MIS patients were more likely to receive dose-dense chemotherapy (61% vs 38%, $P = 0.023$). MIS was initiated in 53 patients and completed without conversion in 44 patients (83%); 11 required a hand port (20.8%); and 14 had a minilaparotomy (26.4%). R0 and optimal resections were achieved in 60.4% and 96.2% of MIS patients, compared with 44.3% and 86.6% of laparotomy patients ($P = 0.07$), respectively. Overall, 10% of patients had a complete pathologic response to NACT (13% and 8%, respectively, $P = 0.494$). There were no differences in preoperative CA-125 or size of largest tumor. Patients who underwent MIS had lower EBL (156 vs 278 mL, $P < 0.001$) were less likely to receive an intraoperative blood transfusion (2% vs 17%, $P = 0.006$) and had a shorter length of stay (3.0 vs 5.7 days, $P < 0.001$). MIS patients were less likely to have any postoperative complication (46% vs 54%), but this was not statistically significant. Operative time was longer in the MIS group (171 vs 150 minutes, $P = 0.007$), but rates of intraoperative complications, ICU stay, and readmission were no different. PFS (27 vs 29 months, $P = 0.45$) and OS (37 vs 35 months, $P = 0.74$) were similar for MIS compared with open surgery.

Conclusion: Minimally invasive surgery is a feasible and effective strategy for interval cytoreduction after NACT in patients with advanced ovarian cancer. MIS is associated with less EBL, lower rate of transfusion, and shorter length of hospital stay with no difference in patient outcomes.

194 - Poster Session

A comparison of sentinel lymph node biopsy to lymphadenectomy for high-grade endometrial cancer staging

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Objective: Sentinel lymph node biopsy (SLNB) is proposed to have equivalent efficacy and reduced morbidity as traditional staging lymphadenectomy for the surgical evaluation of endometrial cancer. This study evaluates the clinical utility and safety of SLNB in patients with high-grade endometrial cancer.

Method: A multiinstitutional retrospective review was conducted for patients with high-grade endometrial cancer undergoing robotic or laparoscopic surgery and SLNB with additional lymphadenectomy between June 2015 and March 2017.

Results: A total of 38 patients received hysterectomy, bilateral salpingo-oophorectomy, and SLNB. Median age was 65.5 years, and tumors averaged 3.7 cm. Distribution of stage was 20 patients (IA), 8 patients (IB), 4 patients (II), 3 patients (IIIA), and 3 patients (IIIC). Successful unilateral mapping of at least 1 SLN was achieved in 35 (92%) patients, and 25 (71%) had successful bilateral mapping. There were 33 (94%) patients who received additional staging lymphadenectomy, and median pelvic lymph nodes sampled were 15.0 (interquartile range [IQR] 9.5–22.3). Paraaortic lymphadenectomy was performed in 73.7% of patients with median nodes sampled of 6.0 (IQR 3.3–10.5). Of the 801 nodes sampled, 2 (6%) patients had macrometastatic SLNs without evidence of positive pelvic or paraaortic nodes, and 1 (3%) patient had grossly metastatic obturator nodes at time of surgery but negative SLNs. Ipsilateral SLNs with isolated tumor cells (ITCs) were present in 5 (13%) patients. None of the other 609 pelvic or 184 paraaortic nodes were positive. Overall, SLNB had a negative predictive value of 96.7% (86.6–99.4% 95% CI) in high-grade disease when nodes containing ITCs were considered negative, and 99.9% (99.2–99.9% 95% CI) when ITCs were considered positive. If the grossly metastatic obturator nodes were not considered falsely negative, the negative predictive value of SLNB in high-grade disease was 100%. No reported complications were associated with SLNB.

Conclusion: SLNB has a high negative predictive value when used to detect early nodal metastases in high-grade endometrial cancer and may be the new standard to replace routine lymphadenectomy.

195 - Poster Session

Asian perspective on the quality of debulking surgery for advanced-stage ovarian cancer: Results of an international survey

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Objective: We investigated the quality of debulking surgery for advanced-stage ovarian cancer (AOC) in Asia.

Method: We designed a questionnaire consisting of general (8 questions), training (7 questions), and procedure information (23 questions) and conducted a survey of Asian gynecologic oncologists using the questionnaire between December 2016 and April 2017.

Results: A total of 253 gynecologic oncologists in Japan (58.9%), Republic of Korea (19%), Taiwan (12.6%), China (7.5%), Indonesia (0.8%), Malaysia (0.8%), and Thailand (0.4%) participated in the survey. The median number of patients undergoing debulking surgery per year was 20, and 47.2% and 38.5% of respondents preferred residual tumors <1 cm and no visible tumor as the criteria-defining optimal cytoreduction, respectively. The most common factors disturbing optimal cytoreduction were performance status (74.3%) and disease involving the porta hepatis (71.5%); 65.1% determined optimal cytoreduction preoperatively, and 79.8% predicted optimal cytoreduction using imaging studies. In terms of training, 63.2% had a fellowship program for gynecologic oncology, and 50.4% had a surgical protocol for debulking surgery. However, 70.4% had no additional training program after fellowship. In terms of procedure, the median percentages of patients who received neoadjuvant chemotherapy and underwent interval debulking surgery were 30% and 80%, respectively. Moreover, 58.6% and 48.4% required 3 to 6 hours for interval debulking surgery and upfront surgery, respectively; 33.2% to 73.9% performed complete procedures for staging operation, whereas only 2% to 19% could perform upper abdominal surgery by themselves.

Conclusion: Gynecologic oncologists in Asia may prefer optimal cytoreduction based on staging operation performed by themselves. However, additional training programs after fellowship are insufficient, and thus the ability to conduct upper abdominal surgery may be relatively low in Asia.

196 - Poster Session

A clinical prediction model stratifies patients by risk and helps with surgical staging decisions in endometrioid endometrial cancer

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Objective: Endometrial cancer is the most common gynecologic malignancy and is diagnosed at an early stage up to 70% of the time. The utility of comprehensive surgical staging in patients with low-grade, minimally invasive disease has been questioned, and to date there is no reliable preoperative predictive model for identifying these patients. The objective of this study is to create a prediction model to stratify patients into risk levels with clinical variables available pre- or intraoperatively.

Method: The Gynecologic Oncology Group has defined risk categories based on patient age, myometrial invasion, histologic grade, and lymphovascular space invasion. Patients were stratified into high- or low-risk categories based on these parameters. Clinical and pathological data were available for 82 patients diagnosed with endometrioid endometrial cancer (EEC) at our institution. After institutional review board approval, clinical data were extracted from patient charts. Univariate and multivariate analyses were performed to identify variables associated with recurrence, survival, and risk levels. Prediction models were constructed using significant variables available at baseline and intraoperatively, analyzed with the lasso regression method, and measured with area under the curve (AUC). Prediction models were compared to those created with clinical and molecular data from The Cancer Genome Atlas (TCGA).

Results: The 5-year survival for low-risk patients was 97% compared to 77% for high-risk patients ($P = 0.02$). On univariate analysis, age, BMI, Charlson morbidity index, myometrial invasion, histologic grade, and positive progesterone receptor were significantly associated with risk levels. The clinical prediction model was built and optimized using age, BMI, grade, and myometrial invasion. It had an AUC of 91% (95% CI 88–93) for detecting high-risk EEC patients; see Figure 1. This validates and improves models utilizing TCGA clinical data (AUC of 90%) in EEC patients.

Conclusion: We validated previous TCGA clinical models to predict risk in patients with EEC in an independent clinical database. Integration of molecular data to this clinical model is likely to improve its performance, resulting in a model that could be translated into a clinical test.

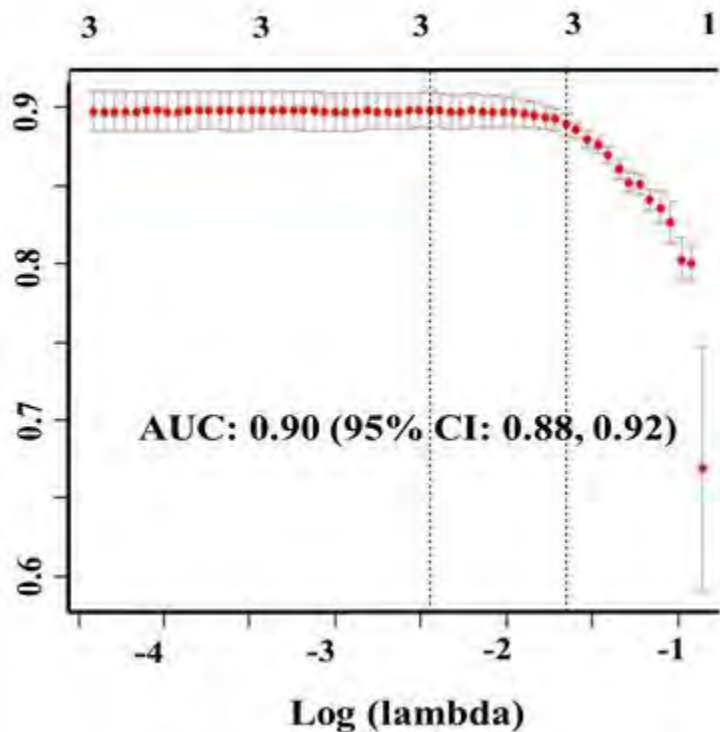


Fig. 1.

197 - Poster Session

Use and safety of minimally invasive hysterectomy for women with non-endometrioid endometrial cancers

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Objective: Minimally invasive hysterectomy is now routinely used for women with uterine cancer. Most studies of minimally invasive surgery (MIS) for endometrial cancer have focused on low-risk, endometrioid tumors with few reports of the safety of the procedure for women with higher risk histologies. We examined the utilization and survival of MIS for women with uterine cancer and high-risk histologies.

Methods: The National Cancer Database was used to identify women with stages I–III uterine cancer who underwent hysterectomy from 2010 to 2014. Women who had laparoscopic or robotic-assisted total hysterectomy were compared to those who had open abdominal hysterectomy. After propensity score-weighted analysis, the effect of MIS hysterectomy on overall, 30-day, and 90-day mortality was examined for each histologic subtype of uterine cancer.

Results: Of 94,507 patients identified, 64,417 (68.2%) underwent inimally invasive hysterectomy. Among women with endometrioid tumors ($n = 81,115$), 70.8% underwent inimally invasive hysterectomy. The rates of MIS in those with nonendometrioid tumors ($n = 13,392$) were 57.6% for serous carcinomas, 57.0% for clear cell tumors, 47.3% for sarcomas, 32.2% for leiomyosarcomas, 47.9% for stromal sarcomas, and 48.5% for carcinosarcomas. Performance of MIS increased across all histologic subtypes between 2010 and 2014. For nonendometrioid subtypes, robotic-assisted procedures accounted for 47.9%–75.7% of minimally invasive hysterectomies by 2014. In a multivariable model, women with nonendometrioid tumors were less likely to undergo MIS than those with endometrioid tumors ($P < 0.05$). There was no association between route of surgery and 30-day, 90-day, or overall mortality for any of the nonendometrioid histologic subtypes.

Conclusion: These data suggest that the use of minimally invasive hysterectomy is increasing rapidly for women with stage I–III nonendometrioid uterine tumors. Importantly, use of MIS does not appear to adversely effect survival.

198 - Poster Session

Intraperitoneal ports placed at the time of bowel resection: Complication rates and surgical outcomes

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Objective: At the time of cytoreduction surgery for ovarian cancer, many delay intraperitoneal (IP) port placement after a bowel resection because of concern for increased risk of IP port complication. The objective was to examine the perioperative outcomes of IP port placement at a cancer center where IP ports are frequently placed at the same time as a bowel resection is performed.

Method: Institutional review board approval was obtained to review the electronic medical records of patients who had an IP port placed between 2005 and 2016. Two groups were analyzed: IP ports placed with concurrent bowel resection (IP-BR) and those without (IP).

Results: Of 256 patient charts reviewed, 32% had concurrent bowel resection at time of IP port placement (IP-BR). Mean age at diagnosis was 61 years IP-BR versus 60 years IP ($P = 0.34$); mean BMI was 26 IP-BR versus 28 IP ($P = 0.13$); and 71% IP-BR versus 51% IP had stage IIIC disease ($P < 0.01$). In the IP-BR group, bowel resections were 71% rectosigmoid, 16% other colon, and 13% small bowel. Patients were optimally cytoreduced to R0 in 52% IP-BR versus 59% IP ($P = 0.33$), R1 in 38% IP-BR versus 26% IP ($P = 0.06$), and "optimal" in 7% IP-BR versus 13% IP ($P = 0.16$). After IP port placement, IV chemotherapy was given before starting IP chemotherapy in 77% IP-BR (median 2 cycles), which was no different than the IP group (76%, median 2 cycles, $P = 0.8$). Ultimately 80% IP-BR and 76% IP went on to receive IP chemotherapy ($P = 0.49$), and the median number of IP chemotherapy cycles was 4 in both groups. Rates of IP port complications were similar (14% vs 20%, $P = 0.26$), including IP port infections (3% IP-BR vs 1% IP, $P = 0.46$). Eleven percent of IP-BR patients had a bowel complication (e.g., bowel obstruction or perforation), while IP port was in situ versus 1% IP ($P < 0.01$). Five percent of both cohorts required revision or replacement of their IP ports, and only 5% IP-BR versus 4% IP discontinued planned IP chemotherapy course because of IP port complication ($P = 0.8$).

Conclusion: Placing an IP port at the same time as a bowel resection for ovarian cancer treatment did not appear to affect initiation of IP chemotherapy nor increase the risk of port complication. This may be due to improved healing of bowel anastomoses when first IP chemotherapy cycle is delayed.

199 - Poster Session

Optimizing blood management in gynecologic cancer patients undergoing laparotomy

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Objective: Perioperative blood transfusion is associated with poor ovarian cancer outcomes and higher complication rates. Our aim was to reduce perioperative red blood cell transfusion by 30% among open cancer cases through implementation of a standardized bundle of interventions.

Method: Multidisciplinary discussion led to identification of a bundled practice change. Interventions included blood transfusion practice standardization utilizing American Society of Anesthesiologists guidelines, an intraoperative hemostasis checklist, standardized intraoperative fluid status communication, and evidence-based use of tranexamic acid. Prospective data from women undergoing laparotomy for ovarian or endometrial cancer from September 28, 2015, to March 31, 2016, defined the study cohort and were compared to historical controls (September 1, 2014, to September 25, 2015). Outcomes were compared in the full unadjusted cohorts and in propensity-matched cohorts.

Results: In the intervention and historic cohorts, 89 and 184 women underwent laparotomy for ovarian cancer ($n = 74$ and 152) or advanced endometrial cancer ($n = 15$ and 32), respectively. Tranexamic acid was administered in 54 (60.7%) patients; a statistical stopping rule for venous thromboembolism was not reached. The perioperative transfusion rate was significantly lower for the intervention group compared to historic controls, 18.0% (16/89) versus 41.3% (76/184) ($P < 0.001$), a 56.4% reduction. This improvement in the intervention cohort remained significant following propensity matching, 16.2% (13/80) versus 36.2% (29/80) ($P = 0.004$). The hospital readmission rate was also significantly lower for the intervention group compared to historic controls, 1.1% (1/89) versus 12.5% (23/184) ($P = 0.002$); however, this improvement did not attain statistical significance following propensity matching, 1.2% (1/80) versus 7.5% (6/80) ($P = 0.12$). Cost analysis demonstrated that this intervention was cost-neutral during index hospitalization plus 30-day follow-up.

Conclusion: Application of a standardized bundle of evidence-based interventions reduced blood utilization in our gynecologic oncology practice. Tranexamic acid is a safe transfusion reduction adjunct for gynecologic cancer patients undergoing laparotomy.

200 - Poster Session

Epidural anesthesia is associated with improved overall survival in patients undergoing primary debulking surgery for ovarian cancer

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Objective: Epidural anesthesia has been associated with improved oncologic outcomes in other solid tumors, presumably because of its effect on surgical stress response. Our objective was to investigate the impact of epidural anesthesia on outcomes of patients undergoing primary debulking surgery (PDS) for advanced ovarian cancer.

Method: Patients with stage IIIB–IV, high-grade ovarian, fallopian tube, or peritoneal carcinoma who underwent PDS from January 2005 to December 2013 were identified. Patients with unknown epidural status were excluded. Demographic and clinical data were collected. Appropriate statistical tests were applied.

Results: Among 729 patients, 638 were included. Median age was 62 years (range 19–88 years). Median BMI was 26 kg/m² (range 16–59 kg/m²). ASA class was 1–2 in 47% and 3–4 in 53% of patients. Stage distribution was stage III, 77%, and stage IV, 23%. Carcinomatosis was noted in 85% and bulky upper abdominal (UAB) disease in 63%. Median length of hospital stay (LOS) was 8 days. Residual disease status was 0 mm in 43%, 1–10 mm in 36%, and >10 mm in 21%. Postoperative intraperitoneal (IP) chemotherapy was used in 46%. Median follow-up was 54.7 months (range 1.3–135.7 months), and the 3-year OS rate was 72% (95% CI 68%–75%). Epidural anesthesia was used in 70% of patients. There were no differences in age, BMI, ASA class, bulky UAB disease, LOS, or adjuvant chemotherapy use between the epidural and no-epidural groups. Compared to the no-epidural group, the epidural group had higher stage disease (stage III, 74% vs 83%; stage IV, 26% vs 17%; $P = 0.01$) and more commonly had carcinomatosis (87% vs 80%, $P = 0.03$), had complete gross resection (49% vs 30%, $P \leq 0.01$), and received IP chemotherapy (49% vs 39%, $P = 0.03$). Median OS was 62.4 vs 40.6 months for the epidural and no-epidural groups, respectively ($P \leq 0.01$), and the 3-year OS rate was 78% vs 59%, respectively. On multivariable analysis, no epidural use (HR = 1.52, 95% CI 1.21–1.9), bulky UAB disease (HR = 1.48, 95% CI 1.15–1.89), any residual disease (HR = 1.56, 95% CI 1.21–2.2), and unknown versus negative *BRCA* status (HR = 1.8, 95% CI 1.42–2.31) were significantly associated with worse OS. The use of IP chemotherapy was associated with improved OS (HR = 0.46, 95% CI 0.37–0.59). See Figure 1.

Conclusion: Despite higher stage disease and greater disease burden, epidural anesthesia use at the time of PDS appears to be associated with improved OS.

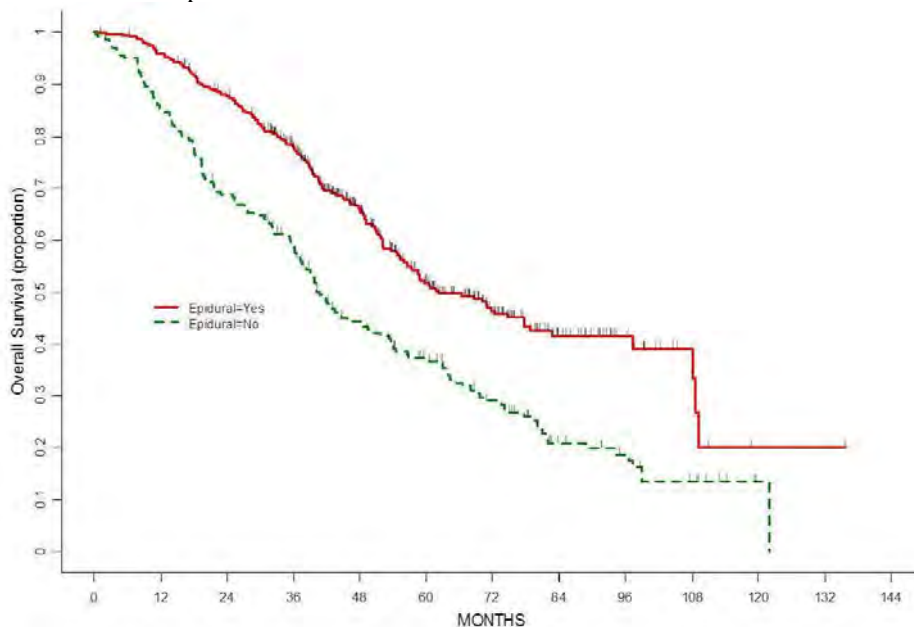


Fig. 1. OS by Epidural Usage.

201 - Poster Session

Does the time interval off neoadjuvant chemotherapy before and after interval debulking surgery affect the overall survival of women with advanced-epithelial ovarian cancer?

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Objective: To examine the impact of the time interval between neoadjuvant chemotherapy (NACT), interval cytoreduction surgery (ICS), and resumption of chemotherapy on the survival of women with advanced high-grade serous ovarian cancer (Ad-HGSC).

Method: This was a retrospective chart review between 2004 and 2012 of women with Ad-HGSC treated with NACT. Baseline characteristics including age, stage, histology, grade, number of chemotherapy cycles, prechemotherapy, and preoperative CA-125 levels as well as operative findings including residual disease (mm) and need for aggressive surgery were abstracted from the medical record. Survival analysis was conducted using Kaplan-Meier curves and Cox proportional hazard ratios, and subgroup analysis was stratified for residual disease.

Results: A total of 82 women met inclusion criteria. All had grade 3 serous histology; 69 were diagnosed with stage III and 13 with stage IV disease. Patients were stratified based on resection status (0 mm vs 1–9 mm residual disease), and there were no differences between these groups in terms of age, number of chemotherapy cycles after ICS, stage, CA-125 levels, or need for aggressive surgery. There was a slight difference in mean number of NACT cycles between the 2 groups (3.5 vs 3.7, $P = 0.045$). There was an overall survival (OS) advantage for patients who underwent 0 mm resection and had a shorter total time off NACT chemotherapy, defined as less than 56 days from last NACT to first consolidation cycle (HR = 0.45, CI 0.24–0.84, $P = 0.011$) and shorter interval from ICS to resuming consolidation chemotherapy (HR = 0.97, CI 0.94–1, $P = 0.022$). The time off chemotherapy had no impact on OS for patients who had 1–9 mm resection.

Conclusion: In patients who receive NACT followed by an ICS that achieves 0 mm resection, consideration should be given to reducing the time off chemotherapy to provide a survival advantage.

202 - Poster Session

Surgeon and patient factors related to false-positive (FP) identification of sentinel lymph nodes (SLN) with indocyanine green (ICG) in women with endometrial cancer

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Objective: The implementation of a sentinel lymph node (SLN) mapping algorithm at a single institution was evaluated. The purpose was to determine patient and surgeon factors that affect SLN identification. Because of the significant impact false-positive identification may have on treatment planning, experience with falsely positive SLN specimens is described.

Method: Women who underwent SLN mapping with indocyanine green (ICG) with or without pelvic and/or paraaortic lymph node dissection from November 2013 to April 2017 were prospectively identified. All patients had pathologically proven endometrial carcinoma. Data collection at the time of surgery was standardized for surgical characteristics. False-positive SLN specimens were those without a pathologically identified lymph node after ultrastaging.

Results: A total of 202 women were identified: 85% had endometrioid pathology, 12% serous, 3% carcinosarcoma, and 3% clear cell. Mixed pathology accounted for percentiles being greater than 100% in sum. The bilateral detection rate of SLN was 56%, and the rate of mapping at least a unilateral SLN 86%. There were 288 specimens removed from the right and left sides altogether after identification with ICG; of these, 29 (14% of all SLN identified) were found to be without nodal tissue (false positive). The overall SLN mapping rate did not change over time. There was a decrease in the rate of false-positive nodes when the first 10 cases (37%), cases 11–30 (28%), and >30 cases (9%) ($P = 0.006$) were compared. BMI >30 kg/m², fibroid uteri, FIGO grade, and uterine histology were not found to have a statistically significant effect on the false positive rate. There was a higher rate of false-positive SLN as the time from cervical injection to identification of the right SLN increased, with a median of 28 (17–63) versus 33 (23–74) minutes ($P = 0.024$).

Conclusion: False-positive SLNs represent a barrier to abandoning lymph node dissection. Intraoperative confirmation of nodal tissue at the time of SLN detection could be of use when adapting a sentinel lymph node technique. However, identification of false-positive SLN specimens decreases with surgeon case experience, suggesting a learning curve. The increase in false-positive associated with time from injection may represent delayed or disrupted uptake of tracer.

203 - Poster Session

Safety of fertility-sparing surgery for non-clear cell epithelial ovarian carcinoma confined to the ovary

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Objective: We aimed to investigate the safety of uterine preservation for women with epithelial ovarian cancer (EOC) using a population-based multiinstitutional database.

Method: The Surveillance, Epidemiology, and End Results database was accessed (1988–2014), and a cohort of women aged 45 years or younger and diagnosed with a unilateral high-grade (grade 2 and 3) non-clear cell EOC confined to the ovary was selected. Patients with grade 1 histology and those with a history of a previous primary tumor were excluded. Based on site-specific surgery codes, we determined whether hysterectomy was performed. Five-year overall (OS) and cancer-specific survival (CSS) rates were calculated following generation of Kaplan-Meier curves. Univariate comparisons were made using the log rank test. A Cox hazard model was constructed to control for possible confounders.

Results: A total of 1,039 women were identified. Median follow-up was 119 months. Rate of uterine preservation was 31.8% (330/1,039). Women who had hysterectomy were older ($P < 0.001$) and more likely to be white ($P = 0.048$). No difference in the rate of hysterectomy was observed between women with stage IA and IC disease (66.6% and 71.2%, respectively, $P = 0.14$) or those with grade 2 and grade 3 tumors (67.1% and 70.8%, respectively, $P = 0.26$). Patients with mucinous tumors were less likely to undergo hysterectomy (58.9%) compared to those with endometrioid (73.9%) and serous (75.9%) tumors ($P < 0.001$). Patients who did not undergo hysterectomy were less likely to receive lymph node sampling/dissection (LND) (55.1% vs 72.9%, $P < 0.001$). There was no difference in CSS between patients who did and did not have hysterectomy ($P = 0.70$) (5-year rates 93.9% vs 92.2%, respectively). Similarly, there was no difference in OS between the two groups ($P = 0.72$) (5-year rates 92.8% and 90.8% for women who did and did not undergo hysterectomy, respectively). After controlling for year of diagnosis, the performance of LND, tumor histology (serous vs nonserous) and grade (grade 2 vs grade 3), hysterectomy was not associated with better cancer-specific mortality (HR = 0.92, 95% CI 0.58–1.45) or overall mortality (HR = 1.13, 95% CI 0.76–1.70).

Conclusion: For patients with high-grade unilateral non-clear cell EOC confined to the ovary, uterine preservation was not associated with a worse prognosis.

204 - Poster Session

Does the use of manipulator for endometrial cancer surgery lead to increased use of adjuvant therapy?

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Objective: (1) To determine whether the use of intrauterine manipulator was associated with an increase in pathologic reporting of pseudo-lymphovascular invasion (LVSI). (2) To assess the potential impact of pseudo-LVSI secondary to balloon uterine manipulator use on adjuvant therapy.

Method: Women with early-stage (I–II) endometrial cancer of all histologies between 2012 and 2016 were included, and clinicopathologic characteristics were abstracted from the medical record including but not limited to race, BMI, grade, age, stage, histology, presence or absence of LVSI, peritoneal cytology, and adjuvant treatment. Slides were blindly reviewed by a gynecologic pathologist for the presence or absence of pseudo-LVSI.

Results: A total of 104 patients met eligibility criteria. Groups were well matched on race, BMI, and grade; however, nonendometrioid histology ($P = 0.046$), older age ($P = 0.02$), and stage 1B–II ($P = 0.01$) were more common in the no-manipulator group. There was no difference on the presence of pseudo-LVSI based on use of manipulator ($P = 0.86$), and in subgroup analysis there was no difference when grade was considered ($P = 0.79$). Six cases of misdiagnosis of LVSI were

identified, of which 3 patients who were in the manipulator group and received adjuvant radiotherapy may not have otherwise been triaged to adjuvant therapy.

Conclusion: Pathologists should remain cognizant of the possibility of pseudo-LVSI when evaluating uterine specimens because it may have an impact on adjuvant therapy. Surgeons may choose to use a uterine manipulator for endometrial cancer surgery because there does not appear to be an increased risk of skewing pathologic findings.

205 - Poster Session

Systematic lymphadenectomy influences adjuvant therapy in presumed localized endometrioid endometrial cancer, meeting Mayo criteria

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Objective: To evaluate the impact of lymphadenectomy for apparent stage I endometrioid endometrial carcinoma meeting Mayo criteria.

Method: Patients with endometrioid endometrial carcinoma who underwent hysterectomy and lymphadenectomy were identified from a tumor registry database. Patients not meeting Mayo criteria were excluded. Algorithms for adjuvant therapy both with and without lymphadenectomy were developed utilizing current NCCN guidelines and the results of PORTEC 1 and PORTEC 2. Each patient served as her own control to determine the frequency of treatment modification.

Results: A total of 357 patients were analyzed. A change in therapy occurred based on the results of lymphadenectomy in 62.8% of patients when whole pelvic external beam radiation was used for patients meeting inclusion criteria for PORTEC 1. A change in therapy occurred in 16.2% of patients when vaginal brachytherapy was used for patients meeting the inclusion criteria for PORTEC 2. When patients were allocated whole pelvic external beam radiation therapy when they met the inclusion criteria for PORTEC (53.8% of patients), there was a reduction in adjuvant radiation from whole pelvic radiotherapy to vaginal brachytherapy alone. When patients were allocated vaginal brachytherapy if they met the inclusion criteria for PORTEC 2, a reduction in therapy occurred in 7.0%. In 9.0% of patients adjuvant therapy was increased to include whole pelvic radiotherapy and chemotherapy. Reduction in therapy occurred more commonly in patients with high intermediate risk (outer half myometrial invasion and grade 2 and grade 3 histology). In patients younger than 70 years, management changed in 56.3% based on lymphadenectomy, whereas in patients older than 70 years adjuvant therapy was altered in 82.8% of patients when whole pelvic external beam radiation was used for patients meeting the inclusion criteria for PORTEC.

Conclusion: Using a standard adjuvant treatment algorithm following hysterectomy for endometrial cancer, using real patient data lymphadenectomy frequently altered treatment allocation.

206 - Poster Session

Incidence of perioperative venous thromboembolism in vulvar cancer

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Objective: To determine the 30-day perioperative incidence of venous thromboembolism (VTE) events in patients undergoing radical vulvectomy for vulvar cancer. Based on the Caprini Risk Assessment Model, patients undergoing radical vulvectomy for invasive cancer are at least moderate risk for VTE. Most patients have additional risk factors that make them high or highest risk. High-risk patients have an estimated 6% risk of VTE and receive both mechanical and pharmacologic anticoagulation. Recent studies report the incidence of symptomatic VTE in vaginal or vulvar cancer to be 1%–4%, though sample size has limited these studies.

Method: This cohort study examined patients undergoing radical vulvectomy, with or without staging inguinal lymphadenectomy for vulvar cancer from 2005 to 2015. Patients were identified from the American College of Surgeons National Surgical Quality Improvement Program database using the International Classification of Diseases ICD-9 and ICD-10. Data regarding the primary outcome, 30-day incidence of VTE, as well as patient demographics and comorbid conditions were collected. Patients who underwent concurrent myocutaneous flap, fecal diversion, or pelvic exenteration were excluded.

Results: A total of 559 patients met inclusion and exclusion criteria. Of these patients, 1 (0.2%) experienced pulmonary embolism, and 3 (0.5%) experienced deep venous thrombosis, thus 4 total reported VTE events (0.7%). Mean age was 66.7 years (SD = 13.8). Mean height was 62.9 inches (SD = 3.1), and median weight was 165 pounds (IQR 140–200) making mean BMI 30.5 (SD = 7.8) and in the obese range. Ten patients (1.8%) had disseminated cancer, and 1 patient (0.2%) received chemotherapy within the 30 days prior to surgery. Fifteen patients (2.7%) were reported to have bleeding disorders; median preoperative INR was 1.0 (IQR 0.98–1.1). There were not enough affected patients to compare the cohort with VTE to those without VTE.

Conclusion: The observed incidence of VTE within 30 days of radical vulvectomy was 0.7%, significantly less than predicted. This incidence calls into question the role for chemical chemoprophylaxis and its inherent risks. Future larger scale studies are necessary to better risk-stratify patients to determine who should receive perioperative anticoagulation.

207 - Poster Session

Timing of robotic hysterectomy after cervical excisional procedure and associated perioperative complications

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Objective: To determine whether the time between cervical excisional procedure (LEEP and CKC) and robotic hysterectomy has an impact on perioperative complication rates.

Method: A retrospective cohort of patients who underwent robotic hysterectomy from August 2006 to December 2013 for cervical dysplasia or cervical cancer at a single tertiary care center was evaluated. Patients were divided into 3 groups depending on the amount of time between cervical excision and robotic hysterectomy: early surgical intervention (less than 6 weeks), delayed surgical intervention (6 weeks or more), and no excisional procedure. Patients who had an excisional procedure less than 6 months prior to hysterectomy were placed in the no-excisional procedure group. Perioperative complications were compared using standard statistical analysis.

Results: A total of 160 patients were identified: 32 (20.0%) had early surgical intervention; 52 (32.5%) had delayed surgical intervention; and 76 (47.5%) had no excisional procedure. There was no difference between groups in aggregate perioperative complication rate (16% vs 12% vs 17%, $P = 0.68$) or individual complications, including estimated blood loss ($P = 0.07$), length of surgery ($P = 0.51$), cystotomy (0 vs 2% vs 1%, $P = 1.0$), ureteral injury (0 vs 0 vs. 0, $P = 1.0$), vessel injury (0 vs 2% vs 0, $P = 0.53$), fever (3% vs 6% vs 8%, $P = 0.76$), anemia (3% vs 0 vs 1%, $P = 0.47$), urinary retention (3% vs 0 vs 4%, $P = 0.41$), infection (0 vs 2% vs 3%, $P = 1.0$), vaginal cuff separation (0 vs 0 vs 0, $P = 1.0$), or venous thromboembolism (0 vs 0 vs 1%, $P = 1.0$, respectively). In addition, there were no differences in length of stay (1.1 vs 1.2 vs 1.4 nights, $P = 0.18$) or 30-day readmission rates (6% vs 6% vs 5%, $P = 1.0$, respectively). Complications were stratified by number of weeks between the 2 procedures to identify an optimal time to perform robotic hysterectomy after cervical excision. There was no time point at which overall complication rate differed between the groups ($P = 0.18$).

Conclusion: Waiting 6 weeks between cervical excisional procedure and robotic hysterectomy does not have an impact on perioperative complications rates. Furthermore, there does not appear to be any time point at which complication risk is affected. This suggests that the time from excisional procedure should not factor into surgical planning for those who undergo robotic hysterectomy.

208 - Poster Session

Stage IV high-grade endometrial cancer: Are outcomes improved by interval surgical debulking?

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Objective: Annually, approximately 61,000 women will be diagnosed with endometrial cancer (EC), with the majority being at an early stage. Unfortunately, some women are found at stage IV, and the treatment for these women involves multimodal therapy. The timing of these treatments varies from institution to institution and often can vary among physicians within a facility. The purpose of this study was to compare progression free survival (PFS) and overall survival (OS) for women with high-grade, stage IV EC who were either treated with neoadjuvant chemotherapy (NACT) followed by interval debulking to those women treated with primary surgery (PS) followed by adjuvant chemotherapy.

Method: This was a retrospective case series of all patients with stage IV high-grade EC treated at a single academic care center between 1990 and 2016. Demographic and operative data were examined using SPSS 20.0 for all statistical analysis. Kaplan-Meier survival curves and log rank tests were used to compare PFS and OS in the two groups. Complications, length of stay, and residual disease were analyzed with Fisher exact and Kruskal Wallis tests for categorical variables, and Mann-Whitney U test for continuous variables. A two-tailed significance level of $P < 0.05$ was used for all statistical tests.

Results: From 1990 to 2016, a total of 186 patients were treated for high-grade EC, with 30 of these patients identified as having stage IV disease. Of the stage IV patients, 20 were treated with PS and 10 underwent NACT. There were no significant differences in demographic data among these patients. Median PFS for the PS cohort was 9 months and for the NACT cohort, 10.5 months ($P = 0.50$). OS did not meet statistical significance, with 10 months in the PS compared to 18.5 months in the NACT cohort ($P = 0.15$). The only statistical difference in the groups was in the rate of blood transfusions; 6 (60%) of the NACT patients required blood transfusions, compared to 4 (20%) PS patients ($P = 0.05$).

Conclusion: In this small cohort of high-grade stage IV EC patients, timing of treatments did not affect PFS or OS. Differences in quality of life and chemotherapy delays were not evaluated. This study did show an 8.5-month improvement in OS for NACT patients, and in a larger cohort this may prove to be significant. Future studies may allow us to better elucidate the most beneficial timing of therapy in managing high-grade stage IV EC.

Table 1. Demographics.

Demographics	Interval Debulking <i>n</i> = 10	Primary Surgery <i>n</i> = 20	P-value
Age - median (range)	68 (59 - 80)	65.5 (56 - 82)	0.61
Race - <i>n</i> (%)			0.29
Black	2 (20)	8 (40)	
White	8 (80)	12 (60)	
BMI - median (range)	29 (22 - 48)	29 (23 - 38)	0.95
Normal (18 - 24) - <i>n</i> (%)	3 (30)	3 (15)	
Overweight (25 - 29) - <i>n</i> (%)	2 (20)	4 (20)	
Obese (> 30) - <i>n</i> (%)	5 (50)	7 (35)	
Comorbidities - <i>n</i> (%)			
HTN	8 (80)	13 (65)	0.67
Diabetes	2 (20)	2 (10)	0.58
COPD	0	2 (10)	0.54
DVT/PE/VTE	2 (20)	4 (20)	1
AFib	1 (10)	1 (5)	1
Tumor Histology - <i>n</i> (%)			
Carcinosarcoma (MMMT)	3 (30)	9 (45)	0.69
Clear Cell	2 (20)	2 (10)	0.58
Grade 3 Endometrioid	0	0	
Serous	5 (50)	9 (45)	1

209 - Poster Session

Prospective validation of sentinel lymph node (SLN) biopsy with indocyanine green (ICG) fluorescence imaging in high-risk endometrial cancer

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Objective: To validate sentinel lymph node biopsy (SLNB) using near-infrared fluorescence imaging (NIR) with indocyanine green (ICG) in high-risk endometrial cancer (EC).

Method: We performed a prospective multicenter cohort study of SLNB by ICG fluorescence imaging in high-risk EC. Patients with clinical stage 1 grade 2 endometrioid or high-grade EC (serous, clear cell, carcinosarcoma, undifferentiated) undergoing laparoscopic or robotic primary surgery at two cancer centres in Toronto, Canada, were recruited for SLNB with ICG by cervical injection. Patients with high-grade EC also underwent pelvic and paraaortic lymphadenectomy (PLND/PALND), and patients with grade 2 endometrioid EC underwent PLND only. Patients with grade 1 EC or evidence of metastatic disease were excluded. SLNs were submitted for frozen section followed by ultrastaging with hematoxylin/eosin and immunohistochemistry for cytokeratin if negative. The primary endpoint was bilateral detection rate (DR), and the secondary endpoint was sensitivity (SN). All patients who underwent ICG injection were included in the primary analysis, and those with least 1 SLN identified were included in the secondary analysis.

Results: Eighty-eight patients with median age 64 years (IQR 59–69) and BMI 27 (IQR 24–33) were accrued (August 2015 to 2017). All patients had SLNB and PLND, and 44/48 patients (92%) with high-grade EC had PALND. Median numbers of SLNs, PLNs, and PALNs removed per patient were 3 (IQR 2–5), 16 (IQR 12–20), and 6 (IQR 4–10), respectively. SLN DRs were 99% per patient (87/88), 89% per hemipelvis (157/177), and 80% bilaterally (70/88). Fifteen (17%) patients had nodal metastases. SLNB correctly identified 14/15 of these patients, yielding an SN of 93.3% (95% CI 0.68–1.00), a false negative rate of 6.7% (95% CI 0–0.32), and a negative predictive value of 99% (95% CI 0.93–1.00). One patient (1.1%) would have been misclassified as node negative by SLNB. In 60% of patients (9/15) with LN metastases, the SLN was the only positive LN.

Conclusion: SLNB by ICG fluorescence imaging has excellent performance characteristics and may be superior to conventional tracers in high-risk EC. SLNB may be an alternative to pelvic and paraaortic LND for high-risk EC once its efficacy has been documented at an institution.

210 - Poster Session

Cardiophrenic lymph nodes resection as part of cytoreduction for primary or recurrent ovarian carcinoma: A cohort study

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Objective: To report our experience and clinical outcomes in patients with epithelial ovarian carcinoma (EOC) in which a resection of cardiophrenic lymph nodes (CPLN) was performed.

Method: Retrospective review in a cohort of patients with EOC who underwent the resection of cardiophrenic lymph nodes. The CPLN must have been the only detectable site of extra-abdominal disease.

Results: Twenty-one patients were included, all with high-grade serous EOC. Ten patients had recurrent disease, while in 11 the cytoreduction was part of primary treatment (4 after neoadjuvant chemotherapy). If the CPLN were suspicious of metastasis by imaging staging and after complete abdominal cytoreduction was achieved, a transdiaphragmatic incision to access the paracardiac space was performed. Sixteen patients underwent a right CPLN dissection, while 3 were on the left side and 2 patients had bilateral resection. The average time of the procedure was 28 minutes with minimal blood loss. No severe complications were noticed, but 4 patients reported moderate or severe pain in the insertion of the tube thoracostomy. The

CPLN were positive in 19 patients; of these, 13 achieved more than 12 months of follow-up. All those patients had recurrent disease. The average disease-free survival was 19 months (17 in the recurrent group, 21 in the nonrecurrent). The mediastinum and/or brain was the site of recurrence in 10 patients. Five patients lived longer than 40 months (14–180) after the CPLN resection. The patients with less than 1-year follow-up are all alive without evidence of disease.

Conclusion: The finding of metastasis at CPLN in ovarian cancer is uncommon. Its resection is a feasible procedure with low morbidity and should be considered in the suspicion of involvement and in the possibility of obtaining complete cytoreduction.

211 - Poster Session

How different histologic components of mixed endometrial carcinomas affect prognosis: Does it really matter?

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Objective: We evaluated the tumor characteristics and clinical outcome of patients with mixed endometrial carcinomas (MEC) and compared them to those of patients with pure endometrial carcinomas.

Method: We retrospectively reviewed data of patients with MEC between 2005 and 2015. Overall survival and disease-free survival rates were evaluated, taking into account the percentage of each histologic component. Clinicopathological variables and treatment strategies were also assessed. Similar data were collected from patients with endometrioid (EC), serous (SC), and clear cell (CC) carcinomas in the same period and compared to MEC parameters. χ^2 tests were used for comparison of proportions. Kaplan-Meier curves were used to compare recurrence and survival.

Results: Sample consisted of 302 cases (52 CC, 74 SC, 128 EC, and 48 MEC) with mean age 66.3 years (SD = 11.5). Early-stage disease was recorded in EC patients compared with CC and SC patients. Adnexal involvement was more frequent in MEC patients compared with pure EC patients ($P = 0.043$). Extra uterine metastasis was more frequent in the SC group compared to the EC group, while lymphovascular space involvement (LVSI) was more frequent in the MEC and CC groups compared to the SC group ($P = 0.001$). EC patients had less omentum involvement compared to CC ($P = 0.035$) and SC ($P < 0.001$) patients. Furthermore, cervical involvement was more common in the CC group compared to the EC group ($P = 0.011$). Both recurrence ($P = 0.265$) and survival ($P = 0.533$) rates were found to be similar in MEC patients compared with pure CC, SC, and EC. In addition, recurrence and survival were similar between EC-CC and EC-SC patients. There were no differences in recurrence and survival in MEC patients with a type II component larger than 10% or 20% ($P > 0.05$).

Conclusion: There is no statistical difference regarding overall survival and disease-free survival among MEC patients with a type II component >10% and SC, CC, or EC patients. Moreover, recurrence and survival rates were similar between EC-CC and EC-SC. Our results demonstrated that MEC patients with type II component >10% show no difference in survival rates compared to those with type II component <10%, contributing to current published literature.

212 - Poster Session

Clinical and surgical predictors of anastomotic leak in gynecologic oncology

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Objective: Anastomotic leak after bowel resection is often accompanied by significant morbidity and prolonged postoperative recovery. Risk factors associated with AL in gynecologic oncology are often abstracted from the colorectal literature. The objective of this study is to determine morbidity and 90-day mortality associated with bowel surgery during gynecologic oncologic procedures. We also aimed to identify perioperative factors and operative techniques associated with anastomotic leak.

Method: The tumor registry at our institution was queried to identify all patients between 2006 and 2016 with a gynecologic malignancy that underwent bowel resection at the time of cytoreductive surgery. Patient charts were reviewed to extract clinical and surgical data. Time to chemotherapy was used as a proxy for postoperative recovery. Logistic and linear regressions were used in the univariate and multivariate analyses to identify variables associated with anastomotic leak, 90-day mortality, and time to chemotherapy. Significance was established at $P < 0.05$.

Results: One hundred and fifty patients met inclusion criteria. Preoperative albumin and anastomotic leak were significantly associated with 90-day mortality in the multivariate analysis. On univariate analysis, two or more bowel anastomoses, longer operative times, American Society of Anesthesiologists Physical Status (ASA) classification >2, and absence of postoperative parenteral nutrition were significantly associated with anastomotic leak. On multivariate analysis, more than 1 bowel anastomosis, not imbricating the anastomotic line, ASA >2, and 90-day mortality were significantly associated with anastomotic leak. No difference in time to chemotherapy was observed between patients with and without anastomotic leak.

Conclusion: Our data confirm findings from prior studies suggesting that multiple bowel resections are a potential risk factor for anastomotic leak. Furthermore, our study is the first in the gynecologic oncology literature to correlate other clinical characteristics and surgical techniques with anastomotic leak and 90-day mortality.

213 - Poster Session

Personalized surgical algorithm for advanced ovarian cancer: Results from a prospective quality improvement project

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Objective: To determine the impact of a laparoscopic triage algorithm in advanced ovarian cancer on complete gross surgical resection (R0) rates and clinical outcomes.

Method: We prospectively triaged patients from April 2013 to December 2016 with suspected advanced-stage ovarian cancer to laparoscopic scoring assessment to determine primary resectability at tumor reductive surgery (TRS). Patients with medically inoperable or distant metastatic disease received neoadjuvant chemotherapy (NACT). Two-surgeon scoring was performed in a blinded fashion using a validated scoring method. Patients with predictive index value (PIV) scores greater than 8 were offered primary surgery, and those with scores 8 or less received NACT. Univariate and multivariate analyses were performed for effects on progression-free survival (PFS).

Results: A total of 621 patients who presented with presumed advanced ovarian cancer were evaluated during the study period, and 488 patients met inclusion criteria. There were 215 patients who underwent laparoscopic scoring, of which 125 patients had a PIV score greater than 8 and 84 had a PIV score of 8 or less. Blinded 2-surgeon PIV scoring resulted in a bivariate discordance in only 2% of cases. Patients were categorized into 3 groups: primary surgery ($n = 138$), NACT/no scope ($n = 243$), and NACT/scope ($n = 104$) with corresponding R0 resection rates at TRS of 88%, 81%, and 76%, respectively. Median PFS was as follows: primary surgery/R0 23.5 months; primary surgery/R1 16.4 months; NACT/R0 12 months; and NACT/R1 10.1 months ($P < 0.001$). On multivariate analysis for PFS, ECOG status (HR = 1.38, 95% CI 1.09–1.75, $P = 0.007$), gross residual disease at TRS (HR = 1.92, 95% CI 1.23–3.01, $P = 0.004$), and primary TRS (HR = 0.56, 95% CI 0.35–0.89, $P = 0.01$) were significantly related to PFS.

Conclusion: Laparoscopic triage assessment allowed for a personalized approach to the management of advanced ovarian cancer patients and resulted in high R0 resection rates at the time of surgery.

214 - Poster Session

Sentinel lymph node biopsy combined with frozen section examination in cervical cancer: A single-institution pilot study

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Objective: To evaluate the accuracy of sentinel lymph node (SLN) biopsy combined with frozen section (FS) examination in detecting nodal metastasis of cervical cancer.

Method: Seventy-five patients with FIGO stage IA2–IIB cervical cancer were enrolled in this prospective study. SLN biopsy and intraoperative FS examination were routinely performed, and the results were compared with those of postoperative paraffin section (PS) examination involving an ultrastaging protocol.

Results: Of the 75 enrolled patients, at least 1 SLN was successfully detected in 69 (92.0%). A total of 15 metastatic SLNs were confirmed in 10 patients. In addition, 1 patient without SLN detected also had nodal metastasis. Micrometastasis and isolated tumor cells (ITC) in SLNs were detected by ultrastaging in 2 FS-negative cases. No pelvic or paraaortic nodal metastasis was detected in patients with PS-negative SLNs. On the basis of PS examination, the sensitivity and negative predictive value (NPV) for SLN biopsy were 100% (10/10, 95% CI 71.7%–100.0%) and 100% (59/59, 95% CI 95.4%–100.0%), respectively, while they were 80.0% (8/10, 95% CI 40.0%–97.2%) and 96.8% (59/61, 95% CI 89.0%–99.6%) on the basis of FS examination, respectively. No significant difference was found in either sensitivity ($P = 0.757$) or NPV ($P = 0.899$) between the FS and PS examinations.

Conclusion: The SLN biopsy combined with FS examination has acceptable accuracy in predicting pelvic nodal metastasis. The FS examination is not significantly worse than the PS one and should be performed as a routine procedure in SLN biopsy for cervical cancer.

215 - Poster Session

Hematologic changes in women with and without infection after splenectomy during primary or interval debulking surgery for ovarian, tubal, or primary peritoneal cancer

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Objective: Splenectomy is a known risk factor for infection, yet infection is difficult to diagnose after splenectomy given frequent postoperative leukocytosis. The objective of this study was to correlate hematologic changes with infection in patients who had a splenectomy during cytoreductive surgery for ovarian cancer.

Method: This was a retrospective review of all patients who underwent a splenectomy during primary (PDS) or interval (IDS) cytoreductive surgery for advanced-stage ovarian, tubal, or primary peritoneal cancer between March 2001 and December 2016. We compared patients who developed an infection within 30 days of surgery (INF) and those who did not (non-I). Infection was defined as a positive culture or classic clinical and/or radiologic findings. For analysis, patients treated empirically with antibiotics were part of the INF group. Appropriate statistical tests were applied.

Results: There were 265 patients who had a splenectomy during PDS or IDS within the study period. Median age of presentation was 64 years (range 22–88 years). A total of 146 patients (55%) presented with stage IIIC disease, and 114 (43%) with stage IV. In 201 (76%) patients, splenectomy was done at the time of PDS. Optimal debulking (≤ 1 cm residual disease) was achieved in 254 (96%). The INF group comprised 132 patients (50%), with urinary tract as the most common (54%), and the non-I group comprised 133 (50%). Median time from surgery to infection was 8 days (range 0–29 days). Figure 1 shows the median white blood cell count (WBC) between postoperative day (POD) 0 and 15 for INF and non-I groups. After an initial rise in WBC in both groups, the INF group had a second WBC peak on POD 10 (median 16.6 K/mcL, interquartile range 12.5–21.2), which was not seen in the non-I group (median POD 10 WBC 12K/mcL, interquartile range 9.3–16.3). There was no difference in the daily median platelet count from POD 0 to 15 between INF and non-I, with both groups showing a progressive increase in platelets between POD 0 and 15.

Conclusion: We identified initial leukocytosis after splenectomy in all patients studied, but the INF group displayed a second peak of WBC on POD 10, which was not present in the non-I group. There was no difference in platelet counts between the two groups. These findings may help guide postoperative management in patients with splenectomy during cytoreduction for advanced ovarian cancer.

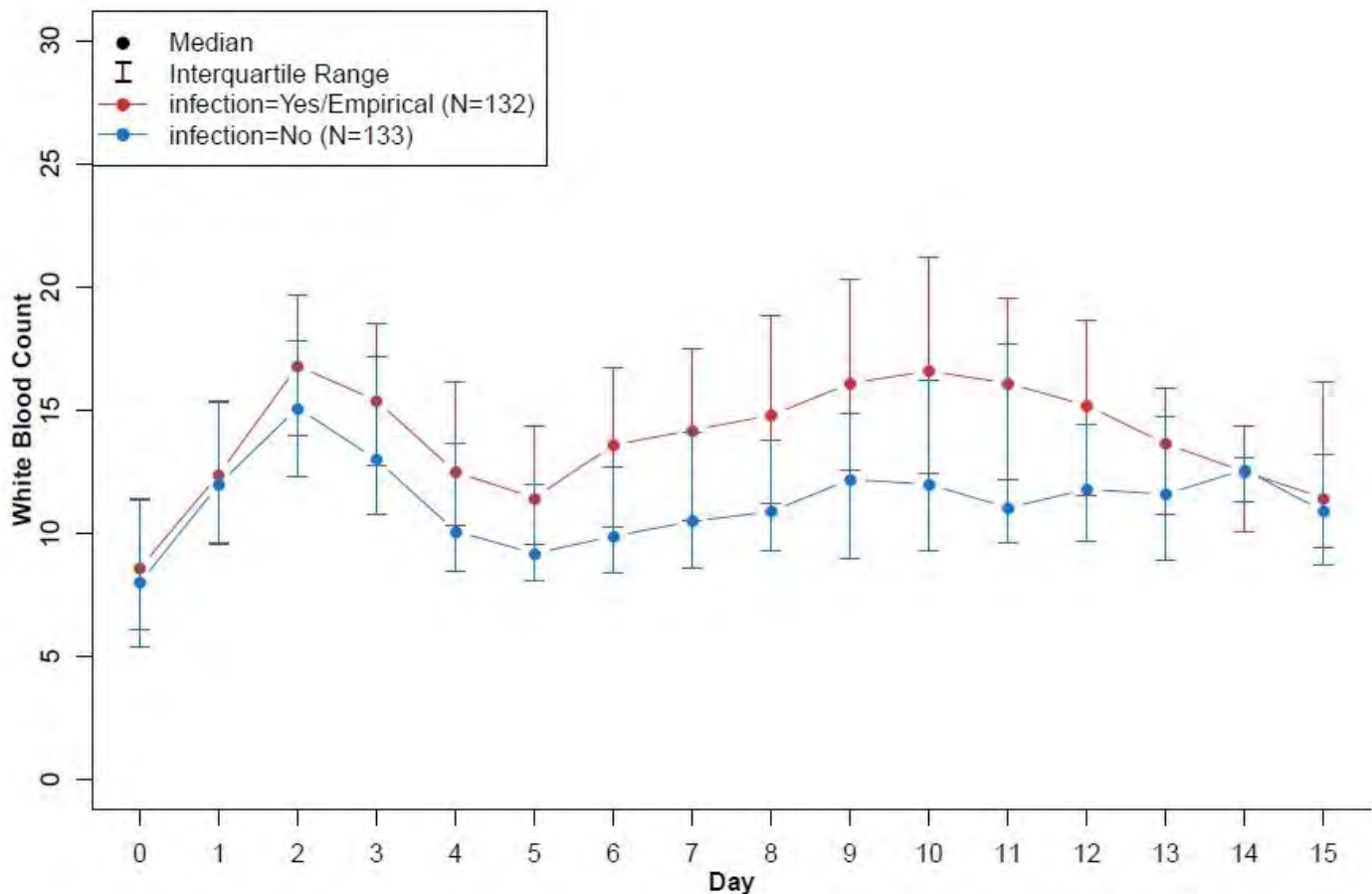


Fig. 1.

216 - Poster Session

Platelet counts and venous thromboembolism after splenectomy in women undergoing primary or interval cytoreduction for ovarian, tubal, or primary peritoneal cancer

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Objective: Thrombocytosis after splenectomy for hematologic disease is common, and venous thromboembolisms (VTE) occur in approximately 10% of these patients. The objectives of this study were to evaluate changes in platelets in patients who underwent a splenectomy during cytoreductive surgery for ovarian cancer, and to evaluate whether there was any correlation to VTE.

Method: We retrospectively reviewed the records of all patients who had a splenectomy during primary (PDS) or interval (IDS) debulking surgery for advanced ovarian, tubal, or primary peritoneal cancer from March 2001 to December 2016. VTE was defined as radiologic evidence of a deep venous thrombosis (DVT) or pulmonary embolism (PE). Thrombocytosis (TBC) was defined as a platelet count above the institutional upper cutoff (400 K/mcL). We compared the postoperative platelet trends for patients who developed a VTE with those who did not. Appropriate statistical analyses were applied.

Results: The 265 patients who had a splenectomy during PDS or IDS during the study period formed the study cohort. The median age was 64 years (range 22–88 years) with 146 cases (55%) of stage IIIC disease and 114 (43%) stage IV. PDS was performed in 201 (76%), while 64 (24%) had IDS. For the entire cohort, gross residual disease was none, 124 (47%); ≤1 cm, 128 (48%); and >1 cm, 9 (3%). Of the total 265 patients, 40 (15%) developed a VTE, while 225 (85%) did not. The median time from surgery to the diagnosis of VTE was 6.5 days (range 1–43 days). Figure 1 represents the daily median platelet count from postoperative day (POD) 0 to POD 15 for patients with and without VTE. Both groups demonstrate a similar and continuous rise in the platelet count from POD 0 to POD 15. TBC was present in 38/40 (95%) patients with a VTE, compared to 183/225 (81%) of patients without a VTE ($P = 0.036$). Among the 221 patients with TBC, the median number of days with TBC was higher in the VTE group (8 days, range 1–15) than in the non-VTE group (6 days, range 1–16 days, $P = 0.049$).

Conclusion: In our study, all patients had a progressive postoperative increase in platelet count after splenectomy. Among patients who developed a VTE, thrombocytosis was more frequent and of longer duration compared to those who did not develop a VTE. These findings may assist in future postoperative preventive management approaches and early detection strategies.

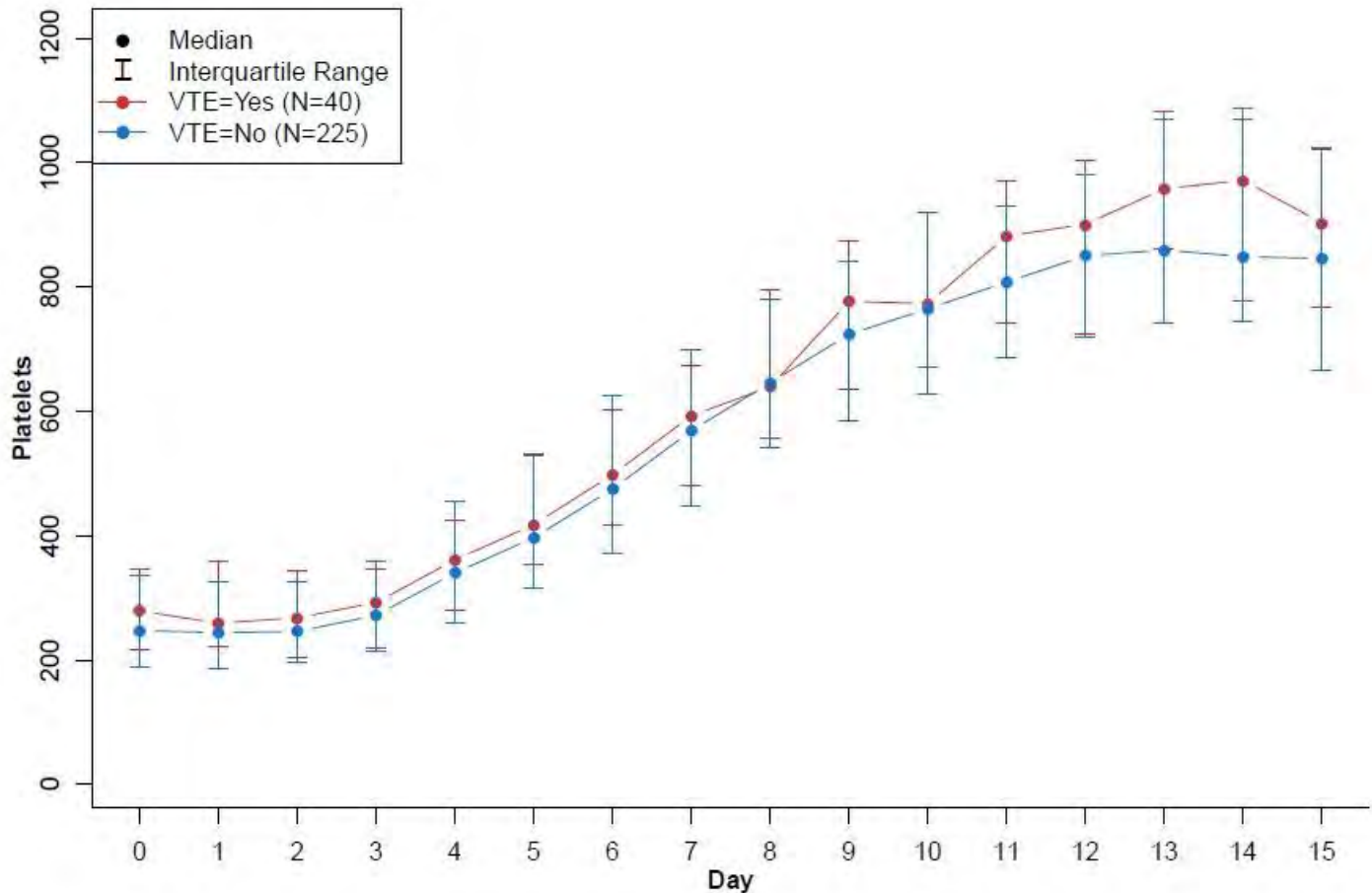


Fig. 1.

217 - Poster Session

Investigating the time intervals between primary cytoreductive surgery and initiation of adjuvant chemotherapy in patients with advanced epithelial ovarian cancer who had optimal cytoreduction surgery with bowel resection

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Objective: Cytoreductive surgery for advanced epithelial ovarian cancer often includes resection of the bowel to achieve optimal or complete cytoreduction. The optimal timing of adjuvant chemotherapy following primary cytoreductive surgery (PCS) that includes bowel resection remains unclear.

Method: A retrospective chart review at 2 tertiary cancer centers was performed. Patients diagnosed between 2002 and 2015 with FIGO stage III or IV grade 3 epithelial ovarian carcinoma who achieved optimal residual disease (0 mm or 1–9 mm) with bowel resection at the time of PCS were eligible. Treatment interval was defined as the time between the date of PCS and the date of the first cycle of adjuvant chemotherapy. Cox regression models were used to determine the impact of interval on overall survival (OS).

Results: A total of 91 patients met inclusion criteria. Median age was 57 years (range 35–86 years), and median follow-up period was 36.0 months (range 2–128 months). During the study period, 20 (22.0 %) deaths were observed. The 5-year OS rate was 71.0%. Residual disease of 1–9 mm was observed in 38.5% (35/91) of patients, and microscopic residual disease of 0

mm was noted in 61.5% (56/91). Median interval was 21 days (range 7–86 days). Rectosigmoid resection was the most commonly performed bowel procedure, 82.4% (75/91); 12.1% (11/91) of patients had multiple bowel resections; 18.7% (17/91) had bowel diversion; and 42.9% (39/91) had upper abdominal surgery including liver, diaphragm, or spleen resection. The rate of anastomotic leak, bowel fistula, or anastomotic abscess was 13.2% (12/91), which had a significant impact on the treatment interval ($P = 0.021$). Intervals were categorized as 2 weeks or less, 2–4 weeks, and 4 weeks or more. Kaplan-Meier analysis showed that intervals between 2 and 4 weeks were associated with improved OS compared to the other groups. On Cox analysis, intervals between 2 and 4 weeks ($P = 0.023$), 0 mm residual disease ($P = 0.013$), young age (older than 70 years, $P = 0.027$), and completing 6 cycles of chemotherapy ($P = 0.002$) were independent prognostic factors of improved OS.

Conclusion: These data suggest that survival outcomes may be affected by the interval between PCS and the first cycle of adjuvant chemotherapy in advanced ovarian cancer. The ideal timing to initiate adjuvant chemotherapy in patients who undergo PCS including a bowel resection appears to be 2–4 weeks postoperatively.

218 - Poster Session

Characteristics and outcomes of reproductive age women with early-stage cervical cancer who underwent trachelectomy

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Objective: To examine trends, characteristics, and survival of reproductive age women who underwent trachelectomy for early-stage cervical cancer.

Method: This is a retrospective observational study examining the Surveillance, Epidemiology, End Results Program between 1998 and 2013. Women younger than 45 years with stage IA and IB1 (tumor size ≤ 2 cm) cervical cancer who underwent trachelectomy were compared to those who underwent hysterectomy. Multivariable models were used to identify clinicopathological factors for trachelectomy use. Survival outcome was compared between the two groups after propensity score matching.

Results: Among 5,534 women, 176 (3.2%, 95% CI 2.7–3.6) underwent trachelectomy. The median age of the trachelectomy group was 31 years (range 18–44 years), and 92 (52.3%) women had stage IB1 disease. The proportion of women who underwent trachelectomy significantly increased during the study period (1.8% in 1998–2003, 3.3% in 2004–2008, and 4.3% in 2009–2013, $P < 0.001$). On multivariable analysis, younger age, single marital status, Eastern registry area, nonsquamous histology, and higher stage were independent factors associated with trachelectomy use (all, adjusted $P < 0.05$). After propensity score matching, women who underwent trachelectomy had 5-year cause-specific survival (96.0% vs 96.1%, HR = 1.33, 95% CI 0.37–4.70, $P = 0.66$) and overall survival (94.5% vs 96.1%, HR = 1.40, 95% CI 0.46–4.29, $P = 0.55$) rates similar to those who had hysterectomy.

Conclusion: Our study found that approximately 1 in 30 women younger than 45 years with stage IA and IB1 (≤ 2 cm) cervical cancer underwent trachelectomy in recent years. Survival with trachelectomy remained acceptable in this population.

219 - Poster Session

A personalized surgical approach to advanced ovarian cancer based on multiple predictive models for R0 resection: A prospective cohort study

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Objective: To present surgical outcomes of advanced epithelial ovarian cancer (AEOC) since implementation of a personalized approach and to validate the performance of multiple predictive models for R0 resection.

Methods Since September 1, 2015, the specialized ovarian cancer unit at FUSCC has implemented a personalized surgical approach to all suspected AEOC. Predictive models and our strategies were (1) a noninvasive model and (2) a minimally invasive model. In the first model, preoperative clinicoradiological assessment was performed according to Suidan Criteria for R0 resection with a predictive score for all. Those with a score 0–2 were almost sent to primary debulking surgery (PDS, group

A), and the others with a score ≥ 3 were counselled about the choices of PDS (group A), neoadjuvant chemotherapy (NAC, group B) or an optional staging laparoscopy (S-LPS). The second model was S-LPS with a predictive index value (PIV) according to Fagotti. Those with a PIV < 8 underwent PDS (group C); otherwise, they received NAC (group D). Clinicopathological data were prospectively collected, including intraoperative assessment of tumor burden (with Eisenkop and PCI score) and surgical results. See Figure 1.

Results: Between September 1, 2015, and August 31, 2017, 161 patients with pathological confirmed EOC were included in the analysis; 52 (32.3%) had a predictive score of 0–2, and 109 (67.7%) had a score ≥ 3 . Among them, 41 (25.5%) patients received S-LPS. Finally, 110 (68.3%) patients underwent PDS (A+C), and 51 (31.7%) patients received NAC (B+D). The optimal resection rate in PDS and NAC patients were 84.5% (56.4% R0 and 28.2% < 1 cm) and 90.2% (60.8% R0 and 29.4% < 1 cm) respectively. For R0 resection, the AUC of clinicoradiological predictive score was 0.548 in the whole PDS group (A+C). The AUC of Fagotti score was 0.702 in group C. The AUC of Eisenkop score and PCI score was 0.808 and 0.797, respectively.

Conclusions: The Suidan criteria was not effective in our patients. S-LPS was helpful for decision making of PDS and should be endorsed in AEEOC in the future.

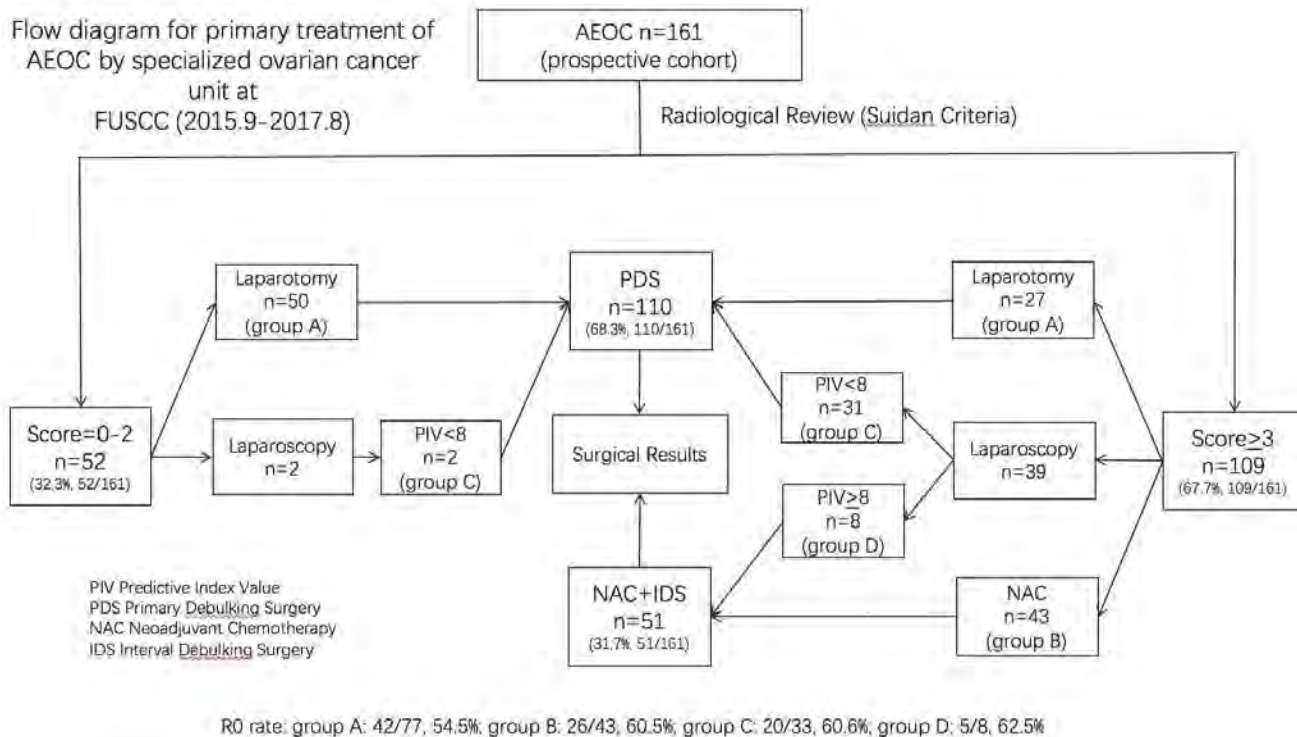


Fig. 1.

220 - Poster Session

Are preoperative antibiotics indicated in vulvar excisions for premalignant lesions?

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Objective: Although strict guidelines on antibiotic prophylaxis exist for most gynecologic surgeries, there is lack of evidence-based recommendations on antibiotic use in patients undergoing vulvar excision for premalignant lesions. We aimed to determine the rate of wound complications after vulvar surgery for premalignant lesions and to evaluate the effectiveness of antibiotic prophylaxis in reducing this seemingly common postoperative morbidity.

Method: We performed a single-institution, retrospective cohort study of women who underwent vulvar surgery for premalignant indications between January 2007 and January 2017. Primary outcome was a composite wound complication rate including breakdown or infection within 8 weeks postoperatively. Data were analyzed using Fisher exact or χ^2 tests, Student t test, and Poisson regression.

Results: Wound complications occurred in 154 (29%) of the 534 patients included. Mean age was 52 years. Most patients were white (84%), were smokers (66%), had no prior vulvar treatment (56%), and had vulvar intraepithelial neoplasia (69%). A total of 227 (43%) patients received preoperative antibiotics. Patients who received antibiotics were more likely to have a higher American Society of Anesthesiologist class score (score 3–4, 38%, vs score 1–2, 29%, $P = 0.03$), greater blood loss (20 vs 10 cc, $P < 0.01$), longer duration of surgery (48 vs 40 minutes, $P < 0.01$), longer mean incision length (3.5 vs 3.0 cm, $P < 0.01$), and width (1.5 vs 1.4 cm, $P = 0.01$), and concomitant reconstructive flap or graft (13.7% vs 2.6%, $P < 0.01$). There was no difference in wound complication rates (30.4% vs 27.4%, $P = 0.45$), tobacco or immunosuppressant use, heart disease, human immunodeficiency virus infection, or chronic kidney disease. Mean length of wound separation in the antibiotic group was significantly shorter (1 vs 2 cm, $P = 0.03$). In multivariate analysis (Table 1), tobacco use (OR = 1.64, 95% CI 1.14–2.38), and primary rather than repeat vulvar surgery (OR = 1.99, 95% CI 1.31–3.01) were associated with increased wound complications.

Conclusion: Over a quarter of women undergoing vulvar surgery for nonmalignant lesions experience wound complications. Future prospective studies are warranted to explore the role of perineal care and prophylactic antibiotics to improve postoperative morbidity.

Table 1. Univariate and multivariate logistic regression model assessing predictors of wound complications ($n = 578$).

Risk Factor ^a	Univariate Unadjusted Odds Ratio (95% CI)	Multivariate Adjusted Odds Ratio (95% CI)
Antibiotic prophylaxis	1.10 (0.79–1.52)	0.96 (0.68–1.36)
Continuous variables		
Incision length	1.10 (1.04–1.16)	1.07 (0.99–1.16)
Incision width	1.14 (1.03–1.27)	1.01 (0.87–1.18)
Categorical variables		
Tobacco use		
Current	1.99 (1.31–3.01)	1.90 (1.26–2.87)
Former	1.52 (0.94–2.46)	1.52 (0.94–2.45)
Never	1.00 (<i>ref</i>)	1.00 (<i>ref</i>)
Prior vulvar surgery		
Yes	0.63 (0.43–0.90)	0.61 (0.42–0.88)
No	1.00 (<i>ref</i>)	1.00 (<i>ref</i>)
Reconstructive flap/graft		
Yes	1.67 (1.02–2.73)	1.36 (0.79–2.34)
No	1.00 (<i>ref</i>)	1.00 (<i>ref</i>)

^a These risk factors remained in the final model of multivariate stepwise selection.

221 - Poster Session

The detection of sentinel lymph node (SLN) in laparoscopic surgery for cervical cancer using carbon nanoparticle: A new method

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Objective: To investigate the feasibility of carbon nanoparticle in the detection of sentinel lymph node (SLN) in cervical cancer.

Method: Carbon nanoparticle (CNP) is a new tracer for SLN mapping. A total of 52 cervical cancer patients (stage IB1–IIA1) who received laparoscopic surgery were retrospectively reviewed. Cervical injection of CNP was performed under anesthesia, and black-stained lymph nodes were identified as SLN. Complete pelvic lymphadenectomy was conducted after removal of SLN. Routine pathological examinations of SLN and other resected specimens were performed separately.

Results: Of the 52 cases, at least 1 SLN was identified in 50 patients (96%), and bilateral SLNs were identified in 37 patients (74%). A total of 380 SLNs was harvested; the average SLN count of each pelvic was 4.4, mostly distributed in the iliac vascular

lymphatic area. The new approach showed an accuracy of 96% (48/50), a sensitivity of 80% (8/10), a false negative rate of 20%(2/10), and negative predictive value of 95% (40/42). Adverse reactions were not observed in all cases.

Conclusion: With high overall and bilateral detection rates, carbon nanoparticle provides a feasible and efficient method in SLN mapping of cervical cancer.

222 - Poster Session

Lymphadenectomy is associated with an increased risk of postoperative venous thromboembolism in early-stage endometrial cancer patients

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Objective: We sought to evaluate the effect of performing lymphadenectomy (LND) on the risk of postoperative venous thromboembolism (VTE) in patients undergoing surgery for early-stage endometrial cancer.

Method: This is a cohort study using the Surveillance, Epidemiology, and End Results (SEER)/Medicare database from 1999 to 2011. We identified stage I–II endometrial cancer patients who underwent primary surgical treatment with hysterectomy. Performance of lymphadenectomy, the 90-day incidence of postoperative VTE (deep venous thrombosis, DVT, and pulmonary embolism, PE), open versus minimally invasive surgery (MIS), demographics, morbidities, stage, and FIGO grade were collected. A washout period of 12 months with no prior VTE was required. Student t test, χ^2 test, and univariate and multivariable Poisson regression with robust variance estimator were used.

Results: A total of 13,334 patients were included, of which 59% ($n = 7,867$) underwent LND. A total of 436 patients developed VTE (acute DVT, 236; PE, 136; and both, 64). There was a higher incidence of VTE (3.9%, $n = 307$) in those who underwent LND compared to those who did not (2.4%, $n = 129$). Those who underwent LND were 65% more likely to develop VTE (RR = 1.65, 95% CI 1.35–2.03). In an unadjusted model, LND increased the risk of developing acute VTE (RR = 1.78, 95% CI 1.38–2.07, $P < 0.001$). After adjusting for age, stage, grade, Charlson morbidity index, and surgical approach, those who underwent LND remained 1.7 times as likely to develop VTE compared to those who did not have LND (RR = 1.7, 95% CI 1.38–2.09, $P < 0.001$). Within a subset of patients who had MIS ($n = 3,452$), those who underwent LND were 78% more likely to develop VTE (RR = 1.78, 95% CI 1.12–2.84). The unadjusted and adjusted models also remained significant (RR = 1.78, 95% CI 1.12–2.84, $P = 0.015$; adjusted RR = 1.79, 95% CI 1.11–2.84, $P = 0.014$).

Conclusion: Lymphadenectomy is associated with an increased 90-day risk of postoperative VTE in patients undergoing surgery for early-stage endometrial cancer, including those who undergo minimally invasive surgery. The risks of postoperative VTE should be considered when counseling patients. The need for extended postoperative VTE prophylaxis in patients undergoing lymphadenectomy in MIS should be explored.

223 - Poster Session

A prospective trial of acute normovolemic hemodilution in patients undergoing cytoreductive surgery for advanced ovarian cancer

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Objective: Our objective was to determine whether acute normovolemic hemodilution (ANH) reduces the requirement for allogenic red blood cell (RBC) transfusions in patients undergoing primary cytoreduction for advanced ovarian cancer.

Method: Patients undergoing primary cytoreduction for advanced ovarian cancer were enrolled on a prospective trial of ANH at time of surgery. Intraoperative blood withdrawal was performed to a target hemoglobin of 8.0 g/dL. A standardized transfusion protocol was applied to all patients intraoperatively and throughout the rest of their hospital stay according to pre-existing institutional guidelines. The primary endpoint was to determine the overall rate of allogenic RBC transfusions in the intra- and postoperative period. A predetermined allogenic RBC transfusion rate less than 35% was deemed a meaningful reduction from a 50% transfusion rate in historical controls.

Results: Forty-one patients consented to ANH at time of primary cytoreduction for advanced ovarian cancer. Median blood withdrawn during ANH was 1,650 mL (range 700–3,000 mL). Cytoreductive outcomes were 0 mm, 30 (73%); 1–10 mm, 8

(20%); and >10 mm, 3 (7%). Estimated blood loss was 1,000 mL (range 150–2,700 mL). Fourteen patients (34%) received allogenic RBC transfusions intra- or postoperatively, thus meeting the primary endpoint. No patients were transfused outside protocol guidelines. The rate of grade 3+ complications (19.5%) was similar to historical controls and met predefined safety thresholds.

Conclusion: For patients with advanced ovarian cancer undergoing primary cytoreductive surgery for advanced ovarian cancer, ANH appears to reduce allogenic RBC transfusion rates versus historical controls without increasing perioperative complications. Further evaluation of this widely available technique is warranted.

224 - Poster Session

Implementation of an abdominal closure bundle to reduce surgical site infection in patients on a gynecologic oncology service undergoing exploratory laparotomy

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Objective: Surgical site infections (SSIs) are associated with increased morbidity, mortality, length of hospitalization, and health care costs. This study aims to investigate whether implementation of an abdominal closure bundle successfully reduces surgical site infection rates.

Method: We conducted a retrospective cohort study. All patients who underwent exploratory laparotomy by a gynecologic oncologist at our institution from January 1, 2011, to April 1, 2017, were identified. The abdominal wound closure bundle, implemented on May 6, 2014, included changing of the surgical gown and gloves, repeat surgical scrub, and usage of new instruments for closure of fascia, subcutaneous tissue, and skin. SSI rates were assessed overall, as well as within subgroups that included multiple demographic and surgical characteristics.

Results: Of the 951 patients identified, 875 were included in the analysis: 471 patients underwent surgery prior to implementation of the closing bundle and 404 patients were in the postbundle group. Overall, the incidence of surgical site infection rate in the prebundle cohort was 48/471 (10.2%); this was reduced to 32/404 (7.9%) in the postbundle group ($P = 0.148$). Multiple subgroup analyses were also completed. In patients who underwent a debulking procedure (485), SSI was noted in 36/277 (13.0%) in the prebundle group, which was reduced to 14/208 (6.7%) in the postbundle cohort ($P = 0.017$). Of the patients who underwent tumor debulking, those who were suboptimally debulked had a prebundle SSI rate of 9/29 (31.0%) compared to 1/17 (5.9%) in the postbundle group ($P = 0.047$). In patients with malignant pathology, the prebundle cohort had an SSI rate of 38/282 (13.5%), which was reduced to 18/215 (8.4%) in the postbundle group ($P = 0.049$). In patients with intraoperative ascites, the rate of SSI decreased from 19/119 (15.9%) in the prebundle cohort to 4/104 (3.8%) in the postbundle group ($P = 0.002$).

Conclusion: Implementation of an abdominal closure bundle was associated with a significant reduction in SSI in patients who underwent debulking surgery. Although there was no associated significant reduction in all groups undergoing exploratory laparotomy, there was a reduction in those patients who were suboptimally debulked, had malignant pathology, and found to have intraoperative ascites.

225 - Poster Session

Concordance of laparoscopy in predicting intraperitoneal spread and residual disease at tumor reductive surgery in advanced ovarian cancer

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Objective: To determine the concordance of laparoscopic scoring assessment in predicting intraoperative tumor dissemination and residual disease at open tumor reductive surgery (TRS) in advanced ovarian cancer.

Method: From April 2013 to June 2017, we prospectively triaged patients with advanced-stage ovarian cancer (stage IIA–IVB) to laparoscopic scoring assessment to determine resectability at primary TRS. Patients with medically inoperable or distant metastatic disease received neoadjuvant chemotherapy (NACT). A validated scoring method was used to determine a laparoscopic predictive index value (PIV) score of 0–14. Patients with PIV scores less than 8 were offered primary surgery, and those with a score of 8 or higher received NACT. Patients who underwent primary TRS received a second PIV score at that

time. Concordance percentages were calculated for PIV scoring at laparoscopy and primary TRS. Positive predictive value (PPV) was used to determine the ability of the PIV score at laparoscopy to predict R0 (complete gross resection) at primary TRS.

Results: A total of 226 patients underwent laparoscopic scoring assessment with advanced-stage ovarian cancer, of which 139 patients (61.5%) had a PIV score of less than 8 and 81 (35.8%) had a PIV score of 8 or higher. Six patients (2.7%) were unscorable. PIV scores were available at laparoscopy and primary TRS for 99 of 139 patients (71%). There was a 96% concordance rate between a PIV score of <8 or ≥8 at laparoscopy and primary TRS. Concordance between PIV scores at laparoscopy and primary TRS were 74.7% for bowel infiltration, 84.6% for mesenteric disease, 86.5% for liver surface involvement, 89.7% for omental disease, 92.9% for diaphragm disease, 94.7% for stomach infiltration, and 94.8% for peritoneal carcinomatosis. The laparoscopic PIV scoring had a PPV of 87.6% at predicting R0 at primary TRS.

Conclusion: Good concordance of overall laparoscopic PIV scoring with actual intraoperative tumor dissemination at primary TRS is seen; however, the lowest concordance was noted for predicting bowel infiltration. Given the potential limitations of laparoscopy at predicting bowel infiltration and residual disease, consideration should be given to the use of additional preoperative predictive modalities.

226 - Poster Session

Intraperitoneal chemotherapy following neoadjuvant chemotherapy and interval surgical cytoreduction for ovarian cancer

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Objective: Although intraperitoneal (IP) chemotherapy (IPC) is well-established in advanced ovarian cancer treatment after primary debulking surgery, outcomes after neoadjuvant chemotherapy (NACT) and interval debulking surgery (IDS) have been less clearly described.

Method: Women with advanced ovarian, fallopian tube, or primary peritoneal cancer received NACT followed by IDS and IP port placement from January 2005 to January 2016. Data abstracted from electronic medical records were analyzed using STATA.

Results: An IP port was placed at the time of IDS after NACT in 49 women with a median age of 63 years. Twenty-nine patients (59.2%) had stage III disease, while 20 (40.8%) had stage IV disease. The median number of cycles of NACT was 3 (range 1–6), with the majority receiving q3 week paclitaxel/carboplatin. Optimal surgical cytoreduction was achieved in all patients; 65.3% were to R0. Bowel resection was performed in 22.4% of patients (11/49), half of which were rectosigmoid. Fifty-three percent had at least 1 complication within 6 weeks of IDS, most commonly blood transfusion (20/49). Of the 45 patients with follow-up after IDS, 25 (55.6%) received at least 1 cycle of IV chemotherapy prior to IPC and 11 (24.4%) never received any IPC, mostly due to change in provider treatment plan ($n = 4$) or a surgical/IP port complication ($n = 3$). Among patients receiving at least 1 dose of IPC ($n = 34$), the median number of cycles was 4 (range 1–6), and 23 (67.6%) received IP carboplatin. A third required an adjustment to their IP regimen, and 20% experienced a complication that led to discontinuing IPC. Most common IPC complications were neutropenia (41.2%), anemia requiring a blood transfusion (17.6%), and grade 3+ neuropathy (8.8%). The median total chemotherapy cycles (NACT, IV, and IP) was 8 (range 3–13). Median follow-up among those who received any IPC was 37 months. Median progression-free survival (PFS) was 19 months for the whole group, 16 months for IP cisplatin, and 19 months for IP carboplatin. There were 16 deaths (47%), and median overall survival (OS) was 54 months. Median OS was similar between IP cisplatin (55 months) and IP carboplatin (54 months).

Conclusion: IPC after NACT remains a viable option for ovarian cancer patients with an optimal cytoreduction at IDS and may lead to long-term survival.

227 - Poster Session

The impact of lymph node status on prognosis in endometrioid endometrial adenocarcinoma

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Objective: Extrauterine disease is an important prognostic factor in endometrial cancer; however, the approach to lymph node evaluation varies widely, particularly in early-stage and low-grade disease. The primary objective is to analyze the

impact of grade and lymph node status on overall survival (OS) with the hypothesis that nodal status will not have a negative impact on OS in low-grade disease.

Method: This is a retrospective analysis of women with endometrioid endometrial adenocarcinoma of the uterus who received treatment at a comprehensive cancer center between 2004 and 2014. Cox regressions were used to evaluate HR for progression and death.

Results: A total of 708 women were eligible for inclusion presentation. Median age at diagnosis was 59 years, and median follow-up time was 30.9 months. Stage distribution was 80% stage I, 4% stage II, 14% stage III, and 2% stage IV. Sixty percent of tumors were grade 1, 26% grade 2, and 14% grade 3. Nodal dissection was performed in 595 patients (84%), of whom pelvic nodes were removed in 594 and paraaortic nodes were removed in 358. Seventy-nine patients (13%) had at least 1 positive node. Among patients with positive nodes, a median of 19 nodes (IQR 11–30) were removed. Among patients with negative nodes, a median of 16 nodes (IQR 9–23) were removed. The 25th percentile of survival was 70 months among all patients: 78 months if grade 1, 57 months if grade 2, and 32 months if grade 3. Among patients with stage I–III disease, positive nodal disease was associated with an increased hazard of death (HR = 2.30, $P = 0.014$) when compared to negative nodal disease after adjusting for depth of invasion (DOI), lymphovascular space invasion (LVSI), age, Charlson comorbidity index (CCI), and adjuvant treatment. Among patients with grade 1/2 disease, positive nodal disease was associated with an increased hazard of death (HR = 4.67, $P = 0.002$) when compared to negative nodal disease after adjusting for DOI, LVSI, age, CCI, and adjuvant treatment. This effect persisted when disease-free survival was analyzed.

Conclusion: In a large cohort, an association between positive lymph nodes and increased hazard of death is sustained across all grades of endometrioid endometrial cancer and when adjusting for tumor factors. This supports the utility of nodal dissection among patients with low-grade disease and may support the implementation of sentinel node dissections in these low-risk groups.

228 - Poster Session

Chemical VTE prophylaxis decreases the risk of postoperative complications in patients undergoing surgery for vulvar carcinoma

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Objective: Vulvar carcinoma is a rare malignancy with little prospective data to guide management. Surgery, including resection of the primary tumor and loco-regional lymph node assessment if indicated, remains the primary treatment. Postoperative complications (POC) are common in this population and can lead to increased health care costs and delay of adjuvant therapy. Our objective was to assess perioperative factors that influence POC in patients undergoing surgery for vulvar carcinoma.

Method: Institutional review board approval was obtained. All patients with a primary diagnosis of vulvar carcinoma who underwent surgical intervention at our institution from September 2001 to May 2016 were identified. Clinical factors including demographics, clinicopathologic data, treatment, and patient outcomes were collected retrospectively. POC included wound breakdown, infections, readmission, transfusion, return to the operating room, venous thromboembolism (VTE), myocardial infarction, stroke, and death within 90 days. The χ^2 test and logistic regression modeling were used for statistical analysis.

Results: A total of 121 patients met the criteria. POC were identified in 83 patients (68.6%). Surgical time ($P = 0.0305$, OR = 1.015, 95% CI 1.001–1.029) and JP drain placement ($P = 0.0281$, OR = 3.630, 95% CI 1.149–11.471) increased the risk of POC. Chemical VTE prophylaxis decreased the risk of POC ($P = 0.0009$, OR = 0.165, 95% CI 0.057–0.480). The rate of VTE in this cohort was 7.4%. There were 69 patients (57%) in the cohort who received postoperative chemical VTE prophylaxis, and 4 (5.8%) of those were diagnosed with a postoperative VTE.

Conclusion: Not surprisingly, longer, more extensive surgeries for vulvar cancer are associated with increased POC. In a patient population with a low incidence of postoperative VTE, chemical VTE prophylaxis decreases the risk of POC, a difference that doesn't seem to be entirely accounted for by prevention of VTE alone. Consideration should be given to prescribing postoperative VTE prophylaxis, especially after longer, more extensive surgeries, to decrease the risk of POC after

surgical management of vulvar cancer.

229 - Poster Session

Performing combined breast and gynecologic surgery does not increase the rate of postoperative morbidity

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Objective: The purpose of this study was to determine and compare the postoperative morbidities in patients undergoing breast surgery only, gynecologic surgery only (bilateral salpingo-oophorectomy and/or hysterectomy), and combined breast surgery and gynecologic surgery.

Methods: We reviewed the National Surgical Quality Improvement Program (NSQIP) Participant Use Files from 2005 to 2015 for subjects undergoing breast surgery, gynecologic surgery, or a combined surgery by utilizing the Current Procedural Terminology (CPT) codes for the different surgical procedures (the database was queried for encounters that contained either one breast, one gynecologic, or both a breast surgery code and a gynecologic procedure code). We then queried the database for postoperative morbidities including surgical site infection (SSI) rates, wound classification, length of hospital admission, postoperative pneumonia, discharge location, postoperative venous thromboembolism (VTE), postoperative sepsis, return to the operating room, and readmission. SSI rates were compared using the χ^2 test with a nominal value of $P < 0.05$ as a test for significance.

Results: We identified a total of 530,415 women undergoing breast and/or gynecologic surgery in the database. A total of 340,234 underwent breast surgery (group 1); 189,539 underwent gynecologic surgery alone (group 2); and 642 underwent combined breast and gynecologic surgery (group 3). The combined surgical approach showed comparable complication rates between group 3 and group 2 for SSI (2.34% versus 2.73%), mean length of hospital admission (2.3 days versus 1.9 days), postoperative pneumonia (0.31% versus 0.34%), VTE rates (0.93% versus 0.54%), and postoperative sepsis (0.31% versus 0.75%). Return to the operating room was similar between group 3 and group 1 (4.98% versus 4.55%).

Conclusion: The rate of complications of combined surgery does not appear to be higher than for gynecologic surgery or breast surgery alone. As more hereditary breast and ovarian cancer genomic alterations are discovered and the number of indications for prophylactic surgery increases, gynecologic oncologists and breast surgeons can coordinate surgical intervention to lower costs and risks from anesthesia while maintaining high-quality care.

230 - Poster Session

Clinical stage II endometrial cancer: Is there a benefit to radical hysterectomy?

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Objective: To determine the effect of radical hysterectomy (RH) versus simple hysterectomy (SH) on recurrence-free survival (RFS) and morbidity in patients with clinical stage II endometrial cancer.

Method: This was a retrospective cohort study from 2000 to 2015 of women with clinical stage II endometrial cancer from 2 institutions. Inclusion criteria were cervical stromal involvement on final pathology, preoperative positive endocervical curettage/cervical biopsy, cervical involvement on imaging, or clinical examination with no evidence of stage III–IV disease. Wilcoxon rank-sum test, Fisher exact test, Kaplan-Meier survivor functions, and Cox proportional hazards multivariable analysis were used.

Results: Ninety patients were included: 33 with SH and 57 with RH. Patients with RH were younger (60.2 vs 64.9 years, $P = 0.04$) and more frequently had tumor visible on cervical examination (63.2% vs 30.0%, $P = 0.004$). Lymphadenectomy was performed in 76% (SH) and 81% (RH). Histologic subtype was endometrioid in 67% of the SH group and nonendometrioid in 53% of the RH group. Fifty-one percent were stage III–IV on final pathology. There was no difference in rates of adjuvant radiation (RT) or chemotherapy between groups. There was no significant difference in surgical morbidity, although the SH group tended to have lower mean blood loss (361 mL vs 546 mL). Mean follow-up was 3.3 (SH) and 3.8 (RH) years.

Recurrences occurred in 11/33 (33%) of the SH group and 19/57 (33%) of the RH group; majority were distant recurrences in 10/11 (SH) and 15/19 (RH). There was no significant difference in 5-year RFS (SH 54% vs RH 63%, $P = 0.72$). After controlling for stage, adjuvant RT, and chemotherapy, RH was not significantly associated with improved RFS (HR = 0.62, 95% CI 0.29–1.33). Among the 44 patients with stage II disease on final pathology, there were 7 recurrences: 4 in the SH group and 3 in the RH group. All but 1 had distant metastases at time of recurrence.

Conclusion: Radical hysterectomy does not appear to be significantly associated with improved RFS or morbidity in patients with clinical stage II endometrial cancer. Fifty-one percent had advanced disease on final pathology, highlighting the importance of surgical staging. Among patients with stage II disease on final pathology, the majority had distant recurrence. Further investigation of adjuvant therapy options in stage II disease is warranted.

231 - Poster Session

Continuous epidural infusion in gynecologic oncology patients undergoing exploratory laparotomy: Less pain and decreased narcotic use with no increased risk of venous thromboembolism

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Objective: There is a lack of consistent data in gynecologic oncology patients regarding perioperative morbidity associated with continuous epidural infusions. We aim to compare the incidence of postoperative venous thromboembolism (VTE), postoperative pain, and postanesthesia care unit (PACU) narcotic use in gynecologic oncology patients who did and did not receive an epidural prior to undergoing exploratory laparotomy.

Method: We performed an institutional review board-approved retrospective chart review of gynecologic oncology patients undergoing laparotomy from January 2012 to October 2015. Patients with a history of VTE, defined as deep vein thrombosis or pulmonary embolism, were excluded. Hydromorphone administration in the PACU was obtained from anesthesia records. Postoperative pain scores were assessed using a Likert scale of 0–10. Bivariate analyses were conducted using Pearson χ^2 or Fisher exact tests as appropriate, and the Student t test or Mann-Whitney U test were used for continuous variables.

Results: Among 538 patients who underwent laparotomy, 304 received an epidural and 234 did not, with no differences in age, race, body mass index, operative time, or estimated blood loss. Presence of an epidural did not have an impact on the risk of developing a VTE within 30 days postoperatively (epidural 5.3% vs no epidural 5.6%, $P = 0.88$) or 30–90 days postoperatively (1.0% vs 0.4%, $P = 0.64$) (Table 1). PACU assessment revealed that women with an epidural reported lower pain scores ($P = 0.01$) and required less hydromorphone ($P = 0.003$) than women without epidural anesthesia. This trend continued throughout postoperative day 0 (median score 3/10 vs 4/10, $P < 0.01$) and postoperative day 1 (median 3/10 vs 3/10, $P < 0.01$), at the expense of longer duration of a Foley catheter (20.41 vs 10.26 hours, $P = 0.02$) and postoperative hypotension (63% vs 37%, $P < 0.01$). However, patients with epidural anesthesia had shorter hospital length of stay (3.5 vs 4.6 days, $P < 0.01$) and no difference in hospital readmissions compared to women without epidural anesthesia.

Conclusion: Perioperative epidurals used in gynecologic oncology patients undergoing major abdominal surgery correlate with decreased immediate postoperative narcotic use and improved pain relief during the first 24 hours after surgery without an increased risk of postoperative VTE within 90 days of surgery.

Table 1. Patient characteristics and perioperative and surgical outcomes.

	Epidural ($n = 304$) ^a	No Epidural ($n = 234$) ^a	<i>P</i> Value
Venous thromboembolism <30 days ^b	16 (5.3)	13 (5.6)	0.88
Upper extremity deep venous thrombosis	2 (0.7)	0 (0.0)	
Lower extremity deep venous thrombosis	4 (1.3)	5 (2.1)	
Pulmonary embolism	10 (3.3)	8 (3.4)	
Venous thromboembolism 30–90 days	3 (1.0)	1 (0.4)	0.64
Upper extremity deep venous thrombosis	0 (0.0)	0 (0.0)	
Lower extremity deep venous thrombosis	1 (0.3)	0 (0.0)	
Pulmonary embolism	1 (0.3)	1 (0.4)	
Age, years (mean \pm standard deviation)	59.25 \pm 13.2	58.88 \pm 13.4	0.75

Race			0.21
White	239 (78.6)	194 (82.9)	
Non-white	65 (21.4)	40 (17.1)	
Black	54 (17.8)	35 (15.0)	
Other	11 (3.6)	5 (2.1)	
Body mass index, kg/m ²	29.5 (25.0, 35.0)	31.0 (25.0, 37.0)	0.27
Operative time, minutes	168 (140, 213)	160 (136, 201)	0.07
Estimated blood loss, milliliters	300 (200, 500)	300 (200, 500)	0.56
Duration of epidural, days	3 (2,3)	--	--
Postanesthesia care unit pain score	3 (0,5)	3 (0,5)	0.01
Postoperative pain score ^c			
Day 0	3 (1,5)	4 (2,6)	<0.01
Day 1	3 (2,4)	3 (2,5)	<0.01
Day 2	3 (1,4)	3 (1,5)	0.17
Day 3	3 (1,4)	3 (1,6)	0.06
Postoperative anticoagulation ^c			0.43
Lovenox	299 (98.4)	231 (99.1)	
Other (Heparin, Xarelto, other)	265 (88.6)	213 (92.2)	
	34 (11.4)	18 (7.8)	
Duration of Foley (hours) ^c	23 (20, 41)	22 (19, 26)	0.02
Foley replaced postoperatively	47 (15.5)	27 (11.7)	0.21
Postoperative urinary tract infection ^d	13 (4.3)	4 (1.7)	0.13
Postoperative hypotension ^e	191 (62.8)	87 (37.3)	<0.01
Length of hospital stay (days)	4 (3,5)	5 (4,6)	<0.01
Readmission			
Within 30 days after surgery	39 (12.8)	33 (14.2)	0.65
30–90 days after surgery	30 (9.9)	27 (11.6)	0.52

^a Median, IQR provided unless otherwise specified.

^b Venous thromboembolism <30 days is reported per person. One person in each cohort had a lower extremity DVT and pulmonary embolism.

^c Missing data.

^d Postoperative urinary tract infection was defined by a positive urine culture.

^e Postoperative hypotension was defined as systolic blood pressure <90 or diastolic blood pressure <50.

232 - Poster Session

SGO member practice patterns for intraoperative assessment of and decision making regarding lymph nodes for cervical cancer: Should we abandon the radical hysterectomy?

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Objective: Radical hysterectomy for cervical cancer is often favored over radiation because it yields comparable outcomes and allows for analysis of pathology. Debated points are the therapeutic benefit of lymph node (LN) dissection and whether patients with positive LN should undergo a radical hysterectomy. The study objective is to describe practice patterns of intraoperative LN assessment prior to radical hysterectomy (RH) and to determine whether LN status influences surgical decision making.

Method: With institutional review board approval, a survey was emailed to the SGO listserv over a 3-week period. All identifiers were excluded. The survey was formatted and distributed with Qualtrics. Descriptive statistics and the χ^2 test were used to report data.

Results: There were 239 respondents. Attendings and fellows alike preferred minimally invasive surgery (MIS) (85.35%) over open technique (14.65%). More respondents (73.22%) preferred robotic RH over laparoscopic (12.13%). Preference for MIS was increased with more physicians in a practice ($P = 0.033$) and fewer years since fellowship ($P = 0.029$). Only 93 (38.9%) of

respondents perform sentinel lymph node (SLN) mapping, and this was more commonly done with more physicians in a practice ($P = 0.007$). A majority of respondents ($n = 205$, 85.77%) reported that positive LN (clinical or pathological) influence their surgical plan, and the top cited reason was concern for increased overall morbidity that can occur with an alternative treatment plan such as radiation therapy. Only 21% of all respondents request pathologic LN assessment routinely, while the majority (63%) will do so only in response to a suspicious appearing LN. Of the 173 respondents who said they were influenced by positive LN on intraoperative pathology, 159 (91.91%) will abort RH in the setting of positive LN on frozen pathology, but continue with some degree of LN dissection. Of the 34 individuals (14%) who aren't influenced by positive LN status (intraoperative pathology or clinical), 10 (29.41%) reported they still send LN for intraoperative pathology despite completing the RH regardless of the result.

Conclusion: Most gynecologic oncologists report that positive LN do influence their surgical plan and will subsequently abort radical hysterectomy due to increased morbidity concerns.

233 - Poster Session

Comparison of MRI, PET-CT, and frozen biopsy in the evaluation of lymph node status before fertility-sparing radical trachelectomy in early-stage cervical cancer

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Objective: To compare the accuracy of magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT), and frozen biopsy before fertility-sparing radical trachelectomy in early-stage cervical cancer.

Method: This was a retrospective study including 132 young women with early-stage cervical cancer who tried fertility-sparing laparoscopic or robotic radical trachelectomy between July 1, 2004, and April 30, 2017. All patients underwent preoperative MRI and/or PET/CT. Pelvic lymphadenectomy was performed during surgery, and all retrieved lymph nodes were sent to frozen biopsy before proceeding to radical trachelectomy. Para-aortic lymphadenectomy was performed when metastasis was suspected in the para-aortic lymph node. The diagnostic accuracy of MRI, PET/CT, and frozen biopsy was compared using the McNemar test and logistic regression with the generalized estimating equation. The final pathologic report on lymph nodes was the gold standard for diagnosis.

Results: The total number of retrieved lymph node stations was 697, and the mean was 20 (range 2–61). Lymph nodes were positive in 20 patients (14.3%). Sixteen patients underwent radical hysterectomy with lymphatic metastasis in frozen biopsy. In comparison between patients, there was significant difference in sensitivity (95.0% vs 40.0%, $P < 0.001$), specificity (100.0% vs 80.0%, $P < 0.001$), and accuracy (99.2% vs 73.8%, $P < 0.001$) of frozen biopsy versus MRI. There was a significant difference in specificity (100.0% vs 84.3%, $P < 0.001$) and accuracy (99.2% vs 82.5%, $P < 0.001$) of frozen biopsy versus PET/CT. See Table 1.

Conclusion: Although sensitivity is not statistically significant in PET/CT, lymph node metastasis is very important for prognosis. Therefore, frozen biopsy of all retrieved lymph nodes during surgery is still the best way to evaluate lymph node status before fertility-sparing radical trachelectomy.

Table 1. Comparison of validity MRI, PET, FROZEN in evaluating lymph node status.

		MRI			PET/CT			FROZEN			Multiple comparison P value		
		N	%	95% CI	N	%	95% CI	N	%	95% CI	MRI vs PET/CT	MRI vs FROZEN	PET/CT vs FROZEN
On patients by patients (n = 134)	Sensitivity	8/20	40.0	21.4-62.0	13/19	68.4	45.2-85.1	20/20	100.0	100.0-100.0	0.065	<0.001	0.009
	Specificity	91/112	81.3	72.9-87.4	90/105	85.7	77.6-91.2	114/114	100.0	100.0-100.0	0.474	<0.001	<0.001
	Accuracy	99/132	75.0	66.9-81.6	103/124	83.1	75.4-88.7	134/134	100.0	100.0-100.0	0.051	<0.001	<0.001
	PPV	8/29	27.6	14.4-46.2	13/28	46.4	29.2-64.6	20/20	100.0	100.0-100.0	0.029	<0.001	<0.001
	NPV	91/103	88.3	80.6-93.3	90/96	93.8	86.8-97.2	114/114	100.0	100.0-100.0	0.104	0.001	0.034

MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; FROZEN, frozen biopsy; PPV, positive predictive value; NPV, negative predictive value.

Multiple comparisons are performed by McNemar's test or Logistic regression using GEE that accounted for the clustering of a patient.

Significance level for multiple comparisons was determined by Bonferroni correction ($P \leq 0.05/3$ for pairwise comparisons).

234 - Poster Session

Risk-reducing surgery for *BRCA* mutations: Are we adhering to the guidelines?

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Objective: Risk-reducing bilateral salpingo-oophorectomy (RRSO) decreases gynecologic cancer-specific mortality by 95% and overall mortality by 76% in women with a pathogenic mutation in *BRCA1/2*. National Comprehensive Cancer Network (NCCN) guidelines recommend RRSO between 35 and 40 years of age and upon completion of childbearing. Several groups have reported a possible association of endometrial cancer with *BRCA* mutations; however, there is no clear recommendation for hysterectomy at time of RRSO (RRSO-H). We sought to evaluate the practice patterns for risk-reducing surgery (RRS) at our center.

Method: We conducted a retrospective chart review at a single institution to identify patients with a *BRCA1/2* mutation who underwent RRS between June 12 and August 8. Statistical analyses were performed with χ^2 and Mann-Whitney *U* tests.

Results: One hundred ninety-seven patients underwent RRS; 97 with *BRCA1* and 99 with *BRCA2* mutations. The median age of RRS in *BRCA1* and *BRCA2* patients was 43 (31–77) and 44 (28–71) years, respectively. Of patients who underwent RRS for *BRCA1* mutation, 93% were older than 35 years and 80% of *BRCA2* mutation carriers were older than 40 years. Seven patients (3.4%) were found to have invasive endometrial cancer at time of RRS; their median age was 43 (41–77) years. Twenty-two percent of patients cited future fertility as the reason for delay in RRS, with *BRCA1* mutation carriers more likely than *BRCA2* (30% vs 15%, $P = 0.03$). Excluding patients who delayed RRS for fertility, the median age of RRS in *BRCA1* and *BRCA2* was 47 (31–77) and 46 (28–71) years, respectively. There was no difference in age at time of RRS for patients with a personal history ($P = 0.35$) or family history of endometrial cancer ($P = 0.68$). Seventy-two (74%) patients with *BRCA1* and 67 (68%) with *BRCA2* mutations had only RRSO; 25 (26%) of women with *BRCA1* and 32 (32%) of *BRCA2* had RRSO-H.

Conclusion: Patients with *BRCA1/2* mutations are undergoing RRS well beyond the NCCN-recommended age. All cases of endometrial cancer in patients undergoing RRS would have likely been prevented if surgery had been completed by 40 years of age. Over a quarter of women delayed surgery because of a desire for future fertility. A large portion of women also underwent RRSO-H for purely risk-reducing reasons, despite mixed data and lack of clear evidence on the role of *BRCA* in endometrial cancer. Further study to better understand reasons for delay may allow for improved adherence in timing of surgery and thereby prevent development of endometrial cancer in patients undergoing RRS.

235 - Poster Session

Survival outcomes of patients with high-grade endometrial cancer undergoing sentinel lymph node (SLN) mapping

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Objective: To evaluate the impact of sentinel lymph node (SLN) mapping on progression-free survival (PFS) and overall survival (OS) in patients with high-grade endometrial cancers.

Method: In this retrospective study, all consecutive patients with high-grade endometrial cancer from December 2007 to August 2014 who underwent SLN mapping and systematic lymphadenectomy (SLN cohort, $n = 85$) were compared to patients who underwent systematic lymphadenectomy only (LND cohort, $n = 62$). Clinical characteristics were extracted from a prospectively gathered electronic database. Thirty-six-month PFS and OS were evaluated at 36-month postoperative follow-up using unadjusted and propensity-score adjusted Cox proportional hazards models controlling for histologic subtype, lymph node metastasis, myometrial invasion, and lymphovascular space invasion.

Results: There was a greater proportion of stage IIIC1 patients among the SLN cohort (23.5% vs 8.1%, respectively, $P = 0.01$) with the SLN as the only positive node in 32% (8/25) of stage IIIC1 patients. In addition, the SLN cohort was found to have improved 36-month overall PFS (HR = 0.48, 95% CI 0.24–0.95, $P = 0.03$). Furthermore, the SLN cohort was found to have

fewer pelvic sidewall recurrences (5.8% vs 24.2%, $P = 0.001$) with improved pelvic sidewall PFS (HR = 0.18, 95% CI 0.06–0.52, $P = 0.002$). As well, the SLN cohort was found to have favorable 36-month OS (HR = 0.30, 95% CI 0.12–0.80, $P = 0.02$).

Conclusion: The addition of SLN mapping may be useful to decrease the risk of recurrences (both overall and in the pelvic sidewall) by enabling the surgeon to efficiently detect the lymph nodes at greatest risk of metastasis, thus helping to guide adjuvant therapy. It may also have a beneficial impact on overall survival.

236 - Poster Session

Mini-laparotomy for large specimen retrieval in robotic gynecologic surgery: Key to a successful minimally invasive procedure

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Objective: Minimally invasive surgery (MIS) is the standard of care for gynecological and gynecological oncology conditions. Furthermore, morcellation has become a controversial option because of concerns of undetected malignancy and dissemination. Our objective is to evaluate the use, safety, and discharge outcomes of minilaparotomy (ML) for specimen retrieval during robotic cases.

Method: This is a retrospective cohort study on patients who underwent robotic gynecologic surgery (RGS) from January 2013 to June 2016 at a single institution. The ML group consisted of patients who at the completion of RGS underwent an abdominal ML incision at the discretion of the surgeon for specimen delivery. Intraoperative and postoperative outcomes were analyzed using Mann-Whitney U and χ^2 tests.

Results: The study included 2,126 patients of whom 155 (7.3%) underwent an ML for specimen retrieval, while 1,971 (92.7%) underwent specimen removal with a laparoscopic approach. Median age and BMI were similar between the two study arms (age, 45 vs 44 years, $P = 0.9$; BMI, 26.2 vs 26.3, $P = 0.9$). Of note, specimen weights were significantly heavier in the ML group (median 391 vs 170 g, $P = <0.0001$). In regard to outcomes, the ML group had a statistically higher estimated blood loss (120 vs 100 cc, $P = 0.003$). In addition, operative time was statistically longer (211 vs 181 minutes, $P = <0.0001$). Discharge time was 450 versus 450 minutes ($P = 0.3$). When comparing same-day discharge to 23-hour observation to full admission, there were no statistical differences (ML, 67% vs 71%, 30% vs 24%, and 3% vs 5%, respectively, $P = 0.2$). Finally, complication (ML 15% vs. 16%, $P = 0.8$), infection (ML 2% vs 3%, $P = 1.0$), blood transfusion (ML 1% vs 3%, $P = 0.5$), and readmission rates (ML 1% vs 4%, $P = 0.2$) were similar.

Conclusion: Although ML for specimen retrieval during RGS statistically increases intraoperative estimated blood loss and operative time, it does not affect postoperative outcomes such as time to discharge, wound infection, complications, need for blood transfusion, or readmission rates when compared to RGS without ML. These results are important because they highlight the role that ML may play when removing large specimens while still enabling a patient to have a successful MIS procedure.

Table 1.

	Minilap (n = 155)	No Minilap (n = 1971)	P value
Age (median +/- SD)	45 +/- 10.54486	44 +/- 11.69253	0.9018
BMI (median +/- SD)	26.2 +/- 7.0035	26.3 +/- 6.584	0.8794
EBL (median +/- SD)	120 +/- 226.3351	100 +/- 234.7236	0.003184
OR time in minutes (median +/- SD)	211 +/- 69.09903	181 +/- 72.56304	< 0.0001
DC time in minutes	450.0 +/- 600.1409	450.0 +/- 2101.0995	0.343
Specimen weight (g)	390.65 +/- 454.2529	170.00 +/- 427.5646	< 0.0001
Cancer diagnosis (n)			0.3032
Yes	22	351	
No	133	1620	
Type of surgeon (n)			0.5092
Onc	49	567	
Benign	106	1404	

Discharge status (n)			0.1706
Same day	105	1407	
23 hr obs	46	472	
Full admission	4	91	
Complication (n)			0.8126
Yes	22	238	
No	122	1211	
Unknown	11	522	
Infection (n)			0.9865
Yes	3	36	
No	141	1411	
Unknown	11	524	
Readmission (n)			0.2211
Yes	2	56	
No	142	1441	
Unknown	11	474	
Blood Transfusion (n)			0.5066
Yes	2	49	
No	153	1922	

237 - Poster Session

Neoadjuvant chemotherapy is associated with a high rate of perioperative blood transfusion at the time of interval cytoreductive surgery

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Objective: To determine the prevalence and oncologic safety of perioperative allogeneic blood transfusion during interval cytoreduction surgery among women receiving neoadjuvant chemotherapy (NACT) for ovarian cancer.

Method: We utilized retrospective chart review to identify a cohort of patients undergoing interval cytoreduction at a large academic tertiary referral center. We compared outcomes in patients who were exposed to perioperative blood transfusion with patients who were not exposed. Our primary endpoint was progression-free survival (PFS); our secondary endpoint was overall survival (OS). Baseline clinical characteristics were collected for patients in each group.

Results: Sixty-six women were included in the final cohort of women undergoing interval cytoreductive surgery after NACT. A total of 51 women (77%) were exposed to allogeneic perioperative pRBC transfusion. Fifteen women (23%) were not exposed to transfusion. The baseline characteristics were generally well matched. Women who were not exposed to a perioperative blood transfusion were more likely to have a normalized CA-125 prior to undergoing cytoreductive surgery. Preoperative hemoglobin concentration was lower in the transfusion group (10.5 g/dL vs 11.5 g/dL, $P < 0.009$). Perioperative transfusion was not associated with a significant difference in PFS (7.6 months for transfused vs 9.4 months for not transfused, log rank test $P = 0.4617$). Similarly, there was no observed difference between groups for OS (23.6 months for transfused vs 22.5 months for not transfused, log rank test $P = 0.1723$).

Conclusion: Women undergoing NACT for ovarian cancer are at high risk of exposure to blood transfusion at the time of interval cytoreductive surgery. Future studies will continue to evaluate the safety and impact of transfusion on ovarian cancer survival in this at-risk population.

238 - Poster Session

Cyberknife therapy for locally recurrent gynecologic cancers after external-beam radiation therapy

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Objective: Management of locally recurrent gynecologic cancers following external-beam radiation (RT) presents a therapeutic dilemma. Treatment options usually involve an exenterative procedure or palliative chemotherapy because of the risk of toxicity associated with re-irradiation. This study aims to analyze the efficacy and safety of re-irradiation using cyberknife for local recurrences involving the pelvis and paraaortic (PA) regions.

Method: A retrospective chart review of patients treated with cyberknife at Winthrop University Hospital between 2005 and 2015 identified 29 patients with prior RT and locally recurrent gynecologic cancer: endometrial ($n = 22$), cervix ($n = 1$), ovary ($n = 2$), and vulvar ($n = 4$). Recurrences were radiologically confirmed. Median dose of pelvic RT given prior to the recurrences was 60 Gy, and the median cyberknife dose delivered was 25 Gy. Efficacy was evaluated by RECIST criteria and toxicity according to CTCAE v3.0 questionnaires. Kaplan-Meier estimates for progression-free (PFS) and overall survival (OS) were calculated. Associations between prognostic factors and survival were determined using Cox proportional hazards regression models. See Figure 1.

Results: Of the 29 patients, 27 had follow-up data and were included in this analysis. Median time between primary RT and cyberknife treatment was 24 months. Seventeen recurrences were located in the central pelvis, 4 in the pelvic sidewall, and 9 in the PA region. Median follow-up was 13.7 months. Overall response rate to cyberknife at 12 months was 89% (9 complete response, 8 partial response, and 7 stable disease). The median PFS and OS were 11.7 months and 20.5 months, respectively. Only 6 in-field disease progressions were observed. Increasing age was significantly associated with higher hazard of progression (HR = 1.07, $P = 0.004$). All patients were able to complete the prescribed cyberknife dose, and only 3 developed grade 3 or 4 toxicities: SBO ($n = 2$) and rectovaginal fistula ($n = 1$).

Conclusion: Our results suggest that use of cyberknife for locally recurrent gynecologic cancers in a prior radiated field can be an effective nonsurgical salvage option providing additional local control with acceptable toxicity. The results of this retrospective chart review warrant further investigation to identify the patients who are more likely to benefit from this approach.

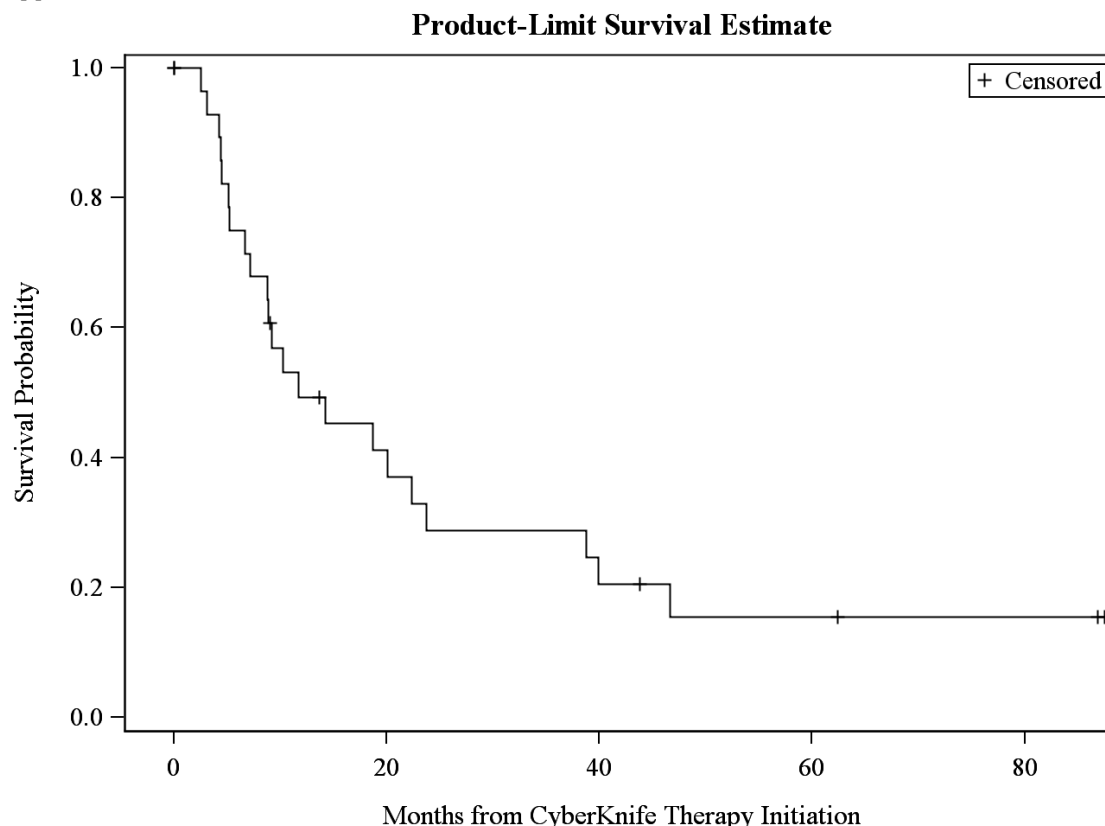


Fig. 1. Kaplan-Meier Estimates for Progression-Free Survival. The median time to progression was 11.7 months with a 95% confidence interval of 8.8 months to 22.4 months.

239 - Poster Session

Routine HbA1c testing in women undergoing major gynecologic surgery to detect prevalence of glucose intolerance

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Objective: To determine the prevalence of undiagnosed diabetes, prediabetes, and overall incidence of glucose intolerance in women undergoing major surgical procedures on the gynecologic oncology service.

Method: This was a retrospective review of preoperative HbA1c levels obtained at preadmission testing in women scheduled for major gynecologic surgery at Winthrop University Hospital by gynecologic oncologists between July 2014 and July 2016. Exclusion criteria were lack of HbA1c within 90 days of scheduled surgery and all women undergoing minor surgical procedures. Diabetes was defined either by established diagnosis or with HbA1c ≥ 6.5 , and prediabetes if HbA1c ranged from 5.7 to 6.4. Values less than 5.7 were considered normal.

Results: A total of 343 women underwent major procedures and had HbA1c levels obtained. Fifty-eight (16.9%) had a known diagnosis of diabetes, and 285 (83.1%) were presumed nondiabetics. The majority (182, 63.9%) had normal HbA1c; 86 (30.2%) were prediabetic; and 17 (6%) met criteria for diabetes, for a 36.2% prevalence of abnormal glucose tolerance in presumed nondiabetics. When all 343 women were considered, the diagnosis of glucose intolerance was present in 161 (46.9%), 64.0% of whom were previously undiagnosed.

Conclusion: Nearly half of the women undergoing major gynecologic surgery procedures on the oncology service had impaired glucose tolerance. The diagnosis was previously not established in 64.0%. Presurgical assessment of HbA1c is warranted in this high-risk population.

240 - Poster Session

Recurrence patterns and survival in patients with endometrial cancer undergoing robotic sentinel lymph node mapping (SLNM)

A.J. Stephens, J.A. Kennard, S. Ahmad, J.L. Gise, K.A. Smith, K.P.A. Wisner, J.E. Kendrick IV, N.D. McKenzie, J.W. Pepe and R.W. Holloway. *Florida Hospital Cancer Institute, Orlando, FL, USA*

Objective: To assess recurrence-free survival (RFS) and overall survival (OS), and to analyze patterns of disease recurrence in patients with apparent uterine-confined endometrial cancer (EC) who underwent robotic sentinel lymph node mapping (SLNM) followed by hysterectomy with or without completion lymphadenectomy.

Method: A database analysis was performed on 417 patients with uterine-confined EC who underwent robotic hysterectomy and SLNM with or without completion lymphadenectomy (LA) from March 2011 to August 2016. The dataset was analyzed for disease recurrence, disease site, prior therapies, sentinel lymph node (SLN) assessments, and surgicopathological findings. Frozen section was used to determine need for paraaortic LA. Death record searches were used to confirm current survival status for all patients lost to follow-up prior to 12 months ($n = 73$). RFS was determined for the remaining 344 patients, and OS for the 417-patient cohort.

Results: Mean age and BMI of 417 patients was 64.9 ± 10.2 years and 33.2 ± 8.3 mg/m² (range 17.8–63 mg/m²), respectively. Histologies included 261 (62.6%) endometrioid (59.8% G1, 30.7% G2, and 9.5% G3) and 146 (37.4%) high-risk subtypes. A total of 204 patients (48.9%) received completion pelvic LA; 188 (45.1%) had pelvic with paraaortic LA; and 25 (6.0%) had SLNM only. Mean SLN was 3.5 ± 2.6 , pelvic 15.0 ± 9.0 , and paraaortic nodes 8.2 ± 6.3 . GOG risk categories included 149 (35.7%) low, 71 (17.0%) low-intermediate, 94 (22.5%) high-intermediate, and 103 (24.7%) high risk. Adjuvant therapy was 11 (2.6%) EBRT, 74 (17.8%) EBRT with chemo, 65 (15.6%) chemo with or without brachytherapy, 16 (3.8%) brachytherapy alone, and 251 (60.2%) no therapy. Mean follow-up time from surgery was 24.4 ± 18.5 months (range 0–76 months). Twenty-four (7.0%) patients had recurrence at a mean 20.9 ± 12.6 months (range 4–43 months). Estimated 3-year RFS was 93%. The 5-year disease-specific OS was 89%. Sites of disease recurrence were 5 (1.5%) vaginal cuff, 4 (1.2%) retroperitoneal pelvic, 3 (0.9%) aortic, 10 (2.9%) peritoneal, and 8 (2.3%) systemic. Recurrent disease was identified in 17/358 (4.7%) endometrioid and 7/59 (11.9%) high-risk subtypes.

Conclusion: Patients with apparent uterine-confined EC undergoing SLN mapping and use of adjuvant therapies based on GOG risk status had excellent retroperitoneal control. Systemic and peritoneal recurrences remain a target for improved outcomes.

241 - Poster Session

Neoadjuvant chemotherapy is associated with more anemia and perioperative blood transfusions than primary debulking surgery in women with advanced-stage ovarian cancer

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Objective: The purpose of this study was to determine the prevalence of anemia and incidence of perioperative allogenic blood transfusions in patients undergoing primary treatment for advanced-stage ovarian cancer with neoadjuvant chemotherapy (NACT) compared to patients undergoing treatment with primary debulking surgery (PDS).

Method: We performed a single-institution retrospective review of patients diagnosed with stage IIIB–IVB epithelial ovarian cancer between 2010 and 2013 undergoing primary therapy with either NACT or PDS. Clinicopathologic characteristics were extracted. Anemia was defined as a hemoglobin concentration of ≤ 11.5 g/dL. Variables were compared by Student *t* test and χ^2 analysis with significance set at ≤ 0.05 .

Results: A total of 131 women were included, 65/131 treated with NACT and 66/131 treated with PDS. There was no difference in age or stage at diagnosis between the two groups. The average hemoglobin prior to treatment was significantly lower in women who received NACT (NACT 11.8 g/dL vs PDS 12.8 g/dL, $P < 0.05$). Women treated with NACT had a significant drop in hemoglobin during chemotherapy treatment prior to interval surgery (11.8 g/dL at diagnosis to 10.7 g/dL preoperatively, $P < 0.05$). Seventy-seven percent of NACT patients were anemic prior to interval debulking surgery compared with 15% of patients prior to PDS ($P < 0.001$, Figure 1). Average estimated blood loss at debulking was higher in patients selected for PDS (871 mL) than in patients undergoing interval debulking after NACT (544 mL); however, the perioperative transfusion rate was higher in patients undergoing interval debulking surgery (NACT 77% vs PDS 56%, $P = 0.01$, Figure 2).

Conclusion: Women selected for NACT were more likely to be anemic at diagnosis compared with women selected for PDS and to become increasingly anemic during neoadjuvant chemotherapy. Despite a lower average blood loss at debulking surgery, NACT patients receive more blood transfusions perioperatively than patients undergoing PDS. This represents a potential opportunity for therapeutic intervention during NACT to correct anemia prior to interval debulking surgery and potentially decrease the perioperative transfusion rate and associated risks in this population.

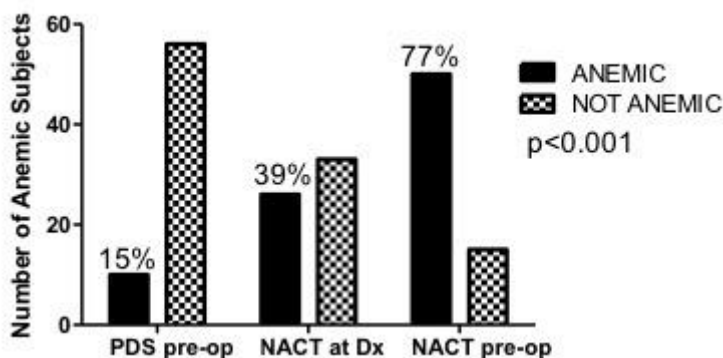


Fig. 1. Rates of anemia by treatment group at diagnosis and prior to surgery.

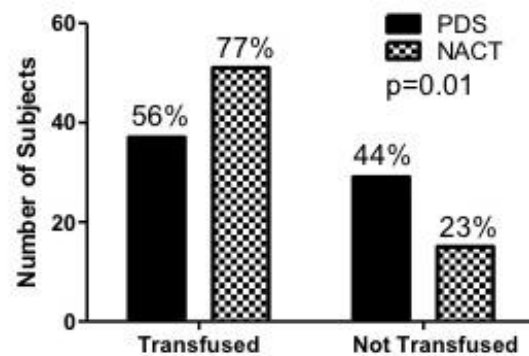


Fig. 2. Rates of transfusion by treatment group.

242 - Poster Session

Does surgical platform impact recurrence and survival? A study of usage of multi-port, single port and robotic-assisted laparoscopy in endometrial cancer staging

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Objective: To identify differences in progression-free survival (PFS) and overall survival (OS) among women undergoing minimally invasive surgery for endometrial cancer (EC) with multiport laparoscopy (MPL), single-port laparoscopy (SPL), and robotic-assisted laparoscopy (RL).

Method: A multicenter single-institution retrospective cohort study was performed in women with EC who underwent minimally invasive surgical staging from 2009 to 2016. Data were collected for demographics, pathologic information, adjuvant treatment, and disease status. Pearson χ^2 and Fisher exact tests were used to evaluate risk factors for outcomes; Kaplan-Meier estimates and Cox proportional hazards were used to evaluate differences in time to progression or death, and a multivariate regression analysis was performed.

Results: In the final analysis, 1,150 women with EC were included who underwent minimally invasive surgical staging with RL ($n = 652$), MPL ($n = 214$), or SPL ($n = 284$). The median age and BMI of women was 62.0 years and 33.5 kg/m², respectively. The majority of patients had endometrioid histology (88.1%), stage IA (74.7%) or IB disease (13.1%), and FIGO grade 1 (57.4%) or 2 (26.0%) histology. Lymphovascular space invasion (LVSI) was present in 24.7% ($n = 283$). Adjuvant radiation (RT) was given in 34.2% of cases with 21.9% receiving vaginal brachytherapy (VBT), 6.6% receiving pelvic RT (EBRT), and 5.4% receiving both. Of all patients, 20.7% received chemotherapy with carboplatin and paclitaxel as the most common regimen. PFS and OS are listed in Table 1. There were no differences between PFS ($P = 0.56$) or OS ($P = 0.99$) at 2, 3, and 5 years for RL, SPL, or MPL, respectively. OS was predicted by age, stage, grade, adjuvant chemotherapy, adjuvant RT, and presence of LVSI ($P < 0.001$ for each). On multivariate analysis, modality of surgery did not have an impact on OS or PFS (RL, HR = 1.19, $P = 0.62$; SPL, HR = 0.93, $P = 0.86$, vs MPL). Age >60 (HR = 4.67, $P < 0.001$), FIGO grade 3 (HR = 2.17, $P = 0.01$), stage III–IV versus I–II (HR = 3.52, $P = 0.002$), LVSI (HR = 2.15, $P = 0.03$) were associated with reduced OS.

Conclusion: This study identifies no difference in PFS or OS in patients undergoing surgical staging for EC with RL, SPL, or MPL. These findings support continued surgeon discretion and hospital administration support for the use of multiple surgical platforms for surgical management and staging of endometrial cancer.

Table 1. Impact of surgical platform on recurrence and survival.

Survival	All ($n = 1,150$)	Robotic-Assisted Laparoscopy ($n = 652$)	Single-Port Laparoscopy ($n = 284$)	Multiport Laparoscopy ($n = 214$)	P Value
Progression-Free Survival					0.56
2 year	91.6%	92.7%	90.3%	90.1%	
3 year	88.9%	90.2%	87.7%	86.8%	
5 year	84.1%	84.2%	85.2%	83.4%	
Overall Survival					0.99
2 year					
3 year	91.6%	95.6%	95.0%	94.4%	
5 year	88.9%	93.4%	93.1%	91.8%	
	84.1%	90.7%	91.8%	91.8%	

243 - Poster Session

Paraortic lymph node dissection pathology in patients with endometrial cancer undergoing robotic sentinel lymph node mapping (SLNM)

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Objective: To describe paraortic and pelvic lymph node pathology in patients with apparent uterine-confined endometrial cancer who underwent robotic hysterectomy with sentinel lymph node mapping (SLNM) and completion pelvic and paraortic lymphadenectomy (LN).

Method: Patients with apparent uterine-confined endometrial cancer underwent robotic hysterectomy and SLNM with completion lymphadenectomy (pelvic or pelvic and aortic) from March 2011 through August 2016 and were enrolled in a database. Intraoperative frozen section was used to determine need for aortic dissections. All GOG high-risk patients were analyzed for standard histopathologic risk factors for metastasis, and a comparison of pelvic and aortic node metastases was performed. Isolated tumor cells (ITC) included H&E or cytokeratin +ve nodes and were counted as metastases for staging.

Results: A total of 417 patients underwent SLNM and were identified. Of these patients, 204 (48.9%) underwent completion pelvic LN, 188 (45.1%) pelvic + paraortic LN, and 25 (6%) SLNM alone. There were 95 (22.8%) patients who had positive LN

(88/95 SLN), and the false negative SLNM algorithm rate was 7/417 (1.7%). There were 103 patients who were high risk by GOG-249 criteria (stage IIIA = 6, IIIB = 1, IIIC1 = 67, and IIIC2 = 28) and constitute the study cohort. The mean age was 65.2 years, and BMI 32.5 kg/m². Histology was 74.8% endometrioid and 25.2% high-risk nonendometrioid. The mean tumor size was 5.3 ± 2.3 cm; >½ DOI, 55.3%; and LVSI, 69.9%. The mean SLN count was 3.4 ± 2.6; pelvic nodes, 18.0 ± 10.0; and paraaortic, 8.5 ± 6.5. The 88 SLN metastasis included 35 (39.8%) ITC. There were significantly more SLN ITCs found in the IIIC1 group than in the IIIC2 group (929/67, 43.3%, vs 6/28, 21.4%, $P = 0.03$). The rate of paraaortic metastasis with pelvic SLN containing ITC was 17.1% (6/35) characterized by 2 macro-, 5 micro- and 1 ITC aortic metastases. There were no isolated aortic metastasis cases in the 417 patient SLNM database.

Conclusion: The SLNM algorithm had a low false negative rate, and approximately 40% of positive SLN nodes had ITC. Despite having “low-volume” ITC metastasis, there was a clinically significant rate of paraaortic metastases. We recommend routine frozen section analysis of the primary tumor to direct paraaortic dissections in the National Comprehensive Cancer Network SLN algorithm.

244 - Poster Session

The feasibility of minimally invasive radical trachelectomy in children with embryonal rhabdomyosarcoma of the cervix: Improving surgical quality and recovery in this pediatric population

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Objective: Embryonal rhabdomyosarcoma (RMS) is a malignancy often affecting young girls and young women. These children have traditionally undergone a total hysterectomy under the care of a pediatric surgeon or a pediatric gynecologist. New data suggest that fertility-preserving radical trachelectomy is appropriate in the management of patients with clinical stage I embryonal RMS of the cervix.

Method: We describe both laparoscopic and robotic minimally invasive surgical approaches to facilitate radical trachelectomy in children with embryonal RMS of the cervix. We describe modifications of the standard surgical technique to facilitate the procedure in the pediatric population.

Results: Three pediatric patients underwent minimally invasive radical trachelectomy between September 2015 and July 2017 for clinical stage I embryonal RMS. A 2-year-old child underwent a laparoscopic-assisted radical trachelectomy. A 6-year-old girl underwent a robotic-assisted radical trachelectomy. A 14-year-old girl underwent a robotic-assisted radical trachelectomy with placement of an abdominal cerclage. None of the patients experienced perioperative complications. All patients were discharged home on postoperative day 1 or 2.

Conclusion: Radical trachelectomy may be an alternative to abdominal hysterectomy in the surgical management of girls with embryonal RMS of the cervix. Minimally invasive radical trachelectomy appears safe and feasible in this pediatric population. The gynecologic oncologist can play an important role in facilitating this fertility-preserving surgery.

245 - Poster Session

Anesthetic and surgical outcomes in obese endometrial cancer patients undergoing robotic hysterectomy

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Objective: To determine the effect of obesity, pneumoperitoneum, and steep Trendelenburg positioning on respiratory system mechanics during robot surgery for endometrial cancer (EC).

Method: We examined a cohort of 89 women undergoing robot surgery for EC. We recorded pulmonary parameters including peak airway pressure, plateau pressure, and static compliance every 5 minutes throughout surgery starting at baseline (after induction of anesthesia, before any skin incisions) and continuing until the end of surgery. The time point of maximum plateau pressure reached during each surgery was used for subsequent calculations. We evaluated the effect of body mass index (BMI) on plateau pressure and static compliance by comparing linear regression coefficients. A nominal value of $P < 0.05$ was considered significant.

Results: Maximum peak airway pressures significantly increased for patients with BMI > 40 kg/m² compared with nonobese patients, those with BMI < 30 kg/m² (38.1 cm H₂O vs 41.5 cm H₂O, $P = 0.01$). There were no intraoperative or postoperative

anesthetic complications associated with increased peak airway pressures; the maximum plateau pressure was achieved for all patients when in steep Trendelenburg with pneumoperitoneum. Median baseline plateau pressures were also significantly lower than when patients had pneumoperitoneum and steep Trendelenburg (22 cm H₂O vs 35 cm H₂O, $P < 0.001$). The median baseline static compliance, 33.5 mL/cm H₂O, was significantly higher than the median static compliance with pneumoperitoneum and steep Trendelenburg (17 mL/cm H₂O, $P < 0.001$). Figure 1 shows that once the patient has a pneumoperitoneum and is in steep Trendelenburg, plateau pressure and static compliance were insensitive to changes in BMI.

Conclusion: The effects of pneumoperitoneum and steep Trendelenburg significantly reduced static lung compliance and increased plateau pressures. Although many anesthesiologists and surgeons assume that class III obesity (BMI > 40 kg/m²) has a negative impact on respiratory mechanics during robotic hysterectomy, we did not identify a relationship between either plateau pressure or static compliance based on BMI.

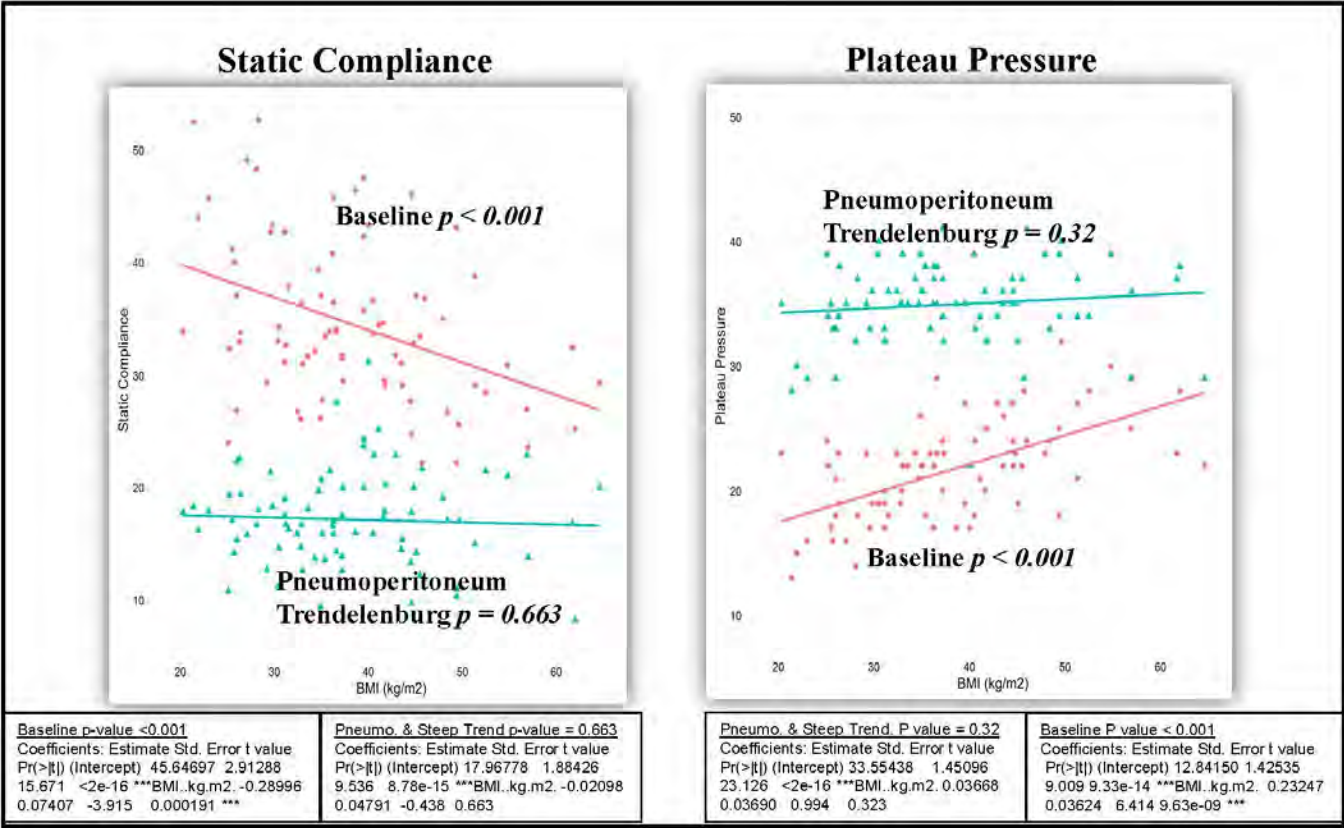


Fig. 1. Respiratory Mechanics.

246 - Poster Session

Near-Infrared angiography during rectosigmoid resection and anastomosis in women with gynecologic malignancies
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Objective: To evaluate the use of near-infrared (NIR) technology with intravenous indocyanine green (ICG) injection and PINPOINT Endoscopic Fluorescence Imaging System (NOVADAQ, Canada) in assessing the perfusion of anastomoses during rectosigmoid resection, in a series of consecutive patients undergoing surgery for gynecologic malignancies.

Method: This is a retrospective study identifying all patients who underwent rectosigmoid resection for a gynecologic malignancy between January 1, 2013, and May 31, 2017, at a single institution. NIR use was based on surgeon preference and device availability. Various clinicopathologic data and outcomes were collected.

Results: Of all patients undergoing rectosigmoid resection during that time, 68 (23%) patients who had rectosigmoid resection that included the use of NIR were identified. The median age was 63 (range 22–83) years; median BMI was 25.5

(range 18.5–40.4) kg/m²; and median preoperative albumin was 4.2 (range 2.4–4.7) g/dL. There were 59 patients (87%) with ovarian cancer and 46 (68%) with high-grade serous histology. Thirty-three patients (49%) underwent primary debulking surgery, and 18 (27%) had interval debulking. Median operative time was 7.7 (range 4.6–13.1) hours; median hospital stay was 8 (range 4–22) hours; median estimated blood loss and intravenous fluids were 950 (range 150–3,050) mL and 3300 (range 1,000–15,000) mL, respectively. Anastomoses <10 cm from the dentate line occurred in 18 patients (27%). Four patients (6%) had a diverting ostomy. Inadequate perfusion identified on NIR assessment was the indication for 1/4 (25%) diversions. One patient (2%) had an anastomotic leak. A postoperative pelvic abscess occurred in 2 patients (3%). Seven patients (10%) were readmitted within 30 days of surgery. There were no allergic reactions to ICG or intraoperative complications associated with NIR.

Conclusion: NIR is a safe and feasible adjunct to standard assessment of primary rectosigmoid anastomosis, associated with low rates of intestinal diversion and anastomotic leaks. These results warrant prospective trials to validate the utility of NIR in rectosigmoid resection for patients with gynecologic malignancies.

247 - Poster Session

Management of STIC lesions in risk-reducing bilateral salpingo-oophorectomy (RRBSO)

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Objective: Serous tubal intraepithelial carcinoma (STIC) is considered the precursor of many ovarian and primary peritoneal serous carcinomas in *BRCA* mutation-positive women. STIC are discovered incidentally in the fallopian tubes via risk-reducing salpingo-oophorectomy in approximately 5%–7% of women. Unfortunately, the biological and clinical relevance of these lesions in *BRCA* mutation-positive women is unknown. The purpose of this study was to review the incidence of STIC lesions in women undergoing risk-reducing salpingo-oophorectomy with a *BRCA* mutation compared to those without a mutation and their outcomes in follow-up.

Method: The authors reviewed pathology reports from 2006 to 2017 that indicated a bilateral salpingo-oophorectomy (BSO) with STIC diagnosis confirmed using the Sectioning and Extensively Examining of the Fimbriated (SEE-FIM) protocol via an electronic database search at our institution. The cases were studied individually for surgical indication. Women undergoing surgery who were symptomatic or had confirmed tumor were eliminated.

Results: Of the 7,073 women who underwent a BSO, 54 women had a STIC lesion upon pathology review. Twenty-six women underwent *BRCA* genetic testing; 13 had a *BRCA* mutation, and 13 were *BRCA* negative. Of those who received genetic testing, we identified 7 women (26.9%) who underwent risk-reducing salpingo-oophorectomy. Of these 7 women, 6 (85.7%) were *BRCA* positive and 1 (14.3%) was *BRCA* negative. After at least 1 year of follow-up, 5 (83.3%) of the 6 *BRCA*-positive women were disease-free, as was the 1 *BRCA*-negative woman.

Conclusion: The frequency of STIC lesions identified via risk-reducing salpingo-oophorectomy, regardless of *BRCA* mutation status, remains very low. Further studies are needed to increase our understanding of the value of opportunistic salpingectomy. Alternative approaches to identifying STIC lesions and investigating the carcinogenic sequence may prove beneficial in enhancing our understanding of ovarian high-grade serous carcinomas.

248 - Poster Session

Outcomes with ultrasound guided transversus abdominal plane (TAP) block after open gynecologic surgery

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Objective: Transversus abdominal plane (TAP) block is a peripheral nerve block placed under ultrasound guidance at the end of surgery to anesthetize the nerves in the anterior abdominal wall. We sought to determine whether TAP block reduces postoperative narcotic use or length of stay after open gynecologic surgery.

Method: This was an institutional review board-approved retrospective review conducted at a single institution from July 2016 to July 2017. Patients were included if they had an open hysterectomy by a gynecologic oncologist. Postoperative pain scores and total oral morphine equivalents were calculated on days 1, 2, and 3. Outcomes were compared between patients with and without TAP block. Statistical analyses were performed using χ^2 and Mann-Whitney *U* tests and univariate regression.

Results: Among the 98 patients identified, 73 (74.5%) received a TAP block. Patient operative characteristics differed between patients with no TAP block versus TAP block (Table 1). The majority of patients with TAP block had vertical incisions (86.3%), while the majority of patients with no TAP block had transverse incisions (64%). Compared to the no TAP group, more patients in the TAP block group underwent ovary cancer debulking (65.7% vs 8%) and experienced postoperative ileus (26% vs 8%). Despite these differences in operative characteristics, there were no differences in pain scores on day 1, 2, or 3 or in total narcotic use by day 3 (Table 1). Length of stay was significantly lengthened with ileus (RR = 9.5, $P < 0.0001$), but median length of stay did not differ between groups (4 days vs 4 days).

Conclusion: Providers preferentially use TAP block in patients with vertical skin incisions and more extensive surgery. Compared to outcomes in patients with less extensive surgery and no TAP block, TAP block results in comparable pain scores, narcotic use, and length of stay.

Table 1. Patient characteristics of no TAP block versus TAP block.

Characteristic	No TAP Block (n = 25)	TAP Block (n = 73)	P Value
Incision			
Vertical	9 (36%)	63 (86.3%)	
Transverse	16 (64%)	10 (13.7%)	
Debulking Surgery	2 (8%)	48 (65.7%)	
Ileus	2 (8%)	19 (26.03%)	0.06
Pain score			
POD1	4.6	4	0.84
POD2	3.8	4	0.51
POD3	3.6	3.8	0.43
POD3 Total Morphine Equivalent	300 mg	327.8 mg	0.53
Length of Stay	4 days	4 days	0.12

249 - Poster Session

Comparative surgical outcomes between robotic radical hysterectomy and abdominal radical hysterectomy in early stage cervical cancer

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Objective: To compare the perioperative morbidity, recurrence rate, and progression free survival (PFS) between abdominal and robotic radical hysterectomy.

Method: A retrospective cohort of patients at the University of Alabama undergoing radical hysterectomy from 2010 to 2016 was identified. Perioperative complications, recurrence rate, and PFS were compared using standard statistical analysis.

Results: A total of 140 patients were identified; 75 underwent abdominal radical hysterectomy and 65 underwent robotic radical hysterectomy. Those who had abdominal surgery had larger lesions (2.7 vs 1.6 cm in largest dimension, $P = 0.0005$) and deeper depth of invasion (8.5 vs 6.0 mm, $P = 0.01$), but there was no difference in histology ($P = 0.87$), the presence of LVSI (28% vs 25%, $P = 0.86$), or number of lymph nodes removed (13.9 vs 13.1, $P = 0.46$). There was no difference between groups in aggregate perioperative complication rate (24% vs 28%, $P = 0.70$), but those who had robotic surgery were more likely to have a vaginal cuff dehiscence (0 vs 6%, $P = 0.04$). All other individual complications, including intraoperative complications (15% vs 2%, $P = 1.0$), GI complications (8% vs 5%, $P = 0.50$), urinary complications (8% vs 11%, $P = 0.77$), infectious complications (11% vs 8%, $P = 0.57$), wound complications (4% vs 8%, $P = 0.47$), pulmonary complications (4% vs 0%, $P = 0.25$), fistula formation (9% vs 9%, $P = 1.0$), venous thromboembolism (1% vs 3%, $P = 0.60$), and lymphedema (1% vs 2%, $P =$

1.0), were not statistically different. In addition, there was no difference in recurrence rates (19% vs 20%, $P = 1.0$), or PFS (27.6 vs 29.9 months, $P = 0.82$).

Conclusion: Robotic radical hysterectomy is associated with an increase in postoperative vaginal cuff dehiscence in this cohort. There do not appear to be any other differences in perioperative outcomes or long-term complications between the two groups. In addition, number of lymph nodes evaluated, recurrence rates, and PFS were similar. Robotic radical hysterectomy appears to be an acceptable alternative to abdominal radical hysterectomy for women undergoing surgery for the treatment of cervical cancer.

250 - Poster Session

Can PET-CT predict complete secondary cytoreduction in ovarian cancer?

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Objective: To analyze the role of PET-CT (18F-FDG) in predicting complete surgical resection in recurrent ovarian cancer.

Method: We included 65 patients who had PET-CT before secondary cytoreductive surgery (SCR) at the A.C. Camargo Cancer Center from February 2008 to March 2017. All patients had platinum-sensitive recurrent epithelial ovarian cancer with no evidence of disease outside the abdomen. False negative PET-CT was considered as the presence of more disease than suggested by the PET-CT.

Results: Median age was 56 (range 31–81) years, and the median interval between primary and secondary cytoreduction was 28.5 (range 8.2–87.7) months. Fifty-six (86.2%) patients had high-grade serous tumors; 59 (90.8%) were stage IIIC; and the median CA-125 was 57 (range 10–698). Fifty-five (84.6%) patients had complete SCR, and 33 (50.7%) had surgical complexity score of ≥ 2 . The median peritoneal carcinomatosis index (PCI) was 6 (range 1–39). PET-CT suggested disease in peritoneum in 44 (67.7%) of cases, intraabdominal lymph node in 11 (16.9%), hepatic in 2 (3.1%), adrenal in 1 (1.5%), and no uptake in 7 (10.8%). Forty (61.5%) cases had false negative PET. Of the patients with peritoneal disease suggested by PET-CT, 19 (43.1%) had ≥ 3 peritoneal implants uptake, and this finding influenced the likelihood of achieving complete SCR. Patients with < 3 and ≥ 3 implants had complete SCR in 94.9% and 68.4% of cases, respectively ($P = 0.012$). Moreover, a low PCI also correlated to complete SCR, with a median PCI of 5 and 19 for patients who had complete or suboptimal SCR, respectively ($P = 0.006$). False negative PET-CT, CA-125 value, histologic type, stage, and disease-free interval did not influence achieving complete SCR. The median follow-up after SCR was 21.3 (range 1–104) months, and the median overall survival was 94 months.

Conclusion: PET-CT had a high false negative rate in predicting the intraabdominal disease. However, presence of < 3 implants in PET-CT correlated to a higher likelihood of complete SCR.

251 - Poster Session

Predictive factors of surgical morbidity for early-stage cervical cancer management: A prospective multicentric cohort of 228 patients

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Objective: The aim of this study was to assess the postoperative morbidity of patients who have undergone a radical surgery for early-stage cervical cancer and to determine the predictive factors of complication.

Method: We analyzed the data of the prospective multicentric trials on sentinel node biopsy for cervical cancer (SENTICOL II). Patients from 28 French oncologic centers between 2009 and 2012 were included.

Results: A total of 228 patients were analyzed. The median age was 43 (range 22–85) years. There were 192 patients who had a radical hysterectomy and 36 a radical trachelectomy. Of all patients, 91.4% had stage IB1 disease. There were 67.7% epidermoid carcinoma and 30.2% adenocarcinoma. Urinary, lymphovascular, and neurologic complications rates were 30.7%, 25.4%, and 21.5%, respectively. In a multivariate analysis, the predictive factors of lymphovascular complications were previous pelvic surgery (ORa = 3.3, 95% CI 1.6–6.8, $P = 0.001$); 1-time surgery (ORa = 7.7, 95% CI 1.6–33.3, $P = 0.01$); associated vaginal complication (ORa = 2.7, 95% CI 1.05–7.12, $P = 0.04$); and adjuvant radiotherapy (ORa = 4.6, 95% CI 1.9–

11.3, $P = 0.001$). In a multivariate analysis, the predictive factors of neurologic complications were BMI $< 25 \text{ kg/m}^2$ (ORa = 2, 95% CI 0.9–1.6, $P = 0.07$), and age < 45 years (ORa = 5, 95% CI 1.4–20, $P = 0.01$).

Conclusion: These complications rates were less important than those found in the literature. The main complications were urinary infections and lower limb lymphedema. The nerve-sparing technique is the most important key to improving the functional outcomes for the surgical management for early-stage cervical cancer.

252 - Poster Session

Survival outcomes of primary versus interval visceral-peritoneal debulking (VPD) surgery in patients with stage IIIC-IV ovarian cancer and complete resection: A cohort study

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Objective: To compare survival outcomes of patients with FIGO stage IIIC–IV primary ovarian cancer (OC) undergoing upfront (group 1) versus interval (group 2) visceral-peritoneal debulking (VPD) surgery after neoadjuvant chemotherapy.

Method: All consecutive patients with FIGO stage IIIC–IV OC were treated with VPD. This surgery aims at complete resection (CR) of all visible disease. Between January 2009 and December 2012 they had upfront VPD. Between January 2013 and December 2016 they had neoadjuvant chemotherapy and proceeded to have interval VPD in case of no progression. All surgical and medical information was prospectively recorded in the Oxford Ovarian Cancer data base. Propensity analysis was performed to verify equal distribution of characteristics, treatment, and risk factors. Baseline characteristics, extension of surgery, and residual disease were compared to minimize bias. Disease-free survival (DFS) and overall survival (OS) were calculated by using the Kaplan-Meier method.

Results: Over the study period, 250 patients had VPD. Full survival data were available for 203 patients, 81 (33.9%) in group 1 and 122 (60.1%) in group 2. Mean age at surgery was 63.4 years, with no statistical difference between the groups ($P = 0.91$). No difference FIGO stage between group 1 and group 2 was observed (stage IV, 18.5% vs 22.1%, $P = 0.53$) and residual disease (CR, 89.9% vs 89.0%, $P = 0.84$). At 30.2 months median follow-up, median DFS was 23.6 and 17.4 months in group 1 and group 2, respectively ($P = 0.70$). Median OS was 48.8 months in group 1 and 31.4 months in group 2, displaying a trend toward significance in favor of group 1 ($P = 0.059$). Survival curves are shown in Figure 1.

Conclusion: In this study patients who underwent upfront VPD had similar DFS but better OS than patients who underwent neoadjuvant chemotherapy despite the latter group excluding patients with tumor resistant to chemotherapy. Although not a clinical trial, this study has the strength of a cohort study with time being the only distinctive factor for patient treatment.

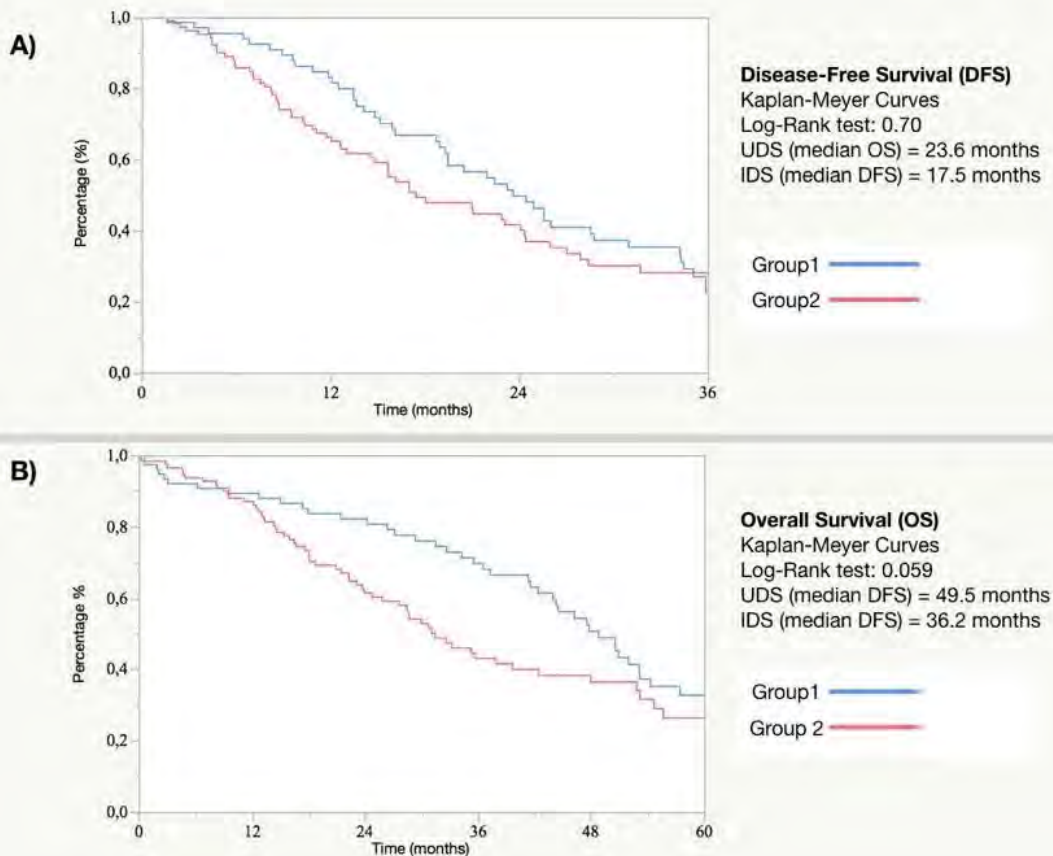


Fig. 1. Disease-free survival (A) and Overall survival (B) of patients undergoing Upfront VPD (Group 1) and Interval VPD surgery (Group 2) for Stage IIIC-IV Ovarian Cancer.

253 - Poster Session

Association between cytoreductive surgery outcomes and postoperative major complication among women with ovarian cancer

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Objective: To compare postoperative major complication rates among ovarian cancer patients who underwent resection to no gross residual (NGR) disease versus optimal cytoreduction (<1 cm) versus suboptimal cytoreduction (>1 cm).

Method: Patients with ovarian cancer who underwent cytoreductive surgery recorded in the National Surgical Quality Improvement Program (NSQIP) in 2015 were identified. The primary exposure was residual disease, which was recorded as NGR disease, residual disease <1 cm (optimal), and residual disease >1 cm (suboptimal). The primary outcome was 30-day grade 3 or higher major postoperative complication defined by the Clavien-Dindo scale. Associations were examined with bivariable tests and multivariable logistic regression.

Results: We identified 1,234 women with ovarian cancer who underwent cytoreductive surgery. Of these patients, 75% underwent resection to NGR; 9.8% had an optimal cytoreduction; and 14.8% had a suboptimal cytoreduction. Optimal patients had the highest rates of major complications (27.3%) compared with those who underwent NGR disease resection (12.4%) or suboptimal cytoreduction (18.0%) ($P < 0.001$). Patients undergoing optimal resection also had the longest operating room times and the most surgically complex procedures (223 minutes, 42.7 RVU) compared with patients undergoing resection to NGR disease (181.5 minutes, 32.5 RVU) or suboptimal resection (170 minutes, 34.1 RVU) (all $P < 0.001$). Optimal resection patients had 3 times the odds of a major complication (OR 2.7, 95% CI 1.7–4.1) compared to those undergoing resection to NGR disease, and nearly twice the odds of an adverse event compared to those undergoing suboptimal resection (OR 1.7, 95% CI 1.0–3.0). With adjustment, optimal resection was associated with more major complications than NGR resection (aOR 1.9, 95% CI 1.2–3.0), but not compared to suboptimal resection (aOR 1.3, 95% CI 0.7–2.3).

Conclusion: Patients who underwent optimal cytoreduction had the highest rates of major complication compared to both NGR disease and suboptimal debulking. Their cases also required the most operating room time and represented the most complex surgeries. The extensive surgical effort required to achieve optimal cytoreduction is associated with the highest rate of major postoperative complications.

254 - Poster Session

Assessment of a scoring system to predict outcomes after interval debulking surgery for advanced ovarian carcinoma

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Objective: A scoring system has recently been proposed by Suidan et al. to predict gross residual disease at primary debulking surgery for advanced epithelial ovarian cancer. This scoring system has not been assessed in patients undergoing neoadjuvant chemotherapy (NACT). The aim of this study is to assess the reproducibility and prognostic significance of the scoring system when applied to women undergoing NACT followed by interval debulking surgery (IDS).

Method: A retrospective cohort study was conducted of patients with advanced ovarian cancer who underwent NACT and IDS between 2005 and 2014. Computed tomography scans at diagnosis (T0) and after initiation of NACT but before IDS (T1) were independently assessed by 2 radiologists. A score for each patient was calculated at each of the 2 timepoints using radiologic and clinical criteria. The change in score between timepoints (T0 score and T1 score) was assessed and compared to residual disease status. Interobserver variability was assessed utilizing Fleiss's kappa (κ). Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method and were compared using the log rank test.

Results: There were 72 patients eligible for analysis. The change in score between T0 and T1 was highly reproducible among radiologists ($\kappa = 0.77$). Residual disease at the time of IDS was compared for patients with a change in score of >1 (denoting an improvement in disease burden) or a change in score of ≤ 1 (denoting stable or worsening disease burden). A change in score of >1 was significantly associated with less residual disease compared to a change in score of ≤ 1 as assessed by both radiologists (residual disease >1 cm, 3% and 2% vs 19% and 21%, $P = 0.04$ and 0.01). A trend towards improvement in OS was observed in patients with a score of >1 compared to those with a score of ≤ 1 as assessed by both radiologists (mean OS = 1,010 and 990 days vs 710 and 716 days, $P = 0.15$ and 0.17).

Conclusion: A change in score between diagnosis and after initiation of NACT for women with advanced ovarian cancer is highly reproducible and demonstrates ability to predict gross residual disease after IDS. This change in score may be helpful in treatment planning and prognostication for women with advanced ovarian cancer receiving NACT and IDS.

255 - Poster Session

An evaluation of bowel resection and ostomy formation among patients undergoing cytoreductive surgery for advanced-stage ovarian cancer

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Objective: The objective of this study was to describe the clinical characteristics and outcomes of bowel resection and ostomy formation among patients undergoing cytoreductive surgery for the management of advanced-stage ovarian cancer.

Method: Patients at 2 academic centers with stage IIIC–IV ovarian, fallopian tube, or primary peritoneal cancer who underwent cytoreductive surgery between January 2010 and December 2014 were identified retrospectively. Demographic and clinical data were collected and analyzed.

Results: Of the 553 patients identified, 384 (69%) had stage IIIC disease. Most patients ($n = 470$, 85%) had high-grade serous histology. A total of 260 (47%) patients underwent primary debulking surgery (PDS), and 293 (53%) underwent neoadjuvant chemotherapy (NACT) with interval debulking surgery (IDS). Patients undergoing PDS were more likely to undergo bowel

resection as compared to IDS patients (37% vs 14%, $P < 0.001$). Of the 138 patients who had a bowel resection, 30 (21%) underwent ostomy formation. Among patients undergoing bowel resection, there were no significant preoperative clinical differences between those who did and did not have an ostomy placed. There was also no significant difference in residual disease when these groups were compared. Rates of ostomy formation were similar when patients undergoing PDS were compared to those undergoing IDS (4% vs 3%). However, patients who had an ostomy placed had longer mean operating times (321 vs 240 minutes, $P = 0.006$), higher rates of blood transfusion (57% vs 34%, $P = 0.03$), higher rates of ICU admission (33% vs. 13%, $P = 0.03$), and higher rates of postoperative small bowel obstruction (13% vs 2%, $P = 0.04$). There were no significant differences in 30-day readmission rates, 30-day reoperation rates, length of stay, or time to NACT. See Table 1. Among patients who had an ostomy placed, 13 (43%) ultimately underwent stoma reversal. Mean time to ostomy reversal was 7.5 months.

Conclusion: Increased perioperative morbidity among patients undergoing ostomy formation at the time of cytoreductive surgery is likely a reflection of the extent of surgery required. Less than 50% of ostomies are reversed, and most reversals occur within 8 months of creation.

Table 1: Comparison of patients who underwent bowel resection at the time of debulking surgery who did and did not have an ostomy placed.

	No Ostomy (n,%)	Ostomy (n,%)	P value
Age, years (mean)	62	62	0.95
BMI, Kg/m²	26.2	26.3	0.91
Race			0.562
White	88 (80)	20 (71)	
Black	2(2)	1(4)	
Asian	3(3)	1(4)	
Hispanic	2(2)	1(4)	
Other/Unknown	15(14)	5(17)	
Comorbidity Index			0.81
0	7(6)	1(4)	
1	6(5)	2(7)	
2	18(17)	6(21)	
≥3	79(72)	19(68)	
Stage			0.62
IIIC	85(78)	20(71)	
IV	25(22)	8(29)	
Histology			0.75
Serous	95(86)	26(93)	
Carcinosarcoma	6(5)	0(0)	
Mixed	7(6)	2(7)	
Mucinous	1(1)	0(0)	
Undifferentiated	1(1)	0(0)	
Pre-operative Ca 125 (mean)	1031	3836	0.69
Primary Treatment			0.46
PDS	82(72)	15(63)	
NACT	32(28)	9(37)	
EBL (cc)	823	1385	0.06
Blood Transfusion	37(34)	16(57)	0.03
Operative Time, minutes (mean)	240	320.5	0.006
Bowel Resection			0.003
Small Bowel	16(14)	0(0)	
Large Bowel	82(72)	13(54)	
Small and Large Bowel	16(14)	11(46)	

Residual Disease Status			0.49
NED	37 (33)	10 (36)	
Optimal (<1cm)	64 (58)	14 (50)	
Suboptimal	9 (8)	4 (7)	
Mean post-operative length of stay (days)	11.5	10.3	0.57
Mean time from surgery to chemotherapy (days)	30.8	27.8	0.51
Readmission within 30 days	8 (33)	20 (18)	0.1
Reoperation within 30 days	2 (8)	7(6)	0.66
Wound Complication	5(21)	18 (16)	0.55
Post-operative ICU Admission	8(33)	15 (13)	0.03
Post-operative VTE	3(13)	8(7)	0.41
Post-operative PNA	0(0)	8 (7)	0.35
Post-operative ileus	5(21)	26 (23)	1
Post-operative SBO	3(13)	2 (2)	0.04
Post-operative intrabdominal infection	3(13)	10(9)	0.7
Post-operative UTI	5(21)	8(7)	0.05
Anastomtic Leak	0(0)	5(5)	1
Unable to receive chemotherapy	0(0)	1(1)	1

256 - Poster Session

Collection of fallopian tube cytology using a novel hysteroscopic tubal catheter

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Objective: To demonstrate the ability of a hysteroscopic tubal catheter to collect samples from the fallopian tube for identification of cytologic abnormalities and correlation with histopathology.

Method: Study subjects were recruited prospectively to an institutional review board-approved trial from three gynecologic oncology centers of women undergoing salpingo-oophorectomy. Eligibility criteria included women older than 18 years undergoing risk-reducing surgery for *BRCA* mutations or surgery for pelvic masses suspicious for malignancy. A novel hysteroscopic catheter (nVision Medical, San Bruno, CA) was used to collect cells from the fallopian tube. Cytology from the collection was evaluated by a pathologist blinded to surgical findings, and subsequently results were compared to pathology findings. Demographic and clinical data, as well as surgical and pathology findings, were collected.

Results: Fifty patients were enrolled, of whom 8 were *BRCA* mutation carriers undergoing surgery for risk reduction, and 42 had a pelvic mass. Four patients were ineligible because of tubal ligation, and 3 patients withdrew. Two cases are pending final results. There were 11 cases of ovarian cancer: 4 stage I, 1 stage II, 5 stage III, and 1 stage IV. In 9 of these cases, cell collection was attempted, with adequate specimens collected in 7 of these cases on the side of the carcinoma. Among 41 evaluable cases, hysteroscopies were performed in 38 women with 71 fallopian tubes, of which 60 ostia were identified, with 57 successful catheterizations. There were 42 adequate samples (42/57, 75%): 32 were benign, 5 were reactive atypical, and 5 were neoplastic or malignant. When a specimen was successfully collected and the tube was involved with carcinoma on histology, cytology was positive in all 3 tubes. In 2 stage I ovarian cancers, tubal cytology was positive on the side of the cancer. There were 3 ovarian cancers with negative tubal cytology and tubal histology: stage I cystic teratoma containing invasive squamous carcinoma, stage Ic endometrioid ovarian cancer, and stage II high-grade serous ovarian cancer. See Figure 1.

Conclusion: Malignancy can be identified in the hysteroscopic collection of cytology from the fallopian tube in cases of ovarian cancer. This device could be used for high-risk surveillance in the outpatient setting.

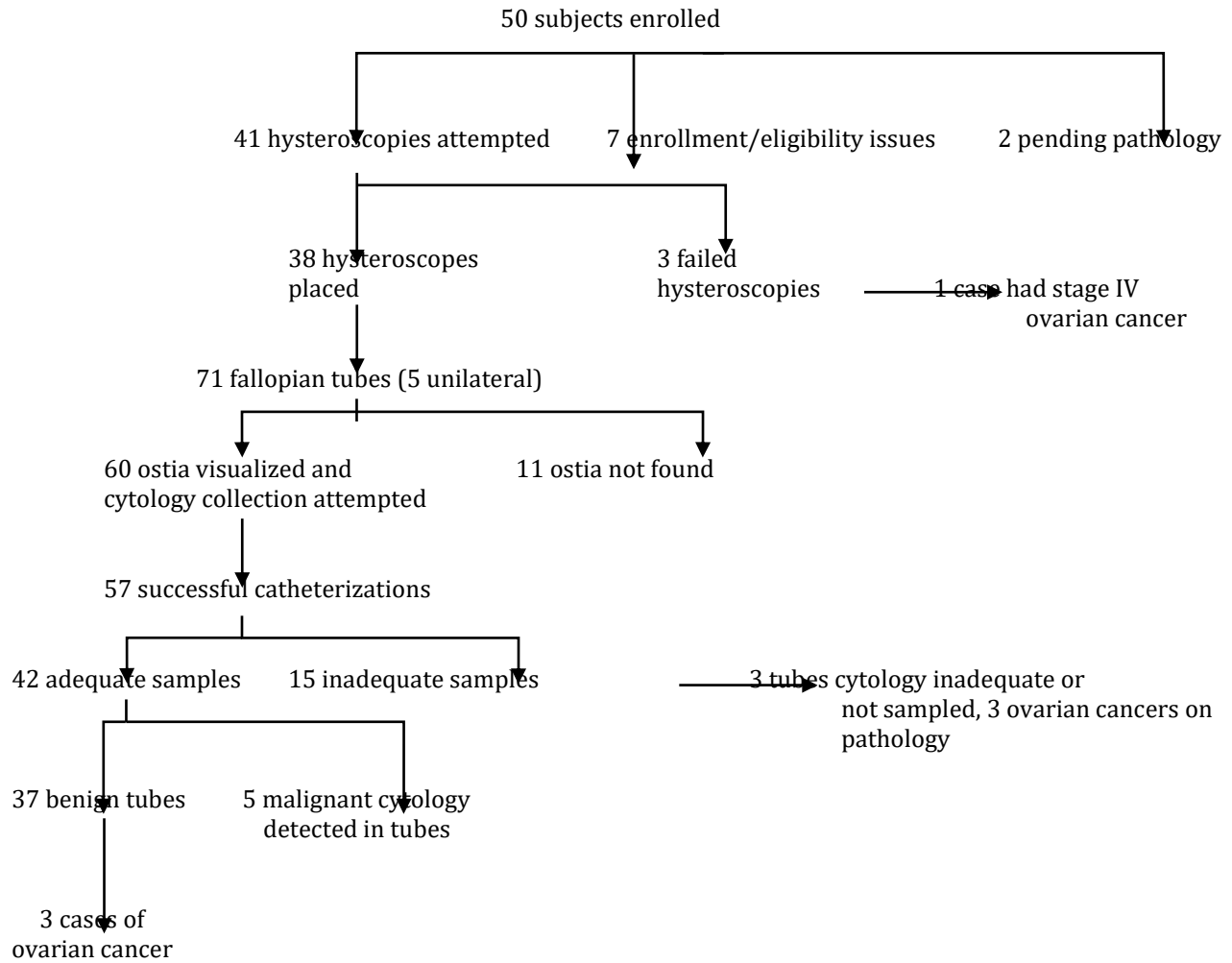


Fig. 1. Diagram of surgical and cytologic findings.

257 - Poster Session

Phase IB dose escalation and expansion trial of the oral hedgehog inhibitor sonidegib (LDE225) and weekly paclitaxel in platinum-resistant ovarian cancer (NCT02195973)

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Objective: Preclinical models suggest that the hedgehog inhibitor-like sonidegib may reverse taxane resistance in patients with recurrent epithelial ovarian cancer (EOC). Our goal was to determine the spectrum of toxicities and maximum tolerated dose (MTD) of sonidegib (LDE225) when given with weekly paclitaxel in women with platinum-resistant EOC.

Method: Eligible platinum-resistant EOC patients were enrolled in a 3+3 phase IB trial. Patients received weekly intravenous paclitaxel 80 mg/m² on days 1, 8, and 15 with daily sonidegib in dose cohorts ranging from 200 to 600 mg daily on a 28-day cycle. Prior studies suggested that 800 mg daily was not tolerated, so this dose level was eliminated. Adverse effects were monitored utilizing CTCAE (Common Terminology Criteria for Adverse Events). Dose-limiting toxicities (DLTs) were predefined drug-related adverse events within the first 42 days from commencement of therapy. Although not a primary goal, antitumor activity was evaluated with imaging performed at baseline and every two cycles.

Results: A total of 17 platinum-resistant EOC patients were enrolled between September 9, 2014, and May 24, 2016. Two ineligible patients were excluded. Patients had previously received a median of 3 (range 1–7) prior lines of therapy. A total of

29 grade 3/4 toxicities occurred in 10 patients; the most common were anemia (5), ascites (3), anorexia (3), worsening pleural effusions (2), neutropenia (2), and fatigue (2). Five patients had no grade 3/4 toxicity. The MTD was not reached as no DLTs were noted. Dose expansion at dose level 3 (LDE225 600 mg daily with weekly paclitaxel) was performed. One of 15 patients (6.7%) had a partial response; 7 patients (46.7%) had stable disease; and the rest had progressive disease. Eleven patients are dead of disease. The median overall survival was 14.60 months (95% CI 13.0–16.2).

Conclusion: Dose escalation of sonidegib with weekly paclitaxel in platinum-resistant EOC patients was well tolerated, and the MTD was not identified. Modest clinical activity in this patient population was noted.

258 - Poster Session

Initial results of a population-based cervical cancer screening program using HPV testing in 1 million women

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Objective: Cervical cancer is unique among common cancers in that it can be almost totally eradicated. High-risk human papilloma virus (HPV) is the primary causative agent in virtually all patients, and since 2006 there have been very effective HPV prophylactic vaccines. In 2014, Turkey redesigned the screening program including a revamped local call and recall strategy and a centralized and fully automatized monitoring of individual screening status, with HPV tests as the primary screening tool, well-defined national algorithms, including extended screening intervals and referral protocols, a single nationwide centralized diagnostics laboratory, and a sustainable agreement with the diagnostics industry.

Method: Women aged 30–65 years (approximately 15 million) are invited for HPV-based screening by primary-level health staff (family physicians and so-called KETEM screening centers) every five years. Two samples are taken from each woman to enable cytology testing in those found to be HPV-positive without the need for a separate visit. HPV-positive women with abnormal cytology or who are HPV 16 or 18 positive are referred for colposcopy, which is performed free of charge in a postscreening diagnostic center.

Results: Based on surveys of general practitioners, there was an approximately 36.5% acceptance rate for HPV-based cervical cancer screening after first invitations (18). This rate was 63.5% for ages 30–45 years, 32.7% for ages 45–60 years, and 13.5% for ages 60 years and older. Overall, 95.1% of the samples were HPV-negative, 1.1% were inadequate, and the remaining 3.5% ($n = 37,515$) were HPV DNA positive. HPV positivity rate by age groups was 4.3% (30–34), 4.0% (35–39), 3.6% (40–44), 3.2% (45–59) and 2.8% (60–65). The highest positivity rates were seen in Istanbul and Mediterranean regions. The most common HPV genotypes were 16, followed by 51, 31, 5, 2 and 18.

Conclusion: HPV DNA testing is currently accepted for primary screening by many professional societies. The low HPV DNA positivity rate (3.5%) facilitated the use of HPV as the primary test, and this is also relevant for other countries with low HPV prevalence rates. This program has demonstrated the feasibility of an HPV-based screening program in a developing country with a large population in varied geographic conditions.

259 - Poster Session

Utero-ovarian preservation and overall survival of young women with early-stage borderline ovarian tumors

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Objective: To examine survival of women who underwent surgical treatment with ovarian and uterine preservation for early-stage borderline ovarian tumors (BOTs).

Method: The Surveillance, Epidemiology, and End Results Program was used to identify women younger than 50 years with stage I BOTs whose surgical treatment included ovarian conservation between 1988 and 2003. Survival outcomes were examined based on the concurrent hysterectomy status at time of surgery.

Results: Among 5,708 cases of BOTs, there were 1,065 women who had utero-ovarian preservation surgery and 52 women who had hysterectomy with ovarian preservation alone at surgery for stage I BOTs. Women who had utero-ovarian

preservation were more likely to be single and diagnosed more recently (both, $P < 0.05$). On univariable analysis, women who had utero-ovarian preservation had BOTs-specific survival similar to those who had ovarian preservation alone without uterine preservation (10-year rate, 99.2% vs 98.1%, $P = 0.42$). However, overall survival was higher in the utero-ovarian preservation group than in the ovarian preservation alone group (95.8% vs 87.6%, $P < 0.001$). On multivariable analysis controlling for age, race, and tumor stage, utero-ovarian preservation remained an independent prognostic factor for improved overall survival (adjusted HR 0.36, 95% confidence interval 0.16–0.82, $P = 0.015$). Cardiovascular disease mortality was lower in the utero-ovarian preservation group compared to the ovarian preservation alone group, but it did not reach statistical significance (20-year cumulative rate, 0.8% vs 3.0%, $P = 0.29$).

Conclusion: Utero-ovarian preservation for young women with early-stage BOTs may be associated with improved overall survival compared to those who had ovarian preservation alone without uterine preservation.

260 - Poster Session

Serum folate, human papillomavirus, and risk of cervical intraepithelial neoplasia: A Chinese population-based cohort study

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Objective: Folate deficiency has long been implicated in the development of cancer, although uncertainties remain concerning the role of folate in cervical cancer prevention. The aim of this study is to evaluate the dose-response association between serum folate and risk of cervical intraepithelial neoplasia (CIN), and potential effect modification by human papillomavirus (HPV) on CIN risk.

Method: We performed a cross-sectional analysis of screening data from 2,304 women aged 19–65 years who participated in an ongoing cohort of 40,000 women in China. Both categorical and spline analyses were used to evaluate the dose-response relationship between serum folate and CIN risk.

Results: The proportion of women with CIN that included women with CIN1 ($n = 564$), CIN2 ($n = 171$), CIN 3 ($n = 47$), and SCC ($n = 19$) accounted for 34.8%. After adjusting for potential confounders including high-risk HPV infection, a statistically significant association between serum folate concentration (<12.9 vs >21.1 nmol/L) and CIN risk was observed (OR 1.41, 95% CI 1.10–1.81, P trend < 0.01). Women with infection high-risk HPV types was associated with 72% increased odds of prevalence of CIN compared with others (OR 1.72, 95% CI 1.43–2.07). An inverse linear relationship between increased serum folate concentrations and risk of higher grade CIN (CIN2+) was also observed (P overall < 0.01 , P nonlinearity = 0.96). The highest risk of CIN2+ was observed for high-risk HPV infection women who had the lowest serum folate concentration (P interaction < 0.01).

Conclusion: These results suggest that while serum folate is inversely associated with risk of CIN and cervical cancer, independently of infection with high-risk HPV types, the magnitude of the risk could be reduced in these women if dietary modifications related to folic acid were taken.

261 - Poster Session

Evaluation of MR imaging with diffusion-weighted imaging for the local response assessment of patients treated with chemoradiation for cervical cancer: A multicenter study

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Objective: To compare MR imaging with or without diffusion-weighted imaging (DWI) and clinical response evaluation (CRE) in the local control evaluation of cervical carcinoma after (chemo)radiation.

Method: This prospective study was institutional review board approved, and all patients provided informed consent. In a multicenter university setting, we included 107 patients with primary cervical cancer treated with (chemo)radiation. CRE and MR imaging (2 readers) were evaluated using cautious and strict criteria for identifying residual tumor. Sensitivity and

specificity were calculated for CRE and MR imaging, and nested logistic regression models constructed for CRE, subsequently adding MR imaging and MR imaging with DWI as independent variables for identifying residual tumor.

Results: In 11% (12/107) local residual tumor was found. Using cautious criteria, CRE and MR imaging with DWI (reader 1/reader 2) have comparable high specificity (83% and 89%/95%, respectively), whereas MR imaging without DWI showed significantly lower specificity (63%/53%) than CRE. Using strict criteria, both CRE and MR imaging with DWI showed very high specificity (99% and 92%/95%, respectively), whereas MR imaging without DWI showed significantly lower specificity (89%/77%) than CRE. All sensitivities were not significantly different. Addition of MR imaging with DWI to CRE has statistically significant incremental value in identifying residual tumor (reader 1 estimate, 1.06, $P = 0.001$; reader 2 estimate, 0.62, $P = 0.02$).

Conclusion: DWI significantly increases the specificity of MR imaging in the detection of local residual tumor. Furthermore, MR imaging with DWI has significant incremental diagnostic value over CRE. Further studies should be performed to analyze the reproducibility of MR imaging findings.

262 - Poster Session

Moving away from cancer exercise trial for overweight/obese cancer survivors: Predicting immediate dropout rates

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Objective: Exercise improves multiple outcomes following a cancer diagnosis, and active intervention trials reduce the rate of functional decline in older cancer survivors. This prospective trial's primary objective was to determine the feasibility of implementing an exercise-based lifestyle intervention program for overweight/obese survivors of endometrial, breast, or ovarian cancers in a rural population; this analysis focused on factors associated with study withdrawal in the first 30 days of a 6-month trial.

Method: Female survivors of endometrial, breast, ovarian, or colon cancer were enrolled in a 6-month program of exercise aimed at improving physical function through increased aerobic (adding 30 minutes of daily walking) and strength-training exercise (with Thera-bands). Support provided included pedometers, bands, and an informational workbook (adapted with permission from the RENEW trial). Participants received weekly telephone monitoring/motivational coaching. Baseline demographics, anthropomorphic measurements, quality of life (QOL), fitness, and readiness to adopt exercise changes were assessed as well as subsequent adherence to the program, daily steps, band use, and periodic weight/BMI /QOL.

Results: Fifty-seven women were recruited. The mean age was 59.2 years (mean age at cancer diagnosis was 55.2 years); mean BMI was 35.4 kg/m²; mean distance travelled to see a physician was 65 miles; 90% of the participants were white; and 38.6% of patients reported current exercise. Thirteen women (22.8%) dropped out of the study within the first month. The following factors were compared for association with study withdrawal and were not significantly different: age, race, height, weight, BMI, blood pressure, type of cancer (yet 0% of ovarian cancer patients dropped out), self-reported fitness, time sleeping, time watching TV, readiness for change, belief in exercise importance, and confidence in doing exercise. Top self-reported barriers to walking were lack of safe place, especially in rain/snow, and pedometer malfunctions; top barriers to strength exercises were that they were "too hard or too easy" and pain.

Conclusions: Immediate dropout rates from an exercise trial in rural cancer survivors are high and difficult to predict. Walking was very acceptable to participants, but alternative strength training options are needed in this population.

263 - Poster Session

RECIST is more sensitive than CA-125 in detecting disease progression in epithelial ovarian cancer patients treated with maintenance bevacizumab: A secondary analysis of the ROSIA trial

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Objective: Data on CA-125 as a predictor of progressive disease (PD) in ovarian cancer come predominantly from patients receiving chemotherapy alone. We assessed concordance between CA-125 and Response Evaluation Criteria In Solid Tumors (RECIST) in diagnosing PD using data from the international ROSIA trial, a single-arm study evaluating extended duration of bevacizumab combined with front-line carboplatin and paclitaxel for epithelial ovarian cancer.

Method: The target patient population comprised women with FIGO stage IIB–IV ovarian cancer treated with carboplatin and paclitaxel, given every 3 weeks, plus bevacizumab, given concurrently every 3 weeks for 5 or 6 cycles and continued as a single agent for up to 24 months or until PD.

Results: Of the 1,021 women enrolled to the ROSiA trial, we identified 556 (54.4%) patients who had a recurrence during a median follow-up of 32 months. In 334 (60.1%) patients, the recurrence was diagnosed by RECIST only, suggesting a 40% false negative rate for CA-125 in the detection of PD. In 222 (39.9%) patients, diagnosis of recurrence was associated with an elevated CA-125, but 18 patients had a recurrence that was diagnosed by an elevated CA-125 only, suggesting a 3.23% false negative for RECIST in the detection of PD. Baseline characteristics including demographics, staging, grading, and other clinical characteristics were not significantly different between patients with or without CA-125 elevation at diagnosis of the first recurrence. Patients with elevated CA-125 were more likely to have lymph nodes involvement at their primary disease ($P = 0.06$). PD presenting with ascites, lymph nodes metastases, or both had a significant percentage of high CA-125 levels at PD compared to pelvic or abdominal PD ($P < 0.001$, $P = 0.03$, and $P < 0.001$, respectively).

Conclusions: In this population with extended duration of bevacizumab treatment after first-line carboplatin and paclitaxel, RECIST was more sensitive in detecting PD than CA-125. Regular clinical and radiologic assessments should be considered during the follow-up of complete response patients after first-line chemotherapy and under maintenance with bevacizumab for earlier detection of PD in general and specifically in clinical trials. The utility of CA-125 in the diagnosis of PD in these settings is uncertain.

264 - Poster Session

Cell cycle biomarker discovery for phase 0 clinical trials in type II endometrial cancer

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Objective: The phase 0 clinical trial mechanism is limited by a lack of practical, economical, and functionally meaningful biomarkers in human samples. The aim of this study was to develop a panel of biomarkers for assaying cell cycle arrest in phase 0 trials of type 2 endometrial cancer.

Method: Immunohistochemical staining for Ki-67, cyclin D1 (CCND1), cyclin E1 (CCNE1), and phospho-Histone H3 (pHH3) was performed on tissue microarrays from 17 patients with type 2 endometrial cancer; 11 patients had uterine serous carcinoma (USC) and 3 had mixed USC. All patients underwent hysterectomy and bilateral salpingo-oophorectomy; the majority underwent lymphadenectomy (82%); 53% had stage III–IV disease; and 47% had lymphovascular invasion (LVI). Two independent pathologists scored an average of 5 tissue cores per patient. Manual enumeration of percent positive staining cancer cells was performed to assign scores to each core for each biomarker. Ki-67, CCND1, and CCNE1 were scored using a 10-point scale equivalent to 10% increments. pHH3 scoring was based on the published mean percent positive cancer cells in other solid malignancies: $\leq 1\% = 0$; $> 1\%$ and $\leq 2\% = 1$; $> 2\%$ and $\leq 4\% = 2$; $> 4\%$ and $\leq 8\% = 3$; and $> 8\% = 4$. A USC cell line and primary antibody omission served as positive and negative controls, respectively. The Cohen κ statistic was used to assess interobserver variability in biomarker scoring. Associations between biomarkers and clinicopathologic variables were tested using the Wilcoxon rank sum test with significance set at $P < 0.05$.

Results: Biomarker scoring was highly reproducible with good interobserver variability. Table 1 reports the κ coefficient as well as the mean, median, and range of scores for each biomarker. No associations were found between biomarkers and depth of myoinvasion or lymph node involvement. LVI and advanced stage were associated with high pHH3 (median score of 2 vs. 1, $P < 0.05$) and CCND1 (median score of 3 vs 2, $P < 0.05$). Patients with suboptimally resected advanced-stage disease had higher pHH3 scores (median score of 2 vs 1, $P < 0.05$). Recurrence was associated with higher mean pHH3 scores (mean score 2 vs. 1, $P < 0.05$).

Conclusions: Quantification of cell cycle biomarkers in type 2 endometrial cancer is feasible and reproducible and may be clinically relevant. This panel will be prospectively validated in an upcoming phase 0 NRG oncology trial.

Table 1. Cell cycle biomarker scores.

Biomarker	\bar{x}	Mean	Median	Range
Ki-67	0.68	5.60	7.00	1-9
Cyclin D1	0.82	3.52	3.00	1-9
Cyclin E1	0.58	7.35	7.75	1-10
phospho-Histone H3	0.52	1.36	1.00	0-4

265 - Poster Session

A phase II, multicenter study to evaluate the efficacy and safety using autologous tumor infiltrating lymphocytes (LN-145) in patients with recurrent, metastatic, or persistent cervical carcinoma

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Objectives: Adoptive cell therapy (ACT) may be effective in treating virally-associated tumors. HPV infection increases mutational load providing additional neoantigen targets ideal for the polyclonal nature of ACT. As outcomes for patients with recurrent, metastatic or persistent cervical cancer remain extremely poor, there is an enormous need for novel immunotherapeutic approaches with curative potential such as ACT.

Methods: Clinical trial C-145-04 (NCT03108495) is a prospective, phase 2 multicenter, open-label study evaluating the efficacy of a single autologous tumor infiltrating lymphocyte infusion (LN-145) followed by IL-2 after a non-myeloablative lymphodepletion (NMA-LD) regimen in patients with recurrent, metastatic, or persistent cervical cancer who have failed at least one prior systemic therapy. The clinical trial protocol requires resection of a tumor lesion for TIL extraction, expansion, and preparation of the infusion product (LN-145). One week prior to LN-145 infusion, patients undergo NMA-LD consisting of cyclophosphamide (60 mg/kg) daily x 2 days followed by fludarabine (25 mg/m²) daily x 5 days. Following LN-145 infusion, up to 6 doses of IL-2 (600,000 IU/kg) is given every 8-12 hours. Simon's two-stage optimal design with one-sided alpha level=0.025 and 80% power will be used to compare an objective response rate (ORR) of 5% vs. 20% in the first stage ($n = 15$ subjects). If two or more ORR are observed, the trial will expand to Stage 2 ($n = 47$). The primary endpoint is the ORR per RECIST v1.1. Secondary endpoints include complete response, duration of response, disease control rate, progression free and overall survival. In addition, the safety summarization of treatment-emergent adverse events (AEs) including serious AEs, AEs leading to discontinuation, and clinical laboratory tests. Other major eligibility criteria include amongst others: adequate bone marrow, liver, pulmonary, cardiac and renal function; ECOG performance status of 0 or 1.

266 - Poster Session

Comparison of the pain scores between tampon, Tao brush and endometrial biopsy as genital tract sampling methods

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Objective: Emerging technology may allow for less invasive sampling methods to evaluate for endometrial cancer (EC). This study compares patient pain scores among 3 genital tract sampling methods and explores variables associated with procedural pain.

Method: A prospective study including 3 sampling methods (tampon first, then Tao brush (TB), followed by endometrial biopsy, EB) was conducted between December 2015 and August 2017 at a tertiary care center and included women 45 years or older presenting with abnormal uterine bleeding, postmenopausal bleeding, or thickened endometrial stripe. Patients reported their pain after each sampling using a 100-point Visual Analog Scale (VAS). Paired comparisons of the VAS scores between the 3 methods were evaluated using Wilcoxon signed rank test; comparisons between independent groups were evaluated using the Wilcoxon rank sum test.

Results: Of 431 enrolled, 191 patients underwent all 3 sampling methods and reported a VAS score for each. The mean age and mean BMI of the 191 patients was 54.8 years (range 33 to 77 years) and 29.9 kg/m². The cohort of 191 comprised 48.7% postmenopausal women, 90.6% parous, and 87.3% with a history of vaginal delivery (VD). The median (IQR) VAS scores were 0 (0, 2), 28 (12, 52), and 32 (15, 60) for sampling via tampon, TB, and EB, respectively. The pain scores during tampon

sampling were significantly lower compared to the other two methods ($P < 0.001$). Among the full group of 431 patients, VAS scoring was completed by all (431) after tampon, 194 of 291 women after TB, and 281 of 388 after EB. Only 6.5% of the 431 women reported a pain score of 10 or higher with tampon insertion. There were 73 patients who did not have TB sampling due to pain or stenosis and among them, 57 (78%) underwent the EB and completed the VAS scoring. Among these 57 patients, median (IQR) VAS scores after EB were significantly higher (60 (33, 70) versus 33 (15, 60) ($P < 0.001$) when compared to the remaining 224 patients who underwent EB. No statistically significant correlation was observed between the VAS scores and menopausal status of women or their history of VD; see Table 1. The correlation between VAS score and parity, age, and BMI is also reported in the table.

Conclusion: Genital tract sampling using a tampon had significantly lower pain than the current methods. Pain scores for TB and EB were not affected by age, parity, menopausal status, or BMI.

Table 1. Comparison of pain scores for genital tract sampling methods^a.

Characteristic	Cohort with Tao Brush Sampling (<i>n</i> = 194)		Cohort with Endometrial Biopsy Sampling (<i>n</i> = 281)	
	Median (IQR) VAS Pain Score	<i>P</i> Value	Median (IQR) VAS Pain Score	<i>P</i> Value
Postmenopausal		0.48		0.29
Yes	25 (8, 50)		37.5 (20, 67)	
No	27.5 (12.5, 44.5)		35 (15, 60)	
History of vaginal delivery		0.46		0.06
Yes	28 (11, 52)		34 (15, 61)	
No	26 (15, 50)		44 (22, 67)	
	Correlation with VAS Pain Score	<i>P</i> Value	Correlation with VAS Pain score	<i>P</i> Value
Age	0.04	0.62	0.03	0.67
BMI	-0.003	0.97	0.01	0.89
Parity	-0.01	0.93	-0.14	0.02

^a The Spearman rank correlation coefficient and Wilcoxon rank sum test were used to explore associations with pain scores.

267 - Poster Session

Incidence and risk factors associated with the development of venous thromboembolism in uterine serous carcinoma
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Objective: To assess the prevalence of venous thromboembolism (VTE) in patients with uterine serous carcinoma and identify risk factors for VTE in this patient population.

Method: After institutional review board approval, all patients diagnosed with uterine serous cancer who received primary treatment at our institution from 2005 to 2016 were identified from our tumor registry. Demographic, clinical, and pathologic data were retrospectively abstracted from patient records including imaging studies. VTE was defined as a deep venous thrombus or pulmonary embolus seen on imaging studies including ultrasound, CT scan, and/or V/Q scan. Data were analyzed with Stata software using the Student *t* test, Mann-Whitney *U* test, χ^2 test, or Fisher exact test as appropriate.

Results: A total of 413 patients were identified for inclusion in the study. Seventy (17%) of the patients were diagnosed with VTE. The majority of patients (83%) were non-white. Bivariate analysis revealed no significant associations between age, BMI, or race with diagnosis of VTE ($P = 0.78$, 0.55, and 0.48 respectively). Patients who had more than 2 risk factors for VTE had a significantly increased likelihood of VTE diagnosis ($P = 0.02$). There was a highly significant association between stage of uterine serous cancer and diagnosis of VTE ($P = 0.005$). Patients with stage III–IV cancer were 2.4 and 3.5 times more likely to develop VTE than patients with stage I cancer (95% CI 1.09–5.30 and 1.74–6.83, respectively). Most patients who developed VTE were not postoperative (64%), and a large proportion developed clots while receiving chemotherapy (36%). Patients who developed VTE while on chemotherapy had a median Khorana score of 1 (IQR 1,2). See Table 1.

Conclusion: There is a very high prevalence of VTE in our population with uterine serous carcinoma. The majority of patients developed a VTE outside of the postoperative period. Patients on chemotherapy had a higher incidence of VTE than predicted by Khorana scores. Patients with advanced-stage carcinoma were significantly more likely to develop VTE and may benefit from thromboprophylaxis beyond the postoperative period.

Table 1. Characteristics of patients with uterine serous cancer diagnosed with VTE during their disease course ($N = 70$).

Characteristic	N (%) [*]	OR	95% CI	P value
Age (years)	68.9 ± 6.9			0.78
Body mass index (kg/m ²)	30.3 ± 6.2			0.55
Total number of risk factors for VTE [†]	3 (2,3)			0.02
Imaging study performed				
Venous duplex ultrasound	38 (54.3)			
CT scan	28 (40.0)			
V/Q scan	4 (5.71)			
Disease status at time of VTE diagnosis				
Presenting symptom	25 (35.7)			
During neoadjuvant chemotherapy	3 (4.3)			
Post-operatively prior to adjuvant treatment	9 (12.9)			
During adjuvant chemotherapy	22 (31.4)			
During adjuvant radiotherapy	1 (1.4)			
After completion of adjuvant treatment	7 (10.0)			
Unknown	3 (4.3)			
On anticoagulation at time of diagnosis	11 (15.7)			
Khorana score (for those receiving chemo at the time of VTE diagnosis) [§]	1 (1,2)			
Race				
White	10 (14.3)	-	-	0.28
Black	43 (61.4)	1.47	0.70- 3.12	
Hispanic	11 (15.7)	0.82	0.33- 2.06	
Asian	3 (4.3)	3.05	0.63-14.66	
Other or unknown	3 (4.3)	1.14	0.28- 4.69	
Dichotomized race				
White	10 (14.3)	-	-	0.48
Non-white	60 (85.7)	1.30	0.63- 2.68	
Stage of cancer				
Stage I	16 (22.9)	-	-	0.005
Stage II	6 (8.6)	1.57	0.57-4.32	
Stage III	14 (20.0)	2.40	1.09-5.30	
Stage IV	30 (42.9)	3.45	1.74-6.83	
Unstaged	4 (5.7)	1.99	0.60- 6.61	

* Data with plus-minus values represent means ± standard deviation, otherwise reported as median (interquartile range).

Categorical data in grey are presented as N (%) associated with odds ratios and 95% confidence intervals.

[†]Composite of risk factors including diabetes, hypertension, hyperlipidemia, cardiovascular disease, prior VTE, recent smoking history, chronic obstructive pulmonary disease, chronic kidney disease, and obesity.

[§]Based on $N = 25$ patients who developed VTE while on chemotherapy

268 - Poster Session

Time to omit pelvic radiation and chemotherapy in stage I high intermediate risk endometrioid endometrial cancer

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Objective: Despite several clinical trials, it is still unclear whether patients with comprehensively staged high-intermediate-risk (HIR) endometrial cancer benefit from systemic therapy. The objective of this study was to examine recurrence patterns in women with comprehensively staged HIR endometrial cancer without adjuvant therapy.

Method: A review of consecutive patients diagnosed with comprehensively staged (with assessment of retroperitoneal lymph nodes) stage I endometrial cancer between 2007 and 2016 was undertaken. Patients classified as HIR by GOG 249 criteria (risk factors, RF: grade 2 or 3 tumor, (+) lymphovascular space invasion, $\geq 50\%$ myometrial invasion; age ≥ 70 years with 1 RF, age ≥ 50 years with 2 RF, age ≥ 18 years with 3 RF), and endometrioid or mucinous histology were included.

Results: A total of 190 stage I patients with HIR endometrial cancer were identified: 121 (64%) received no adjuvant therapy (NAT); 47 (25%) vaginal brachytherapy (VBT) only; 5 (2.6%) external beam radiation (EBRT); and 17 (8.9%) chemotherapy. With a median follow-up time of 59 months, the overall recurrence rate was 14.7%. For patients who received NAT, the recurrence rate was 15.7%, of which 14 (11.6%) were vaginal and 2 (1.7%) were regional. There were no vaginal or regional recurrences for patients with VBT or EBRT, compared to 1 (5.9%) vaginal, 1 regional, and 1 distant recurrence with chemotherapy. Patients who received chemotherapy had higher grade tumors, but were similar in age, depth of myometrial invasion, and LVSI compared to no chemotherapy. Distant recurrence was similar with and without chemotherapy (5.9 vs 5.2%, $P = 0.74$).

Conclusion: Pelvic and distant recurrences are rare in patients with comprehensively staged, stage I, HIR endometrioid endometrial cancer, even in those who receive no adjuvant therapy. Our study confirms that vaginal brachytherapy can prevent most locoregional recurrences, and the additional time and toxicity of EBRT appear to be unjustified. Given the low rate ($\sim 5\%$) of distant recurrence with and without chemotherapy, we believe that it is reasonable to omit chemotherapy, and that lymph node assessment remains helpful to appropriately triage patients for adjuvant (systemic) therapy.

269 - Poster Session

Olaparib in German routine clinical practice: Updated interim results of the non-interventional study c-patrol

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Objectives: The PARP inhibitor olaparib is approved in the European Union for maintenance therapy of *BRCA*-mutated (*BRCA*m+) platinum-sensitive relapsed ovarian cancer patients who are in response to their most recent platinum-based chemotherapy. Thus far, only limited data on real-world olaparib treatment are available.

Methods: The German prospective, noninterventional study C-PATROL (NCT02503436) collects real-world clinical and patient-reported outcome data in *BRCA*m+ platinum-sensitive relapsed ovarian cancer patients treated with olaparib according to label. This first interim analysis (cutoff date, April 6, 2017) provided data on safety and dosing under real-life conditions reflecting the first years after the German market access of olaparib in June 2015. Data were analyzed by descriptive statistics.

Results: The first interim analysis comprised the first 75 patients (median age 61 [45–80] years; ECOG ≤ 1 , 93.3%; patients with ≥ 2 relapses, 49.3%; patients with ≥ 3 prior platinum-based chemotherapeutic regimens, 53.3%) with ≥ 3 months observation after start of olaparib therapy. Patients started with a median daily dose of 800 (300–800) mg olaparib. For 70.7% of patients no dose reduction was reported. For 29.3% of patients dose interruptions (median duration 10.0 [2–51] days) were documented. Olaparib therapy was permanently stopped due to an adverse event in 3 patients. Treatment-emergent adverse events (all grades) were documented for 85.3% of patients. Anemia (34.7% of all patients), nausea (29.3%), and fatigue (26.7%) were the most common events. Updated results comprising data for at least 160 patients from the second interim analysis will be presented.

Conclusion: The first interim analysis indicated that under routine conditions olaparib is well tolerated with a manageable toxicity profile. The toxicity profile is in line with the results of the clinical trial program of olaparib.

270 - Poster Session

Pharmacokinetic analysis of hyperthermic intraperitoneal chemotherapy (HIPEC) with carboplatin during secondary cytoreductive surgery for platinum-sensitive recurrent ovarian cancer

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Objective: To report pharmacokinetics and toxicity of hyperthermic intraperitoneal chemotherapy (HIPEC) with carboplatin from an ongoing multicenter phase II randomized study of HIPEC followed by systemic combination chemotherapy for recurrent ovarian cancer.

Method: Patients with recurrent ovarian, primary peritoneal, or fallopian tube carcinomas undergoing secondary cytoreductive surgery (CRS) to a residual disease ≤ 0.5 cm for first platinum-sensitive recurrence were eligible for enrollment. Patients randomized to the HIPEC arm received a single dose of carboplatin (800 mg/m^2) via intraperitoneal (IP) perfusion for 90 minutes following CRS. Peritoneal fluid and blood samples were collected from 15 HIPEC patients for pharmacokinetic analysis. Toxicity and complications were recorded for 4 weeks post-CRS using Serious Safety Events (SSE) criteria (grades 3–5).

Results: Since January 2013, 55 eligible patients have been enrolled in the study, 27 of whom were randomized to receive HIPEC. To date, 7 grade 3 SSEs were recorded. The following grade 3 complications were observed: pancreatic leak ($n = 2$), colitis ($n = 1$), vascular access complication ($n = 1$), colonic obstruction ($n = 1$), wound infection ($n = 1$), and intraoperative ureteral injury ($n = 1$). No grade 4 or 5 complication was observed. No hematologic or renal grade 3 or higher toxicities were observed, and all patients initiated chemotherapy within 6 weeks of CRS and HIPEC. Pharmacokinetic analysis of platinum exposure in peritoneal fluid (PF) and peripheral blood (PB) samples from 15 HIPEC patients demonstrated favorable PF to PB platinum exposure as expressed by the C_{max} and AUC ratios (17.8 and 2.3, respectively). The mean peak carboplatin dose in PF was $550.5 \text{ } \mu\text{g/mL}$ (AUC $451.5 \text{ } \mu\text{g}\cdot\text{h/mL}$), while the mean peak dose in PB was $31.7 \text{ } \mu\text{g/mL}$ (AUC $220 \text{ } \mu\text{g}\cdot\text{h/mL}$). Platinum concentration-time curves for both sample types are shown in Figure 1.

Conclusion: The data suggest the use of HIPEC with carboplatin in the treatment of recurrent ovarian cancer is safe. Pharmacokinetic analysis of treated patient samples demonstrates high IP platinum and limited systemic platinum exposure without hematologic or renal grade 3 toxicities in the HIPEC arm of our study thus far.

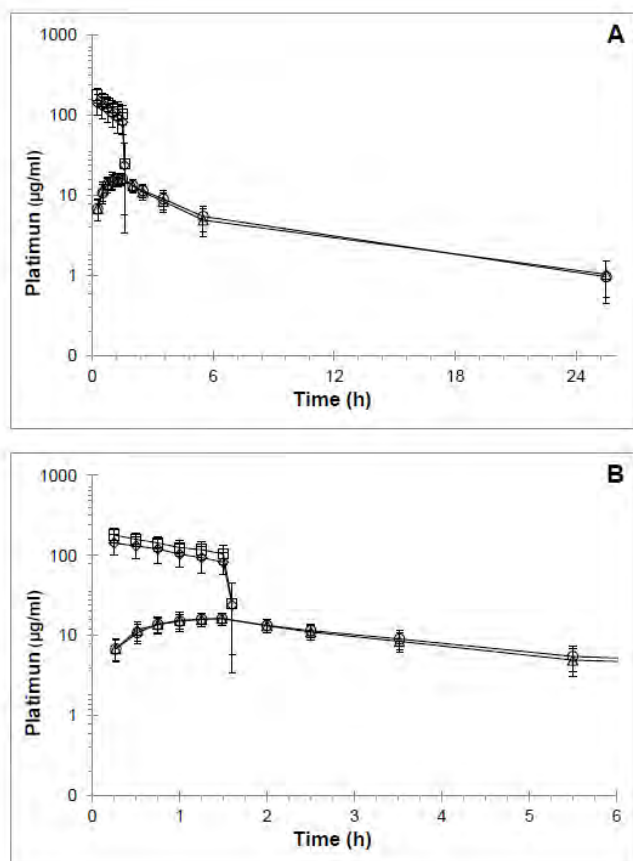


Fig. 1. Total (□) and ultrafilterable (◇) platinum peritoneal perfusate concentrations and total (○) and ultrafilterable (Δ) platinum peripheral blood plasma concentrations in 15 patients (mean±SD) at 24h (A) and 6h (B).

271 - Poster Session

Real-world treatment patterns, health care utilization, and costs associated with recurrence in germline *BRCA*-positive ovarian cancer

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Objective: Estimates of cancer-related health care utilization and costs are largely unavailable for women with recurrent germline *BRCA* (*gBRCA*)-mutated ovarian cancer. The objective of this study was to address this literature gap using real-world medical charts and derived cost data.

Method: A retrospective chart review was conducted in 20 centers across the United States. Patients were 18 years of age or older at initial diagnosis of ovarian cancer, received first-line platinum-based chemotherapy, and experienced at least 1 disease recurrence. Assessments were cancer-related treatment patterns, health care utilization, health care-associated costs from initial diagnosis until first recurrence, health care-associated costs from first recurrence until earliest of second recurrence, death, or loss to follow-up. Costs were obtained by combining utilization counts from the chart review with average service-specific unit costs derived from published literature and analyses of the SEER-Medicare linked database.

Results: Ninety-five patients were reviewed. Mean (standard deviation) age at initial diagnosis and at first recurrence was 55.4 (10.1) and 56.4 (9.8) years, respectively. A majority (85.3%) had locally advanced (42.1%) or metastatic (43.2%) disease at diagnosis. The progression-free interval following first-line therapy was >6 months (platinum-sensitive) for 40% of women and ≤6 months (platinum-resistant) for 60%. Most women (91.6%) received primary cytoreductive surgery after initial diagnosis. After first recurrence, nearly half (47.4%) received additional cytoreductive surgery, and 45.3% initiated second-line treatment. Total direct costs incurred per patient, from initial diagnosis until second recurrence, death, or loss to follow-up are shown in Table 1.

Conclusion: Patients with *gBRCA*-mutated recurrent ovarian cancer carry a high cost burden (\$44,734 annually, or \$3,732 per patient per month, *before* second/later recurrences). Costs are driven by early and downstream surgical procedures, systemic treatment, and frequent follow-up visits with the oncologist.

Table 1. Cancer-related cost per patient (2017 US\$) from initial diagnosis until earliest of second recurrence or end of available follow-up.

Cost Category	Mean	Standard Deviation	Median	Minimum	Maximum
Cytoreductive surgeries	\$39,582	\$17,773	\$28,487	0	\$56,974
Other surgeries ^a	\$22,553	\$15,888	\$28,300	0	\$60,600
Radiotherapy	\$1,888	\$4,767	0	0	\$13,796
Systemic treatments	\$32,548	\$27,667	\$23,735	\$3,480	\$133,926
Maintenance therapies ^b	\$7,929	\$19,981	0	0	\$93,744
Growth factors	\$7,277	\$21,023	0	0	\$96,000
Hospitalizations ^c	\$2,412	\$6,817	0	0	\$28,638
Emergency department visits	\$185	\$346	0	0	\$1,290
Outpatient oncologist visits	\$9,606	\$6,061	\$8,372	0	\$22,724
Outpatient radiologist visits	\$1,517	\$1,745	\$1,096	0	\$8,220
Outpatient surgeon visits	\$1,181	\$1,152	\$1,086	0	\$5,068
Hospice	\$6,114	\$16,512		0	\$68,328
Total cancer-related cost per patient	\$132,791	\$66,638 ^f	\$114,864 ^f	\$20,384 ^f	\$335,319 ^f
Total cancer-related cost per patient per month ^d	\$3,732				
Total annualized cancer-related cost per patient ^e	\$44,734				

^a Includes hysterectomy, bilateral/unilateral salpingo-oophorectomy, exploratory laparoscopy without debulking, exploratory laparotomy, and lymph node dissection.

^b Observed maintenance therapies were bevacizumab ($n = 11$ before first recurrence, $n = 14$ in second-line [after first recurrence]) and rucaparib ($n = 1$ in second-line [after first recurrence]).

^c Excludes hospitalizations for cytoreductive and other surgeries.

^d Calculated as summed total costs over all 95 patients (\$12,615,161) divided by total number of person-months of observation time (3,380) across all 95 patients.

^e Calculated as summed total costs over all 95 patients (\$12,615,161) divided by total number of person-years of observation time (282) across all 95 patients.

^f Standard deviation, median, minimum, and maximum are row-specific values within the table and do not represent column summations.

272 - Poster Session

How we use hospice: Hospice enrollment patterns and costs in elderly ovarian cancer patients

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Objective: To describe disparities in patterns of hospice use, hospice unenrollment, and end-of-life costs among ovarian cancer patients.

Method: Using Texas Cancer Registry Medicare data, ovarian cancer patients deceased 2000–2012 with more than 12 months of continuous Medicare coverage before death were included. Descriptive statistics and multivariate logistic regressions were used to evaluate patterns of hospice use. Cost and resource utilization was obtained from Medicare claims and analyzed using a nonparametric Mann-Whitney test and multivariate linear regressions.

Results: A total of 3,666 patients were assessed: 2,819 (77%) Caucasian, 553 (15%) Hispanic, 256 (7%) African-American, and 38 (1%) other. There were 2,642 (72%) enrolled in hospice prior to death, but only 2,344 (64%) died in hospice. The median hospice enrollment was 20 days. A total of 726 (28%) of 2,642 patients unenrolled from hospice at least once. Of those who unenrolled from hospice at least once, 298 (41%) died without hospice and 18% of these patients unenrolled multiple times prior to dying without hospice. From 2010 to 2012, patients were less likely to unenroll from hospice prior to death compared to previous years (2010 OR 0.17, 0.07–0.44, $P < 0.001$; 2011 OR 0.17, 0.06–0.43, $P < 0.001$; 2012 OR 0.28, 0.12–0.65, $P = 0.003$). Hispanic and African-American patients were less likely to remain enrolled in hospice until death (African-American OR 0.66, 0.50–0.88, $P = 0.004$; Hispanic OR 0.76, 0.61–0.94, $P = 0.01$). Among patients ever enrolled in hospice, African-American patients were more likely to unenroll from hospice (African-American OR 1.63, 1.01–2.62, $P = 0.04$). The median cost to Medicare from diagnosis to death was \$36,334 for those in hospice compared to \$41,138 without hospice ($P = 0.005$). The cost savings to Medicare was lost with any unenrollment from hospice. There were 233 (78%) hospice unenrolled patients and 427 (88%) multiple enrolled hospice patients who received at least one kind of life-extending or invasive procedures or required multiple emergency room visits or an ICU admission following unenrollment from hospice.

Conclusion: Although recent years show decreasing unenrollment from hospice, we found that African-American patients had a higher risk of unenrollment. The majority of patients who unenroll from hospice receive an invasive or life-extending procedure or more intensive care. Hospice enrollment was associated with lower costs as long as a patient did not unenroll from hospice.

273 - Poster Session

High-resolution microendoscopy (HRME) imaging for affordable, point-of-care cervical cancer detection in El Salvador

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Objective: Cervical cancer remains the leading cancer in women living in El Salvador. In low- and middle-income countries health workers may use visual inspection with acetic acid (VIA) to identify precancerous lesions. However, VIA has poor specificity (approximately 50%), leading to unnecessary treatments. High-resolution microendoscopy (HRME) imaging allows

the provider to image epithelial tissue in vivo with subcellular resolution for diagnosis at the point of care. Recent studies have shown that combining VIA with HRME increases the specificity of cervical cancer screening. Interim results are reported from an ongoing study to evaluate the diagnostic accuracy of HRME imaging in comparison to standard screening methods.

Method: Patients undergoing cervical cancer screening at the Instituto de Cáncer de El Salvador in San Salvador were recruited for the study. All women enrolled in the study underwent HPV and VIA screening. Women found to be positive on either screening test, along with 10% of those with negative results on both screening tests, returned for follow-up examination including VIA, colposcopy, visual inspection with Lugol's iodine (VILI), and HRME imaging. Biopsies were taken of any lesions identified by VIA, colposcopy, and VILI, as well as 1 clinically normal site. Clinical examination results and HRME imaging results were compared to histopathology.

Results: To date, 500 of the planned 3,000 patients have been enrolled; 66 screen-positive patients (32 HPV+, 28 VIA+, and 6 HPV+ and VIA+) and 25 patients who screened negative have returned for follow-up testing. HRME imaging results and corresponding histopathology results were obtained for a total of 186 cervical sites in these 91 patients (Figure 1). Six cervical sites in 6 different patients were identified as CIN2+ by histopathology (3 CIN2, 3 CIN3). VIA, colposcopy, and VILI each correctly classified as positive 5 of 6 (83%) CIN2+ sites, while HRME correctly classified 4 of 6 (67%) CIN2+ sites. HRME had a significantly better specificity ($P < 0.003$, McNemar test), correctly classifying 120/180 (67%) <CIN2 sites, followed by colposcopy, VIA, and VILI, which correctly classified 100/180 (56%), 99/180 (55%), and 93/180 (52%) <CIN2 sites, respectively.

Conclusion: These preliminary results show that HRME imaging can be incorporated into a large-scale screening program in a low-resource setting to assist in the early detection of cervical cancer.

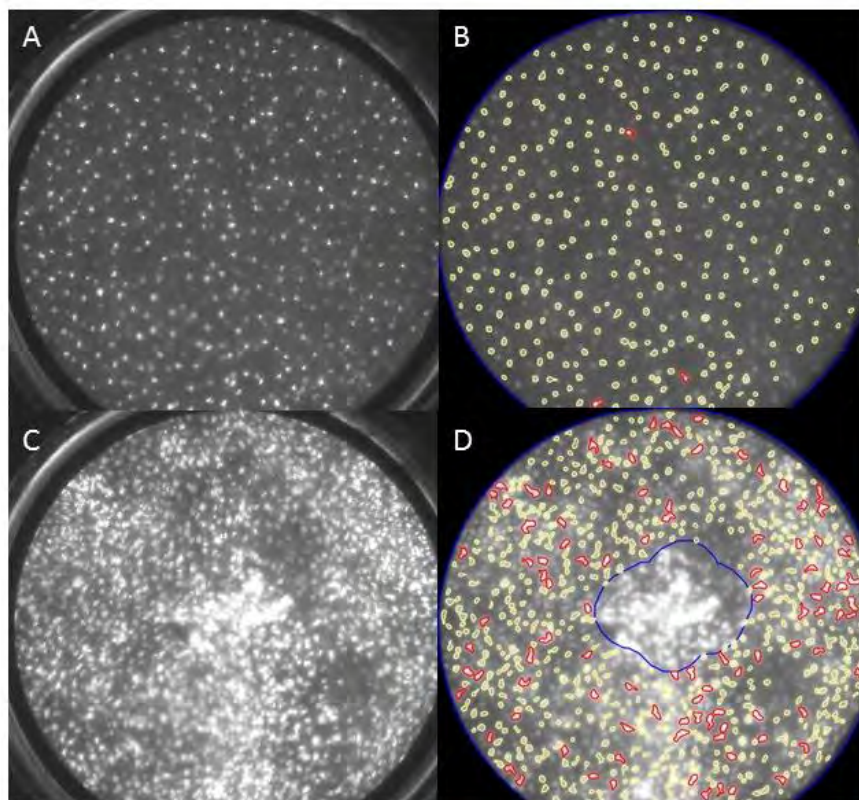


Fig. 1. HRME images A-D were taken of one patient during a follow-up visit. A) HRME image taken of a visibly normal area of the cervix. B) Image A after real-time HRME image analysis. Imaging site A was classified as low-grade by HRME and identified as inflammation by consensus pathology. C) HRME image taken of a cervical lesion. D) Image C after real-time HRME image analysis. Imaging site C was classified as high-grade by HRME and identified as being CIN2 by consensus pathology.

274 - Poster Session

Improving value-based care in cervical cancer through incorporation of consistent value-based teaching in a gynecologic oncology fellowship

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Objective: Gaps in knowledge of cost among learners and practicing clinicians is well described. Although learners provided with charge demonstrate a reduction in clinical spending, it has been reported to be associated with a concomitant reduction in the medical appropriateness of care decisions. The consistent integration of cost awareness concepts in parallel with medical teaching is a crucial element to adopting high-value care. This study examined whether formally compelling a consistent dialogue on cost-effectiveness in parallel with teaching of the Medical Care and Patient Care competencies of the Accreditation Council for Graduate Medical Education in a gynecologic oncology fellowship has an impact.

Method: Cervical cancer care was targeted for the initial pilot study. Weekly didactic conferences were attended by the entire gynecologic oncology division and were modified to routinely incorporate cost and value-based care considerations. These sessions were followed by open-book testing to reinforce concepts introduced in the didactic and further reinforced by pocket cards detailing value-based evidence for (1) initial management, (2) surveillance and survivorship, and (3) recurrence care. A quality review outlining appropriateness of care was performed. Data for the care six months prior to the newly structured educational sessions were compared to those for care occurring within the six months after the change.

Results: During the course of each didactic session, both low- and high-value practices were explicitly identified. Many, but not all, were adopted from the SGO Choosing Wisely Campaign. After the educational intervention, there was a reduction in the following low-value practices: 33% in routine post-treatment PET/CT imaging, 13% in rate of radical hysterectomies performed in women with high-risk pathologic features, and 56% in colposcopies performed for low-grade squamous intraepithelial lesions or less. On the other hand, there was a 100% increase in the rate of smoking cessation prescriptions and referrals.

Conclusion: There are few studies to guide educators on best teaching practices for incorporating value-based care principles. Initial data from this educational intervention pilot reveal a substantial reduction in low-value practices and an increase in a high-value practice in this patient cohort. Its impact on cost and patient outcomes is subject to ongoing study.

275 - Poster Session

Successful implementation of universal genetic testing in a county hospital gynecologic oncology clinic: A quality improvement initiative

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Objective: Assessment of standard-of-care genetics services within gynecologic oncology clinics in county hospitals is limited. We sought to determine genetic counseling and germline genetic testing rates in patients with high-grade, nonmucinous epithelial ovarian, fallopian tube, and primary peritoneal cancers (EC) and Lynch syndrome tumor screening (IHC) in patients with endometrial cancers (EC) at a county hospital serving a diverse, indigent patient population, before and after implementing “universal genetic testing” quality improvement interventions. We sought to ensure that >80% of patients with OC received genetic counseling and genetic testing and >80% of patients with endometrial cancers received IHC with genetic counseling and genetic testing as needed.

Method: We performed a retrospective review of patients with OC and EC diagnosed September 1, 2012, to August 31, 2016 at a county hospital’s gynecologic oncology clinic. Summary statistics were used to describe the patient population and rates of genetic counseling and genetic testing. Run charts visualized trends following the implementation of quality improvement interventions, which were introduced starting in mid-2015 and included integrated genetic counseling (8 appointments/month), provider education for ordering/interpreting IHC tests, and assisted genetic counseling referrals.

Results: A cohort of 244 patients was included in the analysis (60 OC and 184 EC). Prior to implementation of quality improvement interventions, 20.5% (8/39) of OC patients received genetic counseling and genetic testing and 9.6% (13/135) of EC patients received IHC. Following the interventions, overall 83.3% (50/60) of OC patients were referred for genetic counseling and testing; 88% (44/50) completed counseling; 88.6% (39/44) completed genetic testing; 20.5% (8/39) of patients tested positive for a mutation; and 50% (3/6) with a *BRCA* mutation received PARP inhibitor therapy. Of patients with EC, 80.4% (148/184) were recommended to have IHC; 60.1% (89/148) completed IHC; 18% (16/89) had abnormal results; 68.8% (11/16) completed genetic counseling; 72.7% (8/11) completed genetic testing; and 37.5% (3/8) of these had a Lynch syndrome mutation.

Conclusion: “Universal genetic testing” quality improvement interventions can be adapted to ensure that a diverse, indigent patient population in a county hospital gynecologic oncology clinic has access to standard-of-care genetics services, increasing opportunities for targeted therapy (PARP inhibitors) and cancer prevention. For gynecologic oncology clinics with a similar patient volume, 8 genetic counseling appointments per month may be sufficient to meet demands. We achieved genetic counseling and testing rates of >80% among OC patients, while uptake of IHC and genetic counseling and testing for EC patients was lower, in part due to differences in testing and treatment implications and processes.

276 - Poster Session

Implementing universal genetic testing in ovarian cancer

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Objective: Universal genetic testing for all women diagnosed with ovarian cancer as well as first-degree relatives is a fundamental part of oncology care. Despite this, fewer than 1 in 5 individuals with a history of breast or ovarian cancer meeting NCCN guidelines have undergone genetic testing. A recent SGO position statement identified barriers to genetic testing in the clinical setting, including lack of physician awareness of testing benefit and patient misunderstanding of counseling/testing intent.

Method: In our academic urban practice we implemented a low-cost, efficient model for universal genetic testing for ovarian cancer patients that utilized provider education, the creation of quickly accessible standardized texts in the electronic health record (EHR), enhanced EHR patient education, streamlined patient referrals to geneticists, and integration of genetic counselors in the tumor board to improve our genetic counseling and genetic testing completion rates.

Results: Baseline rates for genetic counseling and genetic testing completion were ascertained for our practice by retrospective chart review and were found to be 31% and 26%, respectively, in the combined 4 years prior to our quality improvement model. Genetic counseling and testing completion rates were then determined prospectively after the measures were implemented. In the 3 years since we implemented our practice improvement measures, our genetic counseling completion rates/genetic testing completion rates have increased to 85%/82% (year 1), 91%/86% (year 2), and 82%/79% (year 3), respectively.

Conclusion: The identification of heritable mutations has the potential to have an impact on patient care and needs to become a standard part of clinical practice. Implementation of simple measures has the potential to greatly improve genetic counseling and genetic testing completion rates.

277 - Poster Session

Do patients care who is paying for their ovarian cancer treatment? Patient perspectives on value-based assessments

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Objective: The American Society of Clinical Oncology (ASCO) value snapshot is a visual representation of novel treatments that includes clinical benefit, toxicity, and costs. We assessed whether patients view the value snapshot as a helpful tool during counseling and queried the importance to patients of third-party-payer costs versus out-of-pocket costs when making a treatment decision.

Method: A total of 100 patients with ovarian cancer were prospectively enrolled in a preferences study and educated regarding each component of ASCO's Net Health Benefits (NHB). Patients were asked to evaluate the helpfulness of ASCO's visual value snapshot and its components (clinical benefit, toxicity scores, NHB, and cost). Using a 5-point Likert scale, patients were asked about the importance of both cost to an insurance company and their out-of-pocket costs and whether these would affect their treatment decision.

Results: Average age at diagnosis was 59 years (SD = 9.6); 57% of patients had recurrent disease, with 51% on treatment at time of enrollment. Eighty-three percent of patients thought the ASCO snapshot was appropriate to use as a visual decision aid. Sixty-four percent found the snapshot to be “helpful” or “very helpful.” However, 22% thought that not enough information was presented to be helpful in making a treatment decision. Most patient comments focused on expanding information regarding type and severity of toxicities, removing specific numbers regarding life expectancy, and explaining NHB more

clearly. A few key patient comments regarding life expectancy stated the visual representation was “scary,” “harsh,” and “depressing.” Thirty-nine percent considered the cost of treatment to an insurance company “not important at all,” while 46% reported out-of-pocket costs to be “very important” or “the most important” factor (Figure 1). Thirteen percent of patients would change treatments based on out-of-pocket costs, while none would change treatment based on the cost to insurance.

Conclusion: Most patients considered the ASCO value snapshot to be helpful, suggesting it may be a valuable tool for treatment discussions between oncology providers and patients. However, our findings identified information gaps that should be addressed to further refine the tool and individualize patient treatment decisions. While the cost of cancer treatment to a third-party payer is not a motivating factor for patients, they are highly concerned about out-of-pocket costs.

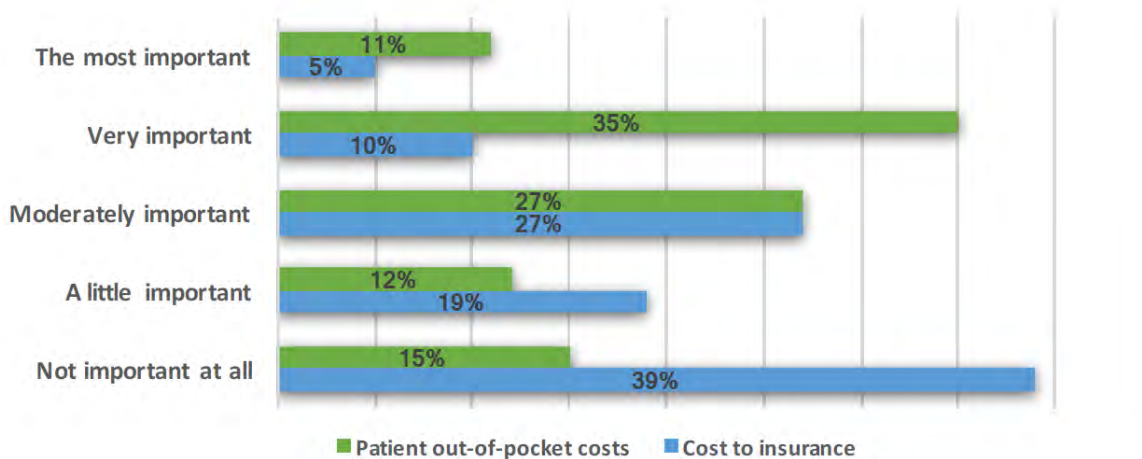


Fig. 1. Importance to patients of cost to insurance and out-of-pocket costs.

278 - Poster Session

A quality improvement initiative to determine and address psychosocial and basic resource needs of patients in the gynecologic oncology clinic

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Objective: Health care disparities are increasing even in high-volume tertiary care centers and are often attributed to unmet psychosocial and basic resource needs. We sought to assess and address the psychosocial needs of patients presenting to a gynecologic oncology clinic through a quality improvement initiative at an urban, academic cancer center.

Method: We conducted a pilot study using a questionnaire validated by Health Leads, a social enterprise that matches patients with community-based resources in an effort to meet basic resource needs as a part of quality health care, in patients presenting to a gynecologic oncology clinic. The domains assessed were food, housing, utility, and transportation insecurity; social support; financial resource strain (“social resource needs”); and mental health. All patients were given resources for identified needs. Patients identified with high levels of resource needs were referred to the Health Leads program for follow-up.

Results: A total of 46 patients were approached, and 100% agreed to participate; 67% ($n = 30$) had a diagnosis of invasive cancer, and 30% ($n = 14$) were undergoing active therapy. Median income was \$46,000; 57% ($n = 26$) had private insurance; and 43% ($n = 18$) had public or no insurance. Fifty-seven percent ($n = 26$) reported at least 1 need; the median number of needs was 1. Social resource needs were reported by 43% ($n = 20$) of patients: 20% ($n = 9$) reported financial strain, 15% ($n = 7$) housing insecurity, 9% ($n = 4$) food insecurity, 9% ($n = 4$) utility needs, 9% ($n = 4$) child-care barriers to care, 9% ($n = 4$) lack of a support system, and 7% ($n = 3$) transportation needs. Thirty-five percent ($n = 16$) had additional mental health needs. While 100% of patients felt comfortable discussing these issues with their provider, only 22% ($n = 10$) had previously done so. Fewer than half ($n = 19$) had ever discussed their respective needs with a social worker. All patients with needs received appropriate referrals to resources, and 11% ($n = 5$) were referred to Health Leads for more intensive follow-up.

Conclusion: In our pilot study, patients presenting to an urban, academic gynecologic oncology clinic had high levels of social resource and mental health needs. Using a validated questionnaire to assess basic resource needs in this setting, with referral to Health Leads when appropriate, may help identify and address these needs.

279 - Poster Session

Genetic testing in elderly patients: Should there be an age cutoff?

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Objective: In the context of a rapidly aging population, limited data are available to guide testing for cancer predisposition genes among older individuals. We sought to evaluate patterns of genetic testing based on age.

Method: Results of all patients who underwent genetic testing at the hereditary breast and ovarian center in a single institution from July 1, 2013, to December 31, 2016, were reviewed. Patients were stratified by age groups ≤ 50 , 51–69, and ≥ 70 years. Statistical analysis was done using Stata.

Results: A total of 1,794 patients were included for analysis: 946 (53%) were ≤ 50 years, 657 (37%) were between ages 51 and 69, and 191 (11%) were older than 70 years. Across all age groups, older patients were more likely to have a personal history of cancer ($P < 0.0001$) and less likely to have a family history of cancer ($P = 0.02$). The median age of patients with genetic testing yielding pathogenic mutations was 45 years versus 50 years for patients with negative results ($P < 0.0001$). However, rates of mutations were similar when comparing patients < 70 and ≥ 70 years (12% vs 9%, $P = 0.78$). Among all patients, *BRCA1/2* were the most commonly mutated genes, accounting for 78% of mutations. Rates of mutations in other cancer-associated genes did not vary by age. Of mutations found in patients ≥ 70 years old, 24% were non-*BRCA*. Despite this, older patients were more likely to undergo single-gene, rather than panel, testing ($P = 0.002$). In patients younger than 50 years, demographic factors including personal history of cancer, family history of cancer, and Ashkenazi Jewish ancestry were predictive of detecting a mutation ($P < 0.0001$, $P = 0.0052$, and $P < 0.0001$, respectively) but not predictive in patients ≥ 70 years ($P = 0.5$, $P = 0.7$, $P = 0.06$, respectively).

Conclusion: Although the average age of patients testing positive for a pathogenic mutation was 5 years younger than those who tested negative, we could not identify an age cutoff at which genetic testing was significantly less likely to yield clinically significant results. Furthermore, rates of mutations in genes other than *BRCA1/2* were similar across all age groups, and demographic factors could not predict which elderly patients would carry pathogenic mutations. Our data suggest that multigene panel testing should not be restricted based on age.

280 - Poster Session

Cancer hospital facility type affects the quality of care and survival in ovarian cancer treatment

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Objective: Treatment of ovarian cancer often requires multimodal care and is resource-intensive. Prior work has shown that treatment at high-volume centers is associated with decreased mortality and improved adherence to evidence-based guidelines. We examined the importance of facility type on survival and adherence to quality metrics for ovarian cancer.

Method: We used the National Cancer Database (NCDB) to identify women with ovarian cancer treated from 2004 to 2013. Data were stratified by American Cancer Society's Commission on Cancer Accreditation program, which classifies facilities based on clinical volume, enrollment in clinical trials, and availability of diagnostic and treatment services as academic comprehensive cancer programs (including NC-designated cancer centers) (ACAD), comprehensive community cancer programs (CCCP), community cancer programs (CCP), and integrated network cancer programs (INCP). For each facility type we examined adherence to quality measures (lymph node dissection for stage I–IIIB tumors, chemotherapy for high-risk early-stage disease, avoidance of chemotherapy for low-risk, early-stage disease, cytoreduction/omentectomy for advanced-stage disease, chemotherapy for advanced-stage disease), and 2-year and 5-year risk-adjusted survival.

Results: A total of 92,428 patients at 1,221 hospitals including 39,982 at ACADs, 37,349 at CCCPs, 4,822 at CCPs, and 10,275 at INCs were identified. Mean hospital-level adherence to all quality metrics was 75.7% (SD = 9.4) at ACADs, 77.0% (SD = 8.6) at INCs, 72.2% (SD = 12.2) at CCCPs, and 69.7% (SD = 17.5) at CCPs (Table 1). Two-year risk-adjusted survival at ACADs was 77.3% (95% CI 76.9–77.6%) compared to 76.6% (95% CI 76.0–77.2%) at INCs, 76.5% (95% CI 76.1–76.8%) at CCCPs, and 75.9% (95% CI 75.1–76.7%) at CCPs ($P < 0.0001$). Similar trends were noted for 5-year survival (Table 1).

Conclusion: ACADs and INCs have higher overall compliance with quality metrics for ovarian cancer. Treatment at ACADs is associated with a small, but statistically significant, improvement in survival compared to CCPs.

Table 1. Quality metrics and 2- and 5-year survival by cancer hospital facility type^a.

Quality Metric	Community Cancer Program (CCP), <i>n</i> = 404	Comprehensive Community Cancer Program (CCCP), <i>n</i> = 567	Academic/Research Program (ACAD), <i>n</i> = 225	Integrated Network Cancer Program (INCP), <i>n</i> = 55	<i>P</i> Value
Lymph node dissection for stage I–IIIB tumors	327 61.9±24	558 59.8±20.9	224 66.5±14.9	55 65.4±16.2	0.0004
Cytoreduction for stage II–IV tumor	314 79.4±21.9	554 81.1±17.7	223 82.5±14.4	55 88.3±8.9	0.0054
Avoidance of chemotherapy for low-risk, early-stage tumors	116 87.9±21.7	372 77.8±23.5	199 70.1±19.9	46 66.2±18.8	<0.0001
Chemotherapy for high-risk, early-stage tumors	208 82.3±24.8	477 70.2±24.4	213 72.9±19	52 69.1±18.1	<0.0001
Advanced-stage chemotherapy	358 84.6±19.3	564 82.5±16.3	224 82.5±12.2	55 84.5±11.6	0.2244
Overall quality	378 69.7±17.5	566 72.2±12.2	224 75.7±9.4	55 77±8.6	<0.0001
2- year survival (%; 95% CI)	75.9 (75.1,76.7)	76.5 (76.1,76.8)	77.3 (76.9,77.6)	76.6 (76.0,77.2)	<0.0001
5-year survival (%; 95% CI)	49.8 (48.6,50.9)	50.5 (50.1,51.0)	51.7 (51.3,52.2)	50.8 (49.9,51.6)	<0.0001

^a Data are *n* or mean (%) ± SD unless otherwise specified.

281 - Poster Session

Cost-effectiveness analysis of tumor testing for *BRCA* pathogenic variants

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Objective: Approximately 15%–17% of women with epithelial ovarian cancer (EOC) will have a germline *BRCA* pathogenic variant, which has major health care implications for them and their relatives. Among those without a germline pathogenic variant, the presence of tumor somatic *BRCA* variants provides important information for therapeutic options. Genetic testing for *BRCA1/2* is recommended for all patients with EOC, but commonly not done. This study objective is to assess the cost-effectiveness of *BRCA* screening with tumor testing.

Method: We compared the cost-effectiveness of *BRCA* screening with initial tumor testing followed by germline testing if indicated with that of routine germline testing followed by tumor testing for those who tested negative, using probability estimates reported in the literature and published cost data. Effectiveness was based on whether testing was completed. A strategy would be favored if it cost $\leq \$5,000$ per additional woman with ovarian cancer tested.

Results: In the base case, tumor testing compared with serum testing cost \$2,580 per additional woman tested. In sensitivity analyses, results were most sensitive to variation in tumor testing costs, serum testing costs, and the probabilities of getting serum testing, of getting tumor testing after serum testing was done, and of getting serum testing after tumor testing. However, tumor testing cost remained $< \$5,000$ per additional test with varying these parameters in clinically plausible ranges. For example, if serum testing cost decreased to \$1,000 (base case \$2,195), the cost per additional woman tested increased to \$3,500. To increase the cost per additional test to $> \$5,000$, the serum testing cost would need to decrease further or the tumor testing cost to increase in addition to decreases in serum testing cost. Tumor testing was not favored if initial serum testing occurred, on average, in $> 67\%$ of cases (base case 30%). In a probabilistic sensitivity analysis, varying all parameters simultaneously over plausible ranges 5,000 times, tumor testing cost $\leq \$5,000$ per additional woman tested in 100% of model iterations.

Conclusion: The average cost per patient of ovarian cancer treatment is estimated as $> \$200,000$. With more than 15% of women harboring a *BRCA* pathogenic variant, having a cost-effective testing strategy, such as the tumor testing strategy proposed, could have a positive impact on care for many women.

282 - Poster Session

Trends in regionalization of care and outcomes for uterine cancer

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Objective: National efforts have been directed toward regionalizing cancer surgery to specialized high-volume surgeons and centers. For endometrial cancer, there is a modest association between procedural volumes and outcomes, and little data on efforts to regionalize care exist. We examined trends in physician procedural volume over time and associated outcomes.

Method: All women diagnosed with uterine cancer who underwent hysterectomy (abdominal, robotic-assisted, laparoscopic) in any hospital in New York state, between 2000 and 2014, were captured in the New York Statewide Planning and Research Cooperative System database. The number of surgeons and procedures performed each year as well as estimates of annualized surgeon and hospital volume were examined. Multivariate models were used to examine the association between surgeon volume and surgical site, medical complications and prolonged length of stay, and excessive charges (> 75 th percentile for each). Trends over time were compared.

Results: A total of 44,558 patients were identified, 29,241 of whom underwent abdominal and 15,317 minimally invasive hysterectomy. The number of surgeons performing cases decreased substantially over time. In 2000, 2,595 hysterectomies were performed by 845 surgeons with a mean surgeon volume of 3 cases. In 2014, 3,119 hysterectomies were performed by 317 surgeons with a mean volume of 10 cases. In a multivariate model increasing surgeon volume was associated with a modest decrease in adverse outcomes. For example, an increase of 1 hysterectomy per year per surgeon was associated with a reduced overall complication rate (RR = 0.997, 95% CI 0.995–0.9995), surgical site rate (RR = 0.996, 95% CI 0.992–0.999), medical complications rate (RR = 0.996, 95% CI 0.993–0.999), length of stay (RR = 0.997, 95% CI 0.995–0.999), and total charges (RR = 0.994, 95% CI 0.991–0.997). Overall morbidity decreased in more recent years of the study.

Conclusion: Regionalization of care for endometrial cancer has resulted in fewer surgeons providing care for a larger number of patients. Concentration to a small number of surgeons with higher volume has resulted in a small, but statistically significant, reduction in morbidity.

283 - Poster Session

Cancer screening correspondence coverage in Ontario, Canada: Factors related to limitations in reach

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Objective: There is significant evidence to show that cervical cancer screening correspondence programs have positive results in promoting uptake of Pap smears. In Ontario a centralized correspondence program has been integrated into the cervical cancer screening program in order to send letters to women newly eligible, due, or overdue for screening. The reach of correspondence in the target population is not well understood, and this study aims to quantify correspondence coverage and to better understand characteristics of women not being reached.

Method: This was a population-based observational study. Women 30–69 years old who were due (last Pap test >3–5 years prior) or overdue (last Pap test >5 years ago or never before screened) for cervical screening, according to the Ontario Cervical Screening Program (OCSPP) guidelines, were the target population for cervical screening correspondence. These correspondence letters contain information about cervical screening and invite women to speak to their health care provider about Pap tests. Administrative databases were linked to determine mailing status and characteristics of individuals who were unsuccessfully mailed letters. Demographic and recent health care utilization patterns (within previous 3 years) were analyzed for the cohort.

Results: More than 1.6 million women were identified as being eligible for cervical mailing correspondence between November 2013 and December 2016, and of these women, unsuccessful mailings due to lack of up-to-date address information ranged from 7.5% (due for screening) to 25.3% (overdue/never screened). Women who failed to receive the mailing were more likely to be ages 30–49 years, to not be affiliated with a primary care provider, and to have not utilized health care services within the last 3 years based on health insurance billings.

Conclusion: Correspondence programs are effective forms of increasing compliance with cancer screening, but there are limitations. There are subgroups of the population who cannot be reached by letter mailing; thus, consideration should be given to alternative strategies to reach these hard-to-reach and underscreened women because the usual methods of outreach are ineffective.

284 - Poster Session

GO-BRCA: A collaborative service model to improve access to ovarian cancer genetic testing

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Objective: At least 15%–20% of women diagnosed with ovarian cancer carry an underlying gene mutation. For every individual with a genetic mutation, there are several close relatives at risk for inheriting the same gene. Diagnosis of a hereditary cancer predisposition helps direct screening and prevention strategies for patients and relatives and, with the advent of poly ADP-ribose polymerase inhibitors, can guide treatment for women with ovarian cancer. Prior to 2016, women were referred to the Hereditary Cancer Clinic (HCC) by the gynecologic oncology team at the time of their cancer diagnosis. The HCC would facilitate genetic testing with pre- and posttest counseling in a publicly funded model. Patients could often wait more than 12 months for genetic testing results; the aim of this study was to improve wait times and ultimately patient care.

Method: In collaboration with the gynecologic oncology team, a pilot program was launched in January 2016 (GO-BRCA). This model transfers pretest counseling and genetic testing responsibilities to the gynecologic oncology team; posttest counseling remains with the HCC. A 5-minute educational video was developed by both teams and provided on a tablet to patients while they waited for their clinic appointment. Primary outcome was time to genetic test results. Patient and gynecologic oncology provider satisfaction were measured using pre- and posttest surveys.

Results: One hundred and twenty-one women were enrolled from January 2016 to January 2017; 111 women had genetic testing completed. Mean time to genetic test results decreased from 306 (± 23) days to 158 (± 7) days. Before testing was completed, 97% of patients thought they made an informed choice about genetic testing. Of those who returned posttest surveys, 97% were happy they had had testing, and 100% appreciated testing by the gynecologic oncology team compared to a separate HCC appointment. The gynecologic oncology team considered it a feasible model.

Conclusion: Transferring pretest counseling and genetic testing to the gynecologic oncology team did not have a significant impact on clinic flow and allowed for expedited test results. With more tailored treatment choices available, this information must be timely to guide treatment decisions. This project demonstrates that this is possible in a publicly funded system and that similar models can be easily adopted in other centers.

285 - Poster Session

Prognostic impact of adjuvant chemotherapy treatment delays for ovarian cancer: A cohort study

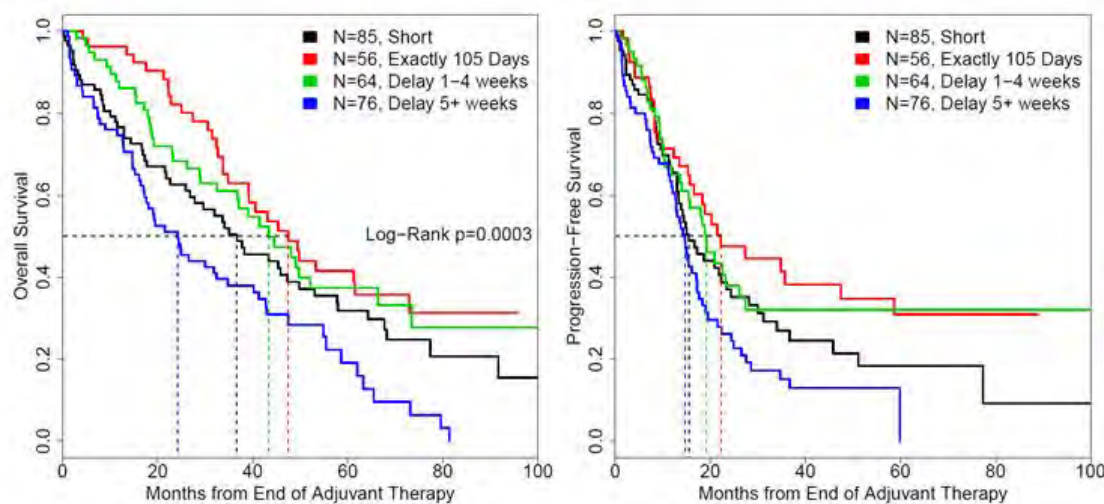
K. Starbuck^a, K.H. Eng^a, K. Morrell^a, W. Duncan^a, J.L. Etter^a, K.B. Moysich^a, K. Odunsi^a, E. Zsiros^a, P.J. Frederick^a, S.N. Akers^a, S.B. Lele^a and J.B. Szender^b. ^aRoswell Park Cancer Institute, Buffalo, NY, USA, ^bSTART Center for Cancer Care, San Antonio, TX, USA

Objective: We aimed to investigate the prognostic impact of duration of first-line chemotherapy administration in patients with epithelial ovarian cancer

Method: Chemotherapy records were abstracted from the electronic medical record. On-schedule completion was defined as 105 days. Patients with on-time completion were compared to patients finishing early (<105 days), with delays of 1–4 weeks, or delays of >4 weeks. A total of 222 women with stage IIIC–IV were identified, and stage-stratified estimates of progression-free survival (PFS) and overall survival (OS) were compared. A delay substudy was performed with outliers removed. Women with completion times of 105 days up to 350 days were considered. Each week of delay was correlated with the change in PFS and OS to identify time points associated with change in outcome

Results: A total of 1,217 women were treated for primary ovarian cancer from May 2006 to December 2016; we focused on 505 women who received platinum/taxane regimens, did not receive neoadjuvant chemotherapy, and had long-term follow-up. Most women had either on-time completion of chemotherapy (23.6%) or a treatment delay of 4 weeks or less (21.8%); 21.6% of women experienced a delay longer than 4 weeks. R0 resection at initial debulking (OR = 1.99, 95% CI 1.18–3.36, $P = 0.010$) and RECIST complete response (OR = 4.88, 95% CI 2.47–9.63, $P < 0.001$) were both strongly associated with on-time completion schedule. Patients with on-time completion and less than 1 month of delay had similar median survivals of 43.1 months (lower 95% CI bound 33.7 months) and 44.5 months (lower bound 37.0, $P = 0.93$ vs on-time). Women with more than 1 month of delay had a significantly decreased median survival of 18.1 months (14.7–24.9 months), while women with short intervals survived 35.0 months (95% CI 21.8–49.8 months). Short-term delays lead to a progressive decrease in overall survival. These differences were significantly different from the on-schedule survival estimate after 6 weeks of delay; a clinically significant trend appears in as little as 2 weeks of delay. See Figure 1.

Conclusion: On-time completion of chemotherapy correlates with increased PFS and OS and higher complete response rates. Progressively increasing delays in chemotherapy completion was associated with decreasing survival.



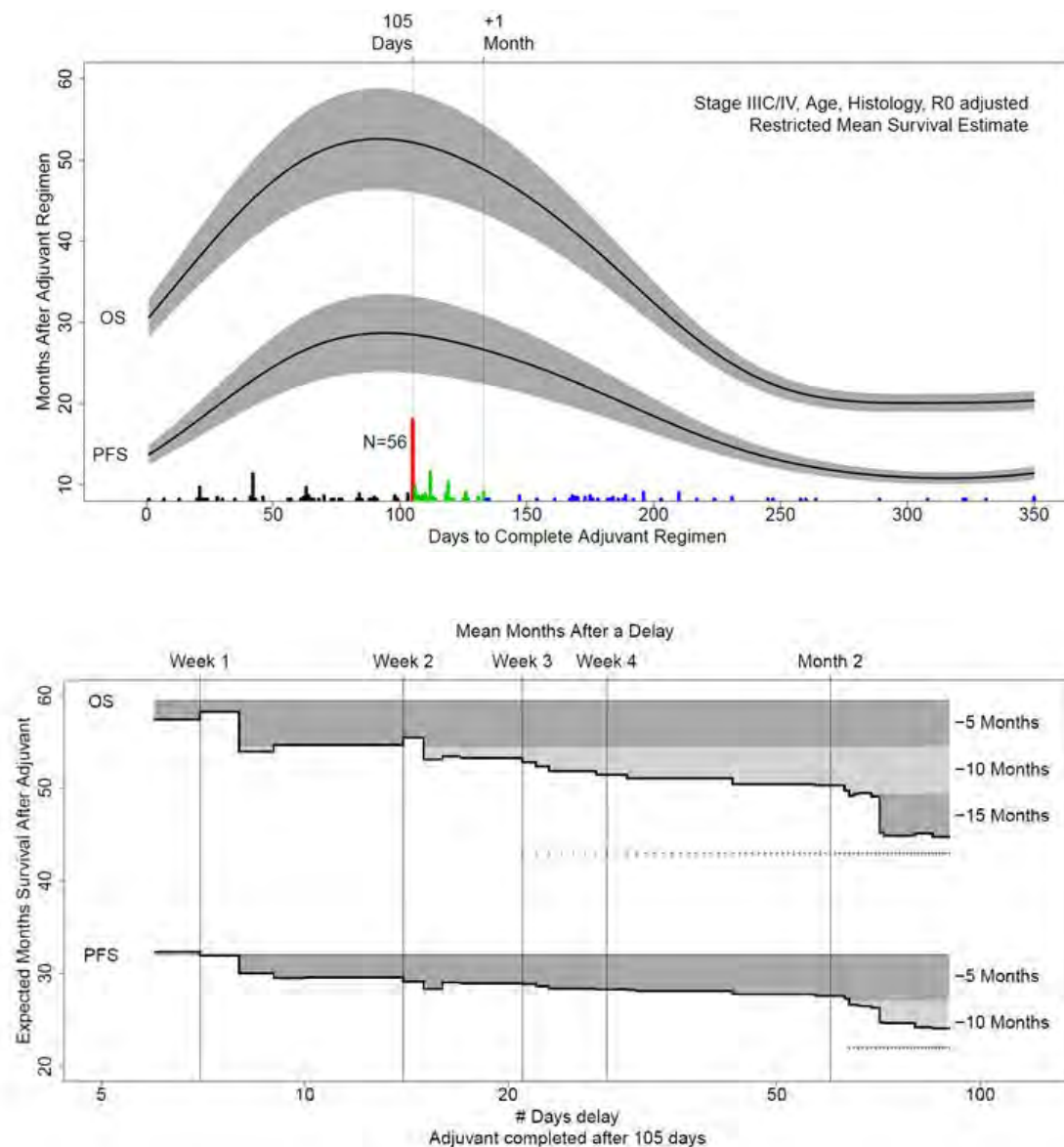


Fig. 1.

286 - Poster Session

Impact of FDA recommendations on patient-reported outcome inclusion in ovarian cancer clinical trials

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Objective: Patient reported outcome (PRO) measurement has gained popularity as a means to elicit otherwise underreported or unreported symptoms or functional issues experienced by patients. In 2009, the Food and Drug Administration (FDA) issued guidance to industry promoting the use of PROs in clinical trials conducted for medical product development to support labeling claims. We sought to determine whether there was an increase in the use of PROs in clinical trials involving interventions for patients with ovarian cancer after the FDA issued its guidance.

Method: We conducted a systematic search using the clinicaltrials.gov online database and reviewed all U.S. protocols received between January 2007 and December 2016 for phase 2–3 “interventional studies” for the condition of “ovarian cancer.” Protocols for trials of nondrug or biologics-based interventions and trials that focused on cancer prevention were excluded. For all included protocols, we collected the date of initial receipt, whether it was industry-sponsored, and whether PROs were included in the trial design. We used descriptive statistics to show the annual trends in PRO inclusion from 2007 to 2016. χ^2 and Fisher exact tests were used to compare the frequency of PRO inclusion before (2007–2009) and after (2010–2016) the FDA issued its guidance and between industry- and nonindustry-sponsored trials.

Results: Of the 368 clinical trials found in our initial search, 291 met inclusion criteria. Overall, 15% (annual range 4%–27%) of ovarian cancer clinical trial protocols included PRO measures. Annual trends in PRO inclusion from 2007 to 2016 are shown in Figure 1. Prior to FDA guidance, 13% (15/113) of trials included PROs compared to 17% (30/178) after the guidance ($P = 0.51$). From 2007 to 2016, 57% (166/291) of ovarian cancer clinical trials were sponsored by industry. PROs were included in 17% (29/166) of industry-sponsored trials and in 13% (16/125) of nonindustry-sponsored trials ($P = 0.33$). Among industry-sponsored trials, 14% (8/58) included PROs before the guidance, and 19% (21/108) did so after ($P = 0.40$).

Conclusion: FDA-issued guidance to include PROs in clinical trials has not had a substantial impact on the rate of PRO inclusion in ovarian cancer trials. PRO inclusion in ovarian cancer clinical trials remains low, and quality improvement efforts should focus on this shortfall.

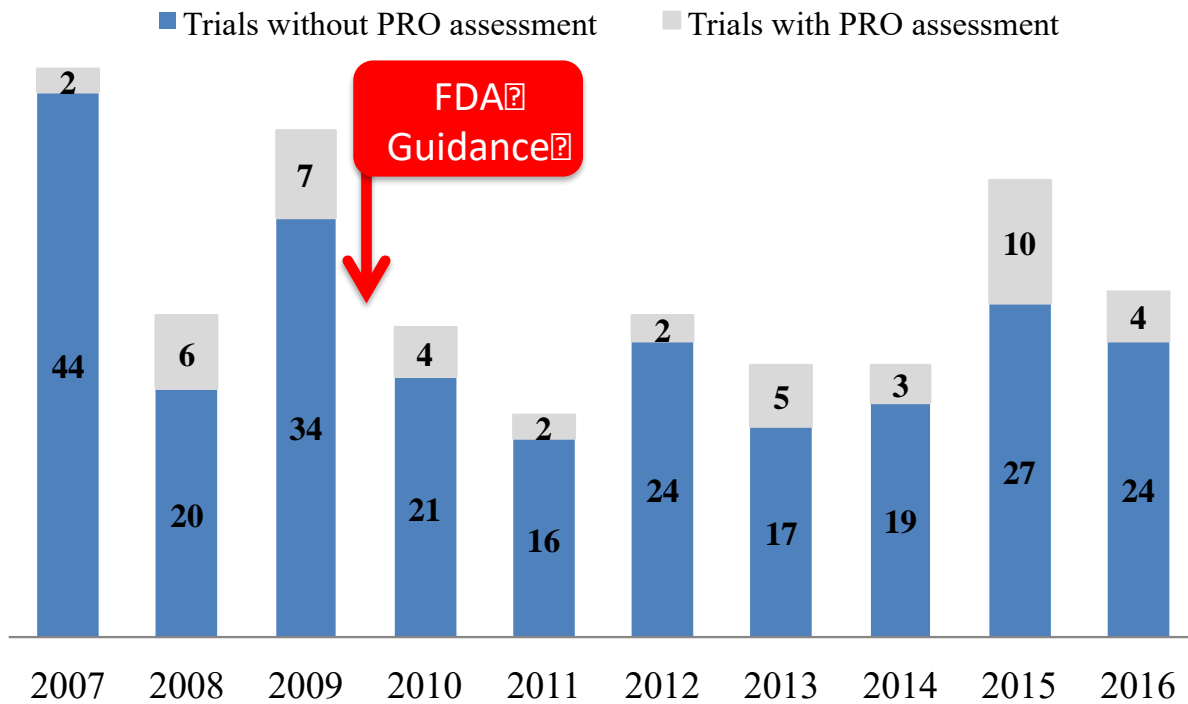


Fig. 1. Temporal trends in PRO inclusion for ovarian cancer clinical trials.

287 - Poster Session

Bundled payment models in cancer: What we know and where to go

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Objective: The number of bundled-payment pilots has surged in recent years; however, the efficacy of bundles in cancer remains unclear. As the gynecologic cancer community works to develop new bundled-payment pilots, we set out to understand the scope of bundled-payment pilots in cancer compared to other diseases in order to identify gaps in the evidence of their impact.

Method: We performed a structured analysis of characteristics of bundled-payment pilots in cancer and other diseases. We conducted a systematic review to identify all published bundled-payment models since the passage of the Affordable Care Act. We collected payer, disease, sample size, and outcome data for each bundle, when available. We compared sample size by payer type using Wilcoxon Rank Sum test in SAS v9.4.

Results: We identified 75 disease-specific pilots, including 29 in orthopedics, 17 in cardiac disease, 10 in obstetrics, 6 in respiratory disease, 6 in cancer, 2 in psychiatry, and 1 in neurology. Table 1 summarizes differences by disease type. The

majority of bundles were contracted through commercial payers ($n = 46, 61\%$), and cancer was the only disease with exclusively commercial contracts. Only 30 pilots (40%) reported sample size data, and the median sample size reported was 1,238 (range 1–51,198). The median sample size for cancer-specific pilots was 515, the lowest of all diseases (range 515–5,805). When we compared sample size by payer type, commercial pilots were associated with a significantly smaller median sample size (153 vs 3,012, $P < 0.01$). Of the six bundled-payment pilots in cancer, only two reported results. The 21st Oncology radiation therapy bundle reported improvements in guideline adherence for patients with bone metastases and prostate cancer and no effect for patients with breast, lung, and skin cancer. The United Healthcare bundle reported decreased hospitalization and therapeutic radiology use and a paradoxical increase in chemotherapy drug costs, with a net savings of \$33.36 million.

Conclusion: The experience with bundled payments in cancer is limited. Initiatives to expand the evidence base, including increased transparency of outcomes, increased samples on which results are based, and targeted efforts to develop bundles with federal payers that have access to larger patient pools, are needed.

Table 1. Characteristics of bundled-payment pilots by disease.

Disease Type ^a	Total, No.	Public Pilots, No. (%)	Sample Size Available, No. (%)	Total Patient Sample, No. ^b	Median Sample Size, No. ^b	Patient Sample, Range ^b
All disease pilots	75	29 (39)	30 (40)	148,131	1,238	1–51,198
Respiratory	6	5 (83)	3 (50)	58,836	5,805	1,833–51,198
Cardiac	17	7 (41)	6 (35)	31,081	4,912	74–11,451
Obstetrics	10	4 (40)	4 (40)	10,938	1,613	1–5,712
Psychiatry	2	1 (50)	1 (50)	1,770	1,770	-
Neurology	1	1	1	1,109	1,109	-
Gastrointestinal	4	3 (75)	2 (50)	1,493	747	29–1,464
Orthopedics	29	8 (28)	10 (34)	41,491	536	60–32,666
Cancer	6	0	3 (50)	1,413	515	88–810

^aBundles that covered multiple diseases were considered separately for each disease-specific pilot. Within the 17 demonstrations reporting patient sample information, 30 disease-specific pilots were evaluated separately in this analysis.

^bCalculations include only bundled-payment pilots with available sample-size data.

288 - Poster Session

Access to gynecologic oncologists in Ohio in 2017: The role of the patient portability and Affordable Care Act

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Objective: To document the role of the Affordable Care Act (ACA) in providing access to gynecologic oncologists in Ohio in 2017.

Method: The goal of the ACA in Ohio is to provide improved access to health insurance utilizing several mechanisms, including Medicaid expansion and health care exchanges, both of which are available through healthcare.org. We obtained information on access and usage of health care exchanges in Ohio in 2017 through healthinsurance.org. We identified gynecologic oncology practices in Ohio through the Society of Gynecologic Oncology, confirmed their functionality by telephone, and identified which practices accepted health insurance provided through a health care exchange. Furthermore, we also gathered information on changes within these exchanges over the past 12 months. Descriptive statistics were then used to document the access to a gynecologic oncologist through these exchanges.

Results: In Ohio in 2017, there were 10 health care exchanges available, and they enrolled 238,843 individuals (2% of the Ohio population) during the 2017 open enrollment period (November 1, 2016, to January 31, 2017). We identified 11 practices in Ohio with 39 gynecologic oncologists; 7 of the 10 health care exchanges provided access to 5 of the 11 gynecologic oncology practices, and these 5 practices encompassed 22 of the 39 (56%) of the gynecologic oncologists in Ohio. Of note, 3 of the 11 (27%) practices were unsure whether they accepted patients on health care exchanges and 3 of the 11 (27%) did not

accept patients on an exchange. Of the three practices that did not accept insurance through a health care exchange, two were located within urban areas where other practices were identified that did accept insurance through an exchange. Of the five gynecologic practices that did accept insurance through an exchange, four accepted insurance through more than one exchange.

Conclusion: We found that about half of the gynecologic oncology practices in Ohio accepted insurance through a health care exchange. Thus, in Ohio in 2017, despite implementation of the ACA, patient access to a gynecologic oncologist may remain limited.

289 - Poster Session

The effect of insurance status on genetic testing patterns and outcomes for inheritable cancer syndromes: A single institution experience

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Objective: National guidelines recommend that genetic testing be offered to women at increased risk for deleterious mutations. Cost has been cited as a barrier to obtaining genetic testing. We sought to identify the role of insurance status on patterns of genetic testing.

Method: Insurance status, patterns of genetic testing, and outcomes of all patients undergoing genetic testing at the hereditary breast and ovarian cancer center at a single institution between January 1, 2013, and December 31, 2016, were reviewed. Patients of Ashkenazi Jewish ancestry were excluded because of the high rates of *BRCA1/2* founder mutations. Comparisons based on insurance status were made before and after January 1, 2014, to allow for the incorporation of legislative changes related to the Supreme Court ruling invalidating single-gene patent rights and New York State health insurance expansion, including access to health insurance exchanges through the Affordable Care Act that came online on January 1, 2014. Insurance status was categorized as private, Medicaid, Medicare, and uninsured.

Results: A total of 1,864 patients met with genetic counselors; 998 patients met inclusion criteria. Study cohort demographics are shown in Table 1. Physician referrals for genetic testing surged after 2014 ($P < 0.01$). After 2014, panel testing increased (46.2% vs 8.6%, $P < 0.001$), which was most significant among patients with private insurance ($P < 0.001$). Private insurance status increased among patients (80.1% vs 66.1%, $P < 0.001$), while the number of uninsured patients decreased after 2014 ($P < 0.001$). While the number of deleterious mutations identified decreased, the detection of variants of uncertain significance (VUS) increased significantly after 2014, which correlated with an increase in panel testing ($P < 0.001$). Patients with known mutations undergoing prophylactic screening or surgery increased after 2014 ($P = 0.04$), but the clinical management of patients with VUS remained unchanged ($P = 0.50$).

Conclusion: Since 2014, the decline in uninsured patients has been commensurate with the sharp rise in patients with private insurance and use of panel testing. With insurance expansion, more cost-effective testing platforms, and improved identification of cancer-related genes, improved access to genetic testing should be made available for all patients.

Table 1. Demographics of the study cohort ($n = 998$).

Characteristic	Number	Percentage
Age at testing ^a		
<45 years	405	40.6
45–59 years	362	36.3
60+ years	231	23.2
Race/Ethnicity		
Non-Hispanic White	699	70.0
Hispanic	85	8.5
Non-Hispanic Black	101	10.2
Asian	113	11.3

Insurance status		
Private	778	78.0
Medicaid	52	5.2
Medicare	119	12.0
Other	48	4.8

^a Mean 49.1, range 22–89.

290 - Poster Session

The impact of the Affordable Care Act on young women with gynecologic cancer

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Objective: The 2010 Affordable Care Act (ACA) dependent coverage mandate allows young adults to stay on their parents' insurance through age 26. This provision led to significant gains in insurance for young women. Our objective was to evaluate the impact of the ACA on insurance status, stage at diagnosis, and receipt of fertility-sparing treatment among young women with gynecologic cancer.

Methods: We used a difference-in-differences (DD) approach to assess insurance status, stage at diagnosis, and receipt of fertility-sparing treatment before and after the 2010 ACA among young women aged 21–26 years compared to women aged 27–35 years. We used the National Cancer Database with the 2004–2009 surveys as the pre-reform years and the 2011–2014 surveys as the postreform years. Women with uterine, cervical, ovarian, vulvar, and/or vaginal cancer were included. We analyzed outcomes for women overall and by cancer and insurance type, adjusting for race (white, non-white), nonrural area (metropolitan size $\geq 50,000$ people), and area-level household income and education level.

Results: A total of 1,912 gynecologic cancer cases pre-reform and 2,059 postreform were identified for women aged 21–26 years compared with 9,782 cases pre-reform and 10,456 postreform for women aged 27–35 years. The ACA was associated with increased insurance (DD = 2.3%, $P = 0.04$) for young women aged 21–26 years compared to woman aged 27–35 years, as well as with a significant improvement in early-stage at cancer diagnosis (DD = 3.5%, $P = 0.04$) for young women. For fertility-sparing treatment, there was a nonsignificant trend toward increased receipt for young women under the ACA (DD = 2.0%, $P = 0.19$). Trends in early-stage diagnosis or fertility-sparing treatment did not differ by gynecologic cancer type. Privately insured women were more likely to be diagnosed at an early stage and receive fertility-sparing treatment than publicly insured or uninsured women throughout the study period ($P < 0.001$).

Conclusion: Under the Affordable Care Act dependent coverage mandate, young women with gynecologic cancer were more likely to be insured and diagnosed at an early stage of disease. Given the small number of cancers in this age group (~500 cases annually), these positive trends post-Affordable Care Act implementation may be clinically important to cancer and fertility outcomes in young women.

291 - Poster Session

Cost-effectiveness of preoperative chest X-rays in low-grade endometrial cancer and atypical endometrial hyperplasia

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Objective: To determine the cost-effectiveness of obtaining routine preoperative chest X-rays in women with atypical endometrial hyperplasia or low-grade endometrial cancer.

Method: In this institutional review board-approved study, the charts of women with newly diagnosed atypical endometrial hyperplasia or grade 1 or grade unspecified endometrioid endometrial cancer treated at one institution in 2016 were reviewed to identify whether preoperative chest X-rays were cost-effective or altered the treatment plan. Women with grade 2 or grade 3 endometrioid, clear cell or serous carcinoma, or carcinosarcoma, or hyperplasia without atypia were excluded. Patient charges were determined by the institutional department of financial services. Health care costs were estimated with the Healthcare Blue Book data.

Results: Ninety-two women were included, and 52 had grade 1 endometrioid adenocarcinoma, 12 had endometrioid adenocarcinoma with unspecified grade, 25 had complex hyperplasia with atypia, and 3 had simple hyperplasia with atypia. Of

the 92 women, 46.7% (43/92) had preoperative chest imaging: 45.7% (42/92) had a preoperative chest X-ray, and 1.1% (1/92) had a preoperative CT, which was ordered by the referring physician. Of the 42 chest X-rays, 2 demonstrated lung nodules, which were evaluated with a CT and showed no evidence of metastatic disease. Initial preoperative chest imaging resulted in \$29,720 in charges (\$20,020 for the chest X-rays and \$9,700 for the preoperative CT), and \$4,950 in cost (\$2,856 for the chest X-rays and \$2,094 for the preoperative CT). Follow-up CT imaging resulted in \$12,905 in charges and \$2,794 in cost. Total preoperative chest imaging resulted in \$42,625 in charges and \$7,744 in cost. Preoperative chest imaging did not change the treatment plan of any of these women.

Conclusion: None of the women with newly diagnosed low-grade endometrial adenocarcinoma or atypical endometrial hyperplasia who had preoperative chest X-rays were found to have metastatic disease nor did the treatment plan change. The cost of routine preoperative chest X-rays in the initial evaluation of nonaggressive endometrial pathology may unnecessarily raise health care costs and escalate a woman's anxiety at the time of her cancer diagnosis without benefiting her clinical care.

Table 1. Costs and charges of imaging for patients with low-grade endometrial cancer and atypical endometrial hyperplasia

Imaging	n	%	Charge	Cost
Preoperative Imaging				
Chest x-ray 2 views	40	43.5	\$19,160	\$2,720
Chest x-ray 1 view	2	2.2	\$860	\$136
CT chest/abdomen/pelvis with contrast	1	1.1	\$9,700	\$2,094
Subtotal	43	46.7	\$29,720	\$4,950
Follow-up Imaging				
CT Chest	1	-	\$3,205	\$700
CT Chest/abdomen/pelvis with contrast	1	-	\$9,700	\$2,094
Subtotal	2	-	\$12,905	\$2,794
Total			\$42,625	\$7,744

292 - Poster Session

Implementation of a genomic profiling program for gynecologic malignancies: An achievable clinical option

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Objective: To describe the clinical application of an institutional program of next-generation sequencing (NGS) testing on gynecologic malignancies.

Method: Beginning in September 2015, our institution began offering comprehensive genomic profiling of archived tumor tissue for patients with a gynecologic malignancy. Patient assistance programs were utilized to eliminate cost barriers, and a dedicated pharmacist provided patient counseling and therapy modifications. The decision to test archived specimens was at the discretion of individual providers and patients. Under an institutional review board-approved protocol, we prospectively collected data on all participating patients.

Results: A total of 199 patients have undergone genomic profiling to date; 158 patients had ovarian cancer, and 41 had nonovarian histologies including uterine and vulvar cancers. In the ovarian cohort, 89 patients (56%) were found to have a targetable mutation with potential clinical significance; 85% of nonovarian samples had a targetable mutation. A total of 31 patients received treatment based on their genomic profile, 13 with nonovarian tumors and 18 with ovarian tumors. Average treatment length was 4.2 months. Three patients were treated for 12 months or more. Cessation of treatment was most

commonly due to disease progression. Currently, 9 patients continue on targeted therapy, and 1 patient has been treated with 2 different drug classes sequentially based on genomic profiling.

Conclusion: Institutional genomic profiling of gynecologic malignancies can identify patients who could benefit from individualized targeted therapies. Less common tumor types were more likely to have a targetable mutation and more likely to receive targeted therapy. Genomic profiling is both feasible and affordable to patients with the proper multidisciplinary infrastructure. In addition, it has the potential to provide treatment options for patients beyond traditional chemotherapeutics, particularly those with rare tumor types.

293 - Poster Session

A single-visit algorithm to improve breast care efficiency in rural Zambia

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Objective: A major cause of late-stage presentation of breast disorders in resource-constrained environments is delay in diagnosis and treatment. Simulating Zambia's "screen and treat" approach to cervical cancer prevention, we designed and implemented a single-visit algorithm to improve breast care efficiency.

Method: A cadre of mid- and high-level Zambian health care providers was trained to provide the various services involved in the breast cancer care pathway. Two breast care outreach camps were then implemented, each of 1-week duration, during which breast self-awareness, psychosocial counseling, clinical breast examination, ultrasound, ultrasound-guided biopsy, imprint cytology of biopsy specimens, and surgical treatment or referral were offered to participants within a single-visit format.

Results: A total of 1,129 women were evaluated. Their mean age was 35.9 years. The majority were multiparous (79.4%) and breast-fed (76.0%); 50.0% reported hormone use. Abnormalities were detected on clinical breast examination in 122 (10.8%) women, 114 of whom required ultrasound. Of the 114 women who underwent breast ultrasound, 48 had identifiable lesions and were further evaluated with ultrasound-guided core needle biopsy (39) or fine-needle aspiration (9). The concordance between imprint cytology and histology, for both benign and malignant lesions, was 100%. For pathologic subtypes, cytologic and histologic concordance was 85.7% for benign and 100% for malignant lesions. Overall, 6 invasive cancers were detected. Eighteen women with symptomatic breast lesions had next-day surgery, following histologic confirmation.

Conclusion: Similar to the "see and treat" approach for cervical cancer prevention, a single-visit algorithm has the potential to vastly improve breast care efficiency in low-resource environments.

294 - Poster Session

Cervical cancer screening: The first step in cancer care for women in Haiti

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Objective: Cervical cancer is a leading cause of cancer-related death for women in the developing world. Haiti has one of the highest rates of cervical cancer in the Western Hemisphere; however, little is being done to promote screening and treatment. Visual inspection of the cervix with acetic acid (VIA) is the inexpensive cervical cancer screening modality used in low-resource countries such as Haiti. Our goal is to determine the most efficacious screening modality for cervical cancer in Haiti.

Method: We reviewed data of 500 women undergoing cervical cancer screening in Cazale, Haiti, using VIA, conventional PAP smears, and liquid-based cytology (LBC). Each woman served as her own control. We utilized the χ^2 test to compare these modalities. With the kappa statistic, we explored the level of agreement between the three methods and with the Intraclass Correlation Coefficient (ICC) compared the reliability of the tests.

Results: The mean age of women in our study was 38 \pm 12 years, and 96% never had a PAP smear. With VIA, 303 normal, 191 abnormal, and 6 inconclusive results were identified. LBC identified 456 normal versus 466 normal results on PAP. LBC identified 18 ASCUS versus 17 ASCUS on PAP. LBC also identified 15 LGSIL versus 5 LGSIL on PAP. Both LBC and PAP tests identified 6 patients with HGSIL. LBC identified 3 patients with AGUS versus 2 AGUS on PAP. LBC identified 2 patients with

HGSIL/SCC versus 3 on PAP. LBC identified 0 patients with squamous cell carcinoma (SCC) versus 1 on PAP. The χ^2 test demonstrated poor concordance between PAP results and VIA results (3.02, $P = 0.08$). The low kappa value also indicated low concordance (0.04). Similarly, there was poor concordance between LBC and VIA ($\chi^2 6.06$, $P = 0.01$; kappa coefficient = 0.06). The estimated reliability between PAP and LBC was 0.89 with 95% CI, 0.87, 0.91.

Conclusion: There is poor concordance between both VIA and PAP, and VIA and LBC. This finding suggests VIA should not be an acceptable tool for cervical cancer screening for women in Haiti. There is excellent reliability between PAP and LBC, however; LBC identifies more women with low-grade disease, and PAP identifies more women with high grade disease. A prospective study that includes follow-up testing with colposcopy, biopsy, and pathology is needed to validate these observations.

295 - Poster Session

Ethnic disparity in the use of definite surgical treatment for stage IA2/IB1 cervical cancer

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Objective: To investigate the presence of disparities in the surgical management of stage IA2/IB1 cervical cancer.

Method: The NCI's Surveillance, Epidemiology, and End Results database was accessed, and women diagnosed between 1988 and 2013 with stage IA2 or IB1 squamous, adenosquamous, or adenocarcinoma of the cervix were identified. Those who received primary surgery were selected for further analysis. Based on site-specific surgery codes, treatment was categorized into radical/modified radical hysterectomy (RH), simple hysterectomy (SH), and local excision (LE).

Results: A total of 11,840 women were identified: 57% were Caucasian, 22.9% Hispanic, 10.3% Asian, and 9.7% African-American. Overall, 49.6% underwent RH, while 36.8% and 13.6% had SH and LE, respectively. Higher rates of RH were observed for those with adenosquamous (62.3%) and adenocarcinoma (55.1%) compared to squamous (46.1%) carcinoma ($P < 0.001$). Also, women with stage IB1 were more likely to receive RH compared to those with stage IA2 disease (59.1% vs 33.1%, $P < 0.001$). Rates of RH among Caucasian, Hispanic, Asian, and African-American women were 50.4%, 49.1%, 55.3% and 40.2%, respectively, while rates of SH were 36.7%, 38.4%, 33.1% and 38.8%, and those of LE were 12.8%, 12.5%, 11.6% and 21.1%, respectively ($P < 0.001$). After controlling for age, histology, year of diagnosis, and stage, African-American women were less likely to receive RH compared to White women.

Conclusion: Almost half of women diagnosed with stage IA2/IB1 did not receive appropriate surgical treatment. African-American women are less likely to receive definite surgical treatment. Further research should investigate the cause of this disparity.

296 - Poster Session

Factors associated with navigation failure among medically underserved women screened for cervical cancer

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Objective: To identify factors associated with the ability of a comprehensive real-time patient navigation system to ameliorate health disparities inherent in cervical cancer screening.

Method: After institutional review board approval was obtained, demographics and clinical outcomes were abstracted for all women navigated for abnormal cervical cytology by an urban, safety net health system between September 1, 2014, and August 31, 2015. Navigation failure was defined as more than one missed appointment following enrollment. The χ^2 and Mann-Whitney tests were used to evaluate statistical significance.

Results: A total of 3,526 women were diagnosed and navigated for abnormal cervical cytology (>ASCUS, atypical squamous cells of unknown significance) within the defined study window. When compared to successfully navigated patients ($n = 3,298$), women with more than one missed appointment ($n = 228$, 6%) disproportionately self-identified as African-American (44% vs 22%, $P < 0.0001$) and current tobacco user (30.0% vs 13%, $P < 0.0001$). They were also more likely to have a public source of external funding for their health care ($P < 0.0001$) and have been diagnosed cytologically with low-grade dysplasia. Median time to diagnostic resolution among unsuccessfully navigated women was 166 days (range 8–1,271), significantly

longer than that for women without missed appointments (75 days, range 1–472, $P < 0.001$). Median time from referral to colposcopy was also longer (58 days, range 0–383) vs 45 days (range 1–513), $P < 0.01$, respectively. No differences in age, prior history of dysplasia, distance traveled, or acknowledged exposure to intimate partner violence were observed between successfully and unsuccessfully navigated women.

Conclusion: African-American women may be disproportionately vulnerable to navigation failure. If this disparity is confirmed, potential causes should be carefully delineated and addressed.

297 - Poster Session

Does race play a role in genetic screening for hereditary cancer syndromes?

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Objective: Knowledge of genetic mutations can influence cancer screening, prevention strategies, and options for targeted therapy. We sought to identify ethnic differences in patterns of genetic testing.

Method: We reviewed genetic testing at the hereditary breast and ovarian cancer center at a single institution. Self-reported race/ethnicity was stratified as non-Hispanic white, Hispanic, non-Hispanic black, and Asian. Ashkenazi Jews were excluded ($n = 668$) because of known high rates of *BRCA1/2* founder mutations.

Results: A total of 998 patients met inclusion criteria: 699 whites, 85 Hispanics, 101 blacks, and 113 Asians. There were no differences in rates of mutations by race/ethnicity, with *BRCA 1/2* gene mutation being the most common. VUS were more common in non-whites ($P < 0.001$). Blacks and Hispanics were more likely to be referred for testing because of a personal history of cancer, while more whites and Asians were referred for a family history of cancer ($P < 0.001$). Blacks and Hispanics were more likely to have advanced-stage cancer at the time of testing ($P < 0.04$). Whites were more likely to undergo cancer screening and prophylactic surgery following genetic testing than non-whites ($P < 0.01$). See Table 1.

Conclusion: Non-whites were less likely to be referred for genetic testing based on a family cancer history, suggesting that there is a missed opportunity for mutation detection and cancer prevention based on race/ethnicity. Furthermore, even when pathogenic mutations were identified, non-whites were less likely to undergo cancer screening and risk-reducing surgery. Efforts to improve racial/ethnic disparities in early access to genetic testing and guided cancer prevention strategies are essential.

Table 1. Characteristics of patients who underwent testing ($n = 998$).

Characteristic	Non-Hispanic White ($n = 699$)	Hispanic ($n = 85$)	Non-Hispanic Black ($n = 101$)	Asian ($n = 113$)	P value
Age at testing (mean, range)	49.9 (22–89)	46.8 (25–72)	49.4 (23–80)	44.9 (29–75)	<0.001
	Number (%)	Number (%)	Number (%)	Number (%)	
Age at testing					<0.001
<45 years	262 (37.5)	39 (45.9)	38 (37.6)	66 (58.4)	
45–59 years	250 (35.8)	32 (37.7)	44 (43.6)	36 (31.9)	
60+ years	187 (26.8)	14 (16.5)	19 (18.8)	11 (9.7)	
Insurance status					<0.001
Private	557 (79.8)	56 (65.9)	67 (66.3)	98 (86.7)	
Medicaid	12 (1.7)	18 (21.2)	17 (16.8)	5 (4.4)	
Medicare	96 (13.8)	4 (4.8)	14 (13.9)	5 (4.4)	
Other	33 (4.7)	7 (8.2)	3 (3.0)	5 (4.4)	

Referring medical specialty					0.03
Breast	206 (29.5)	28 (32.9)	37 (36.6)	48 (42.5)	
IM/FM	68 (9.7)	9 (10.6)	14 (13.9)	9 (8.0)	
Ob/Gyn and Gyn/Onc	195 (27.9)	16 (18.8)	17 (16.8)	32 (28.3)	
Heme/Onc	207 (29.6)	26 (30.6)	31 (30.7)	20 (17.7)	
Other	23 (3.3)	6 (7.1)	2 (2.0)	4 (3.5)	
Type of test sent					0.73
Single	415 (59.4)	54 (63.5)	65 (64.4)	68 (60.2)	
Panel	284 (40.6)	31 (36.5)	36 (35.6)	45 (39.8)	
Reason for referral ^a					<0.01
Family history only	269 (38.5)	26 (30.6)	31 (30.7)	39 (34.5)	
Personal history only	78 (11.2)	19 (22.4)	20 (19.8)	25 (22.1)	
Family and personal history	351 (50.2)	38 (44.7)	50 (49.5)	49 (43.4)	
Personal cancer history					
Breast	394 (56.4)	54 (63.5)	64 (63.4)	73 (64.6)	0.18 ^b
Positive receptor	251 (86.0)	35 (83.3)	38 (80.9)	49 (86.0)	0.81
Negative receptor	41 (14.0)	7 (16.7)	9 (19.2)	8 (14.0)	0.45 ^b
GYN (ovarian/uterine)	31 (4.4)	2 (2.4)	5 (5.0)	2 (1.8)	0.16 ^b
Other	27 (3.9)	7 (8.2)	2 (2.0)	4 (3.5)	
Stage of cancer (among those with any personal history) ^c					
Zero	87 (22.4)	13 (25.5)	13 (20.6)	23 (31.9)	
One-Two	256 (66.0)	30 (58.8)	36 (57.1)	44 (61.1)	
Three-Four	45 (11.6)	8 (15.7)	14 (22.2)	5 (6.9)	0.09 ^d

^a Three women had neither family nor personal history (1 non-Hispanic white, 2 Hispanic).

^b Comparing frequency of women with history of specific cancer type across race/ethnicity.

^c Fifty-six women with personal history of cancer did not have stage information available.

^d $P = 0.04$ when comparing stage 0-2 versus 3-4.

298 - Poster Session

Impact of age at diagnosis on racial disparities in endometrial cancer patients

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Objective: Although black patients with endometrial cancer (EC) have worse survival than white patients, the interaction between age/race has not been examined. We evaluated the impact of increasing age at diagnosis on racial disparities in disease presentation and outcome in EC.

Method: We evaluated women diagnosed with EC between 1991 and 2010 from the Surveillance, Epidemiology, and End Results. Mutation status for *TP53* or *PTEN*, or with the aggressive integrative, transcript-based, or somatic copy number alteration-based molecular subtype, was acquired from the Cancer Genome Atlas. Odds ratio and hazard ratio with 95% CI were calculated. Interaction tests compared differences in odds or hazard between age at diagnosis and race.

Results: A total of 78,184 white and 8,518 black patients with EC were analyzed. Mean age at diagnosis for black versus white patients with endometrioid cancer (EEC), serous cancer, and carcinosarcoma was 61 versus 63, 67 versus 70, and 67 versus 69 years old, respectively ($P < 0.0001$). The increased presentation of non-EEC histology with age was larger in black than in white patients ($P < 0.0001$). The racial disparity in survival and cancer-related mortality was more prevalent in younger than in older patients ($P < 0.0001$). Mutations in *TP53*, *PTEN*, and the three aggressive molecular subtypes each varied by race, age, and histology. (See Figures 1–4.)

Conclusion: Aggressive histologies or molecular features were more common in black patients and older age, with greater impact of age on poor tumor characteristics shown in black than in white patients. Racial disparities in outcome were larger in younger patients. Intervention at early ages may mitigate racial disparities in EC.

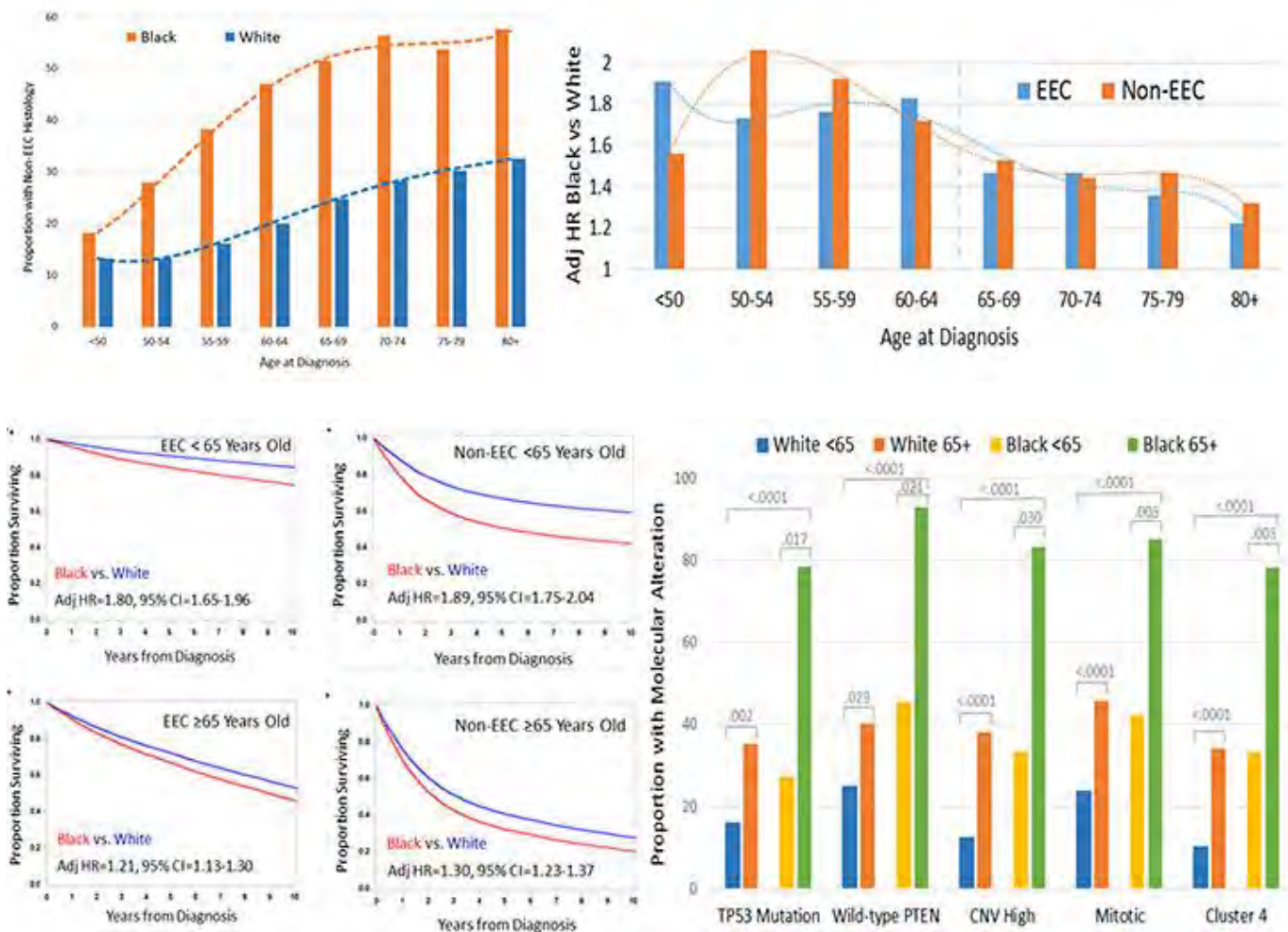


Fig. 1. Impact of Age on Racial Disparities in Endometrial Cancer.

299 - Poster Session

Race and route of hysterectomy: Examining disparities in postoperative complications

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Objective: To investigate associations between race, route of hysterectomy, and complications from hysterectomy while controlling for patient-level factors.

Method: We examined all patients undergoing benign hysterectomy recorded in the National Surgical Quality Improvement Program and its targeted hysterectomy file in 2015. Our primary exposure was self-reported race. Our primary outcome was route of hysterectomy (open versus minimally invasive). Secondary outcomes were 30-day major and minor complications. Major complications were defined as grade 3 or greater on the Clavien Dindo scale and minor as grade 2 or less. Associations were examined using bivariable tests and multivariable logistic regression.

Results: We identified 15,136 women of white ($n = 11,330$) and black ($n = 3,806$) race who underwent hysterectomy for benign indications. Black women were more likely to undergo open hysterectomy than white women (50.1% vs 22.0%, $P < 0.0001$, OR 3.37, 95% CI 3.11–3.64). Black women had larger uteri (median weight 262 vs 123 g, 60.7% vs 25.6% with uterus >250 g), more prior pelvic surgery (58.5% vs 53.2%), and higher BMI (32.4 vs 30.2) (all $P < 0.001$). After adjusting for these

factors, as well as age, prior abdominal surgery, and prior endometriosis, black women remained more likely to undergo open hysterectomy (aOR 2.04, 95% CI 1.87–2.23). Black women also experienced more major complications than white women (4.0% vs 2.3%, OR 1.74 CI 1.42–2.14) and more minor complications (11.4% vs 6.7%, OR 1.78 CI 1.57–2.02). Again, these disparities persisted when adjusting for route of surgery, uterine weight, prior abdominal and pelvic surgery, history of endometriosis, age, and BMI (major aOR 1.52 CI 1.21–1.9; minor aOR 1.26 CI 1.10–1.45).

Conclusion: Significant disparities exist for both route of hysterectomy and complication rates between black and white women even when accounting for confounding patient-level factors. Although open surgical approach and complications are associated, this alone does not explain the increased rate of complications experienced by black women. The decreased association between race and complication when route of surgery is adjusted for suggests that increased access to minimally invasive surgery for black women would likely improve disparities in complication rates.

300 - Poster Session

Identifying disparities in germline and somatic testing in patients with ovarian cancer in a university health system

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Objective: Germline mutations are present in approximately 25% of patients with epithelial ovarian cancers, and testing is recommended for these patients. Somatic mutations have been estimated to be 5–7%. Our objective was to assess the disparities in germline and somatic testing for patients treated at a comprehensive cancer center and a safety net hospital.

Method: Patients treated for ovarian cancer at our institution from 2011 to 2016 were included. Abstracted data included sociodemographic factors, genetic testing results, and treatment histories. The Fisher exact and χ^2 tests and logistic regression analysis were used.

Results: Of the cohort, 50.9% of women received germline testing, and 24.4% of women received somatic testing. Women treated at the comprehensive cancer center were significantly more likely to be tested for germline mutations (55.2% vs 39.1%, $P = 0.01$) and somatic mutations (31.9% vs 3.4%, $P < 0.0001$) than those treated at a safety net hospital. Non-Hispanic black patients were less likely to be tested than non-Hispanic white patients for germline mutations (OR = 0.45, 95% CI 0.21–0.95, $P = 0.037$). Hispanic women were less likely to have germline testing performed compared to non-Hispanic white patients, although the difference was not significant. Patients with Medicare/Medicaid were less likely to receive germline testing (OR = 0.50, 95% CI 0.32–0.80, $P = 0.004$) and somatic testing (OR = 0.36, 95% CI 0.18–0.71, $P < 0.001$) than those privately insured. Testing rates increased significantly with recurrence versus those who had received only primary treatment for both germline (OR = 2.46, 95% CI 1.49–4.05, $P < 0.001$) and somatic (OR = 5.74, 95% CI 2.39–13.77, $P < 0.001$) mutations.

Conclusion: Disparities in germline and somatic testing among different ethnic backgrounds exist at both a public safety net hospital and a comprehensive cancer center. Identifying and overcoming barriers to testing is critical and may improve cancer-related mortality by allowing for more tailored treatments.

301 - Poster Session

Endometrial cancer survival outcomes differ by geographical region

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Objective: To determine whether treatment in different geographical regions in the United States has an impact on overall survival (OS) in endometrial cancer patients.

Method: Using the Surveillance, Epidemiology, and End Results (SEER)/Medicare database from 1999 to 2011, we identified stage I–III endometrial cancer patients who underwent primary surgical treatment with hysterectomy for endometrioid (EAC), serous (USC), clear cell (UCC), and carcinosarcoma (MMMT). Demographic, surgical staging, pathology, type of adjuvant treatment (radiation and chemotherapy), and survival outcomes were collected. Treatment location was defined by SEER/Medicare into the following regions: Northeast, Midwest, South, and West. Descriptive, Kaplan-Meier curves, and Cox modeling were used to assess impact on OS.

Results: OS by region was compared individually for stage I–III endometrial cancer for the four histologies. In unadjusted analyses, significant differences in OS were found in patients with stage I EAC ($n = 12,945$), stage II EAC ($n = 846$), stage III MMT ($n = 257$), and stage III USC ($n = 485$). After controlling for age, race, type of adjuvant treatment, Charlson score, and FIGO grade, differences in OS for stage I and stage II EAC and stage III USC were significant. For all, patients in the South had worse outcomes compared to the Northeast with risk of death 1.2 times in stage I EAC (95% CI 1.12–1.38, $P < 0.01$), 1.6 times in stage II EAC (95% CI 1.18–2.20, $P < 0.01$), and 1.5 times in stage III USC. In addition, for stage I and II EAC (95% CI 1.06–2.12, $P = 0.02$), OS in the West was worse with risk of death 1.1 times (95% CI 1.02–1.21, $P = 0.02$) and 1.3 times (95% CI 1.01–1.75, $P = 0.04$), respectively. Overall, the Northeast administered more adjuvant treatment; there were more blacks in the South; Charlson scores were better for stage I EAC in the West; and the West had a slightly higher portion of substage 1A EAC.

Conclusion: In the United States, patients who underwent endometrial cancer treatment in the South and West had worse OS compared to the Northeast for stage I and stage II endometrioid, and the South had worse survival for stage III serous endometrial cancer even after controlling for age, race, Charlson score, grade, and receipt of and type of adjuvant treatment. Further investigation should be performed to better understand this geographic disparity.

302 - Poster Session

Patient profile, patterns of care, and mortality among Asian and white women with uterine cancer

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Objective: Immigration of Asian women to the United States has increased substantially. However, little is known about the incidence and outcomes of uterine cancer in this population. We examined the patterns of care and outcomes of Asian women compared to white women with uterine cancer.

Method: The National Cancer Data Base was used to identify Asian and white women with uterine cancer diagnosed from 2004 to 2014. Clinical and demographic characteristics and patterns of care were compared between the two groups. Multivariable proportional hazards models were developed to examine differences in survival.

Results: A total of 7,799 Asian and 238,697 white women were identified. Compared to white women, Asian patients were younger at diagnosis, had fewer comorbid conditions, more often had nonendometrioid and high-grade tumors, and more frequently presented with stage III–IV disease ($P < 0.05$ for all). Asian women were more likely to receive chemotherapy (72.3% vs 64.8%) for stage III–IV tumors and often underwent lymphadenectomy (71.1% vs 66.1%) for stage I–IIIC disease ($P < 0.05$ for both). Multivariable models indicated that Asian women with early-stage tumors had a 29% (HR = 0.71, 95% CI 0.63–0.80) lower mortality rate compared with white women, as well as a 15% reduction in mortality (HR = 0.85, 95% CI 0.74–0.97) for advanced-stage neoplasms. Five-year adjusted survival for early-stage tumors was 91.6% (95% CI 90.7%–92.5%) for Asian women versus 89.0% (95% CI 88.8%–89.2%) for white women and for advanced-stage tumors 52.3% (95% CI 49.6%–55.1%) and 47.8% (95% CI 47.1%–48.4%), respectively. Survival disparity was also observed across Asian nativity. Chinese women had a more favorable prognosis, and Filipino patients were at increased risk of death.

Conclusion: Asian women with uterine cancer are diagnosed at a younger age and have more aggressive tumors than their white counterparts. Despite these negative prognostic factors, Asian women have a more favorable prognosis and improved survival compared to white patients.

303 - Poster Session

Racial disparities in incidence and mortality in adenocarcinoma or adenosquamous carcinoma compared with squamous cell carcinoma of the cervix

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Objective: Incidence of adenocarcinoma (AC) and adenosquamous carcinoma (ASC) of the cervix appears to be rising, and these histologic subtypes seem to be less likely to respond to standard of care treatment. This study evaluated racial disparities in trends in the proportion of AC/ASC and in cancer-related mortality (CRM) and noncancer mortality (NCM) in AC/ASC compared with squamous cell carcinomas (SCC) of the cervix.

Method: Data were evaluated from the 18-region Surveillance, Epidemiology and End Results registry for women with a diagnosis of AC/ASC or SCC of the cervix between 1990 and 2014. The proportion of patients with AC/ASC was compared over 5-year increments in patients who self-designated to be non-Hispanic white, non-Hispanic black, Hispanic, or Asian/Pacific Islander. CRM and NCM were estimated using Fine and Gray's subdistribution hazard modeling with adjustments for age, race, and stage in AC/ASC or SCC in non-Hispanic black, Hispanic, or Asian/Pacific Islander patients relative to non-Hispanic white patients.

Results: There were 62,887 evaluable patients including 16,645 with AC/ASC and 46,242 with SCC. The racial breakdown was 54.8% non-Hispanic white, 13.8% non-Hispanic black, 22.2% Hispanic, and 9.2% Asian/Pacific Islander. Figure 1A illustrates the incremental increase in proportion of cervical cancer patients with AC/ASC in 5-year periods between 2000 and 2014 in the non-Hispanic white, Hispanic, and Asian/Pacific Islander racial groups ($P < 0.0001$) with a more modest trend in non-Hispanic black patients during this time. Non-Hispanic black (HR = 1.39, 95% CI 1.24–1.55) and Asian/Pacific Islander (HR = 1.12, 95% CI 1.01–1.26) patients had worse CRM than non-Hispanic white patients with AC/ASC of the cervix (Figure 1B). Among those with SCC of the cervix, non-Hispanic black patients had worse CRM (HR = 1.17, 95% CI 1.11–1.23), whereas Hispanic (HR = 0.80, 95% CI 0.77–0.83) and Asian/Pacific Islander (HR = 0.69, 95% CI 0.64–0.74) patients had better CRM than non-Hispanic white patients (Figure 1B). Non-Hispanic black patients with AC/ASC (Figure 1D) also had worse NCM (HR = 1.38, 95% CI 1.16–1.65). NCM in patients with SCC (Figure 1E), however, was worse in non-Hispanic black (HR = 1.22, 95% CI 1.13–1.31) and better in Asian/Pacific Islander (HR = 0.75, 95% CI 0.68–0.83) patients.

Conclusion: The prevalence of AC/ASC in non-Hispanic white, Hispanic, and Asian/Pacific Islander patients has risen incrementally from 1990 to 2014. Relative to non-Hispanic white patients, CRM and NCM were worse in non-Hispanic black patients with AC/ASC than SCC. In Asian/Pacific Islander patients the relationship was mixed with worse CRM in SC/ASC and improved CRM in SCC. CRM was better in Hispanic patients with SCC but not AC/ASC.

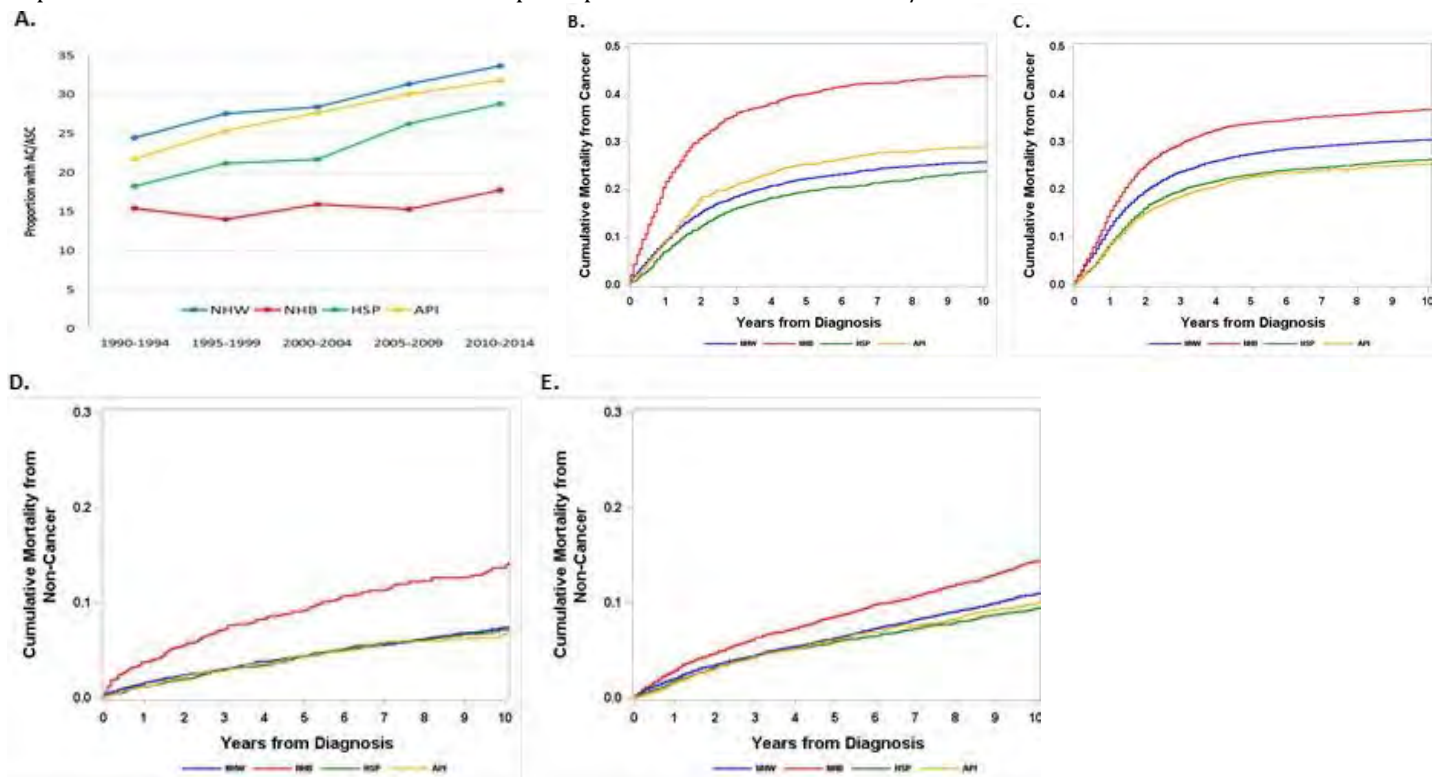


Fig. 1. The proportion of non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic (HSP) or Asian/Pacific Islander (API) patients with adenocarcinoma (AC) or adenosquamous carcinoma (ASC) of the cervix in five-year increments between 1990 and 2014 (A). Cumulative cancer-related mortality in NHW, NHB, HSP or API patients with AC/ASC (B) or in squamous

cell carcinoma (C). Cumulative non-cancer mortality in NHW, NHB, HSP or API patients with AC/ASC (D) or in squamous cell carcinoma (E).

304 - Poster Session

Factors associated with the access and use of a high-volume cancer center by black women with ovarian cancer: A qualitative study

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Objective: Disparities between population subgroups exist in the utilization of gynecologic oncologists and high-volume hospitals. The objective of this study was to explore the experiences of black women obtaining ovarian cancer (OC) care at a high-volume center (HVC) and to identify the patient, provider, and systems-related factors that play a role in accessing and utilizing this level of care.

Method: In this formative qualitative research study, 22 one-on-one semistructured interviews were conducted as part of an institutional review board-approved protocol with women who had been treated for OC and self-identified as black or African-American at a single HVC institution from January 2013 to May 2017. The interviews were transcribed, and recurring themes were identified through the process of independent and collaborative thematic content analysis.

Results: Qualitative analysis identified 5 primary themes: (1) internal attributes that contributed to black women's ability/desire to be treated at an HVC, (2) pathways to high- and low-volume centers, (3) obstacles to obtaining care at an HVC, (4) potential barriers for other black women to be treated at an HVC, and (5) suggestions to improve HVC utilization by black women. Black women successful at accessing care at the HVC were comfortable navigating the health care system, knew the importance of self-advocacy, and valued the expertise of a comprehensive cancer center. Those who did not possess these attributes were connected to someone who did, either a diagnosing physician or member of their social network. Barriers to utilizing care at an HVC included a lack of knowledge of the HVC, lack of referral, difficulty travelling, and insurance coverage.

Conclusion: In this qualitative study of factors associated with access to ovarian cancer care, we found black women treated at an HVC shared attributes and experiences that likely helped them successfully access care at an HVC. Based on themes identified in this study, there is a need for collaboration with black communities and interventions to reduce barriers and disseminate information about the importance of receiving ovarian cancer care at an HVC.

305 - Poster Session

Survival disparities for black race persist despite treatment at high-volume centers for ovarian cancer

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Objective: To investigate whether survival disparities persist for black women with ovarian cancer who receive multiagent chemotherapy (MAC) and surgery when treated at high-volume centers throughout the United States.

Method: Women with stage II–IV high-grade serous ovarian cancer treated with MAC and cytoreductive surgery between 1998 and 2013 were identified using the National Cancer Data Base (NCDB). All women received care at high-volume centers (more than 20 ovarian cancer surgeries/year). The primary outcome was overall survival (OS). The effect of race on OS was estimated using the method of Kaplan-Meier. Multivariable Cox proportional hazards regression models tested associations of race and survival.

Results: We identified 8,798 women treated for ovarian cancer at high-volume centers with 4,571 deaths. White women ($n = 7,458$, 85%) accounted for the majority of the cohort with a smaller number of patients of other races: black ($n = 559$, 6.4%), Hispanic ($n = 389$, 6.3%), others ($n = 272$, 4.4%), and unknown ($n = 120$, 3.6%). White patients were more likely than black patients to have private insurance ($n = 4,091$, 54.9%, vs $n = 242$, 43.3%, $P < 0.001$), receive treatment at an academic center ($n = 4,668$, 62.6%, vs $n = 317$, 56.7%, $P < 0.001$), present with stage III disease ($n = 4,567$, 60.8%, vs $n = 312$, 55.8%, $P < 0.001$), and undergo primary debulking surgery ($n = 5,406$, 72.5%, vs $n = 380$, 68%, $P < 0.001$). Black race was associated with decreased median OS (43.1 months, 95% CI 39.5–51, vs 52.9 months, 95% CI 50.9–54.2; HR = 1.15, 95% CI 1.02–1.3081).

Survival disparities increased when the cohort was further limited to patients treated at high-volume academic centers (HR =1.33, 95% CI 1.13–1.56) for black race.

Conclusion: After adjusting for confounding factors and limiting our cohort to patients who received consistent cancer care, black race was associated with increased hazard of death. Further investigation into the factors driving these disparities, including tumor biology, is warranted.

306 - Poster Session

Evidence of provider implicit bias toward women with cervical cancer: A study of physicians and nurses caring for gynecologic oncology patients

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Objective: Implicit prejudice and stereotyping may operate in health care providers automatically without awareness or intentions by the perceiver. These biases can then correlate with outcomes that may be consequential for the patient. This project examined 2 forms of implicit bias towards cervical versus ovarian cancer among gynecologic oncology medical care providers.

Method: Participants were recruited through the SGO listserv and regional internet searches. Physicians, trainees (residents, fellows), nurse practitioners, and nurses then participated in an anonymous online survey. The Implicit Association Test (IAT) was used to assess implicit stereotypes and prejudice. The prejudice IAT measured how quickly participants associated cervical cancer with anger and ovarian cancer with empathy. The stereotype IAT measured how quickly participants associated cervical cancer with risk and ovarian cancer with compliance. Linear models and Student t tests were used to examine average levels of implicit bias as well as moderators of the implicit bias effects.

Results: A total of 176 (132 female, 43 male, 1 nonresponse; $M_{age} = 39.18 \pm 10.58$ years) providers were recruited. Respondents demonstrated evidence of implicit prejudice ($M = 0.17 \pm 0.47$) by more quickly associating cervical cancer with anger and ovarian cancer with empathy. They also expressed implicit stereotyping ($M = 0.15 \pm 0.42$) by more quickly associating cervical cancer with risk and ovarian cancer with compliance. Nurses demonstrated greater implicit bias than did physicians ($P < 0.01$), and individuals without cultural competency training demonstrated greater bias than those who had completed such training ($P < 0.05$). White providers demonstrated greater implicit prejudice than non-white providers ($P < 0.01$). Older and more experienced providers demonstrated higher levels of implicit bias ($P < 0.05$).

Conclusion: This research provides the first evidence that medical providers hold implicit biases related to cervical cancer. Interventions may benefit by targeting particular types of health care providers, including majority group nurses, older providers, and providers who have been practicing for a longer amount of time.

307 - Poster Session

Sexual dysfunction disparities in ethnically/racially diverse women with history of gynecologic malignancies

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Objective: To prospectively identify the prevalence of sexual dysfunction (SD) in women with gynecologic malignancies and evaluate the association of sexual function with race, ethnicity, and treatment modality—surgery, chemotherapy, radiation, or combination therapy.

Method: After institutional review board approval, women with gynecologic malignancies (uterine, cervical, vaginal, or vulvar) were consented to fill out a one-time validated survey, the Female Sexual Function Index (FSFI), to assess sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. Prevalence of SD was estimated, and its association with demographic and clinical covariates was analyzed using χ^2 and t tests (Wicxon rank sum test) and multivariable logistic regression.

Results: Among the 155 participants, 49% had SD. The majority of our participants identify as non-white, 35% as black, and 40% as other (which includes Hispanic and Asian). Our patients were significantly more likely to have SD if they reported not currently having a partner (66% vs 19%, $P < 0.0001$). Abstinence within 6 months of cancer diagnosis was associated with an increase in SD (74% vs 28%, $P < 0.0001$). Black women were 3 times more likely to have SD than white women (OR = 3.877, 95% CI 1.054–14.269). Participants who identified their race as other did not have an increase in SD (OR = 0.556, 95% CI 0.095–3.260). Hispanic ethnicity was not associated with SD (OR = 2.259, 95% CI 0.605–8.433). While chemotherapy and radiation did not have a significant association with SD in our cohort (OR = 1.696, 95% CI 0.696–4.134), if patients received surgery and adjuvant radiation/chemotherapy, there was an increase in sexual dysfunction (OR = 3.473, 95% CI 1.216–9.922). See Figure 1.

Conclusion: Our study highlights the significant rates of SD in women with gynecologic cancers, specifically in our diverse patient population. Black women were significantly more likely to suffer from SD. Further research will explore interventions to improve sexual function in women with gynecologic malignancies.

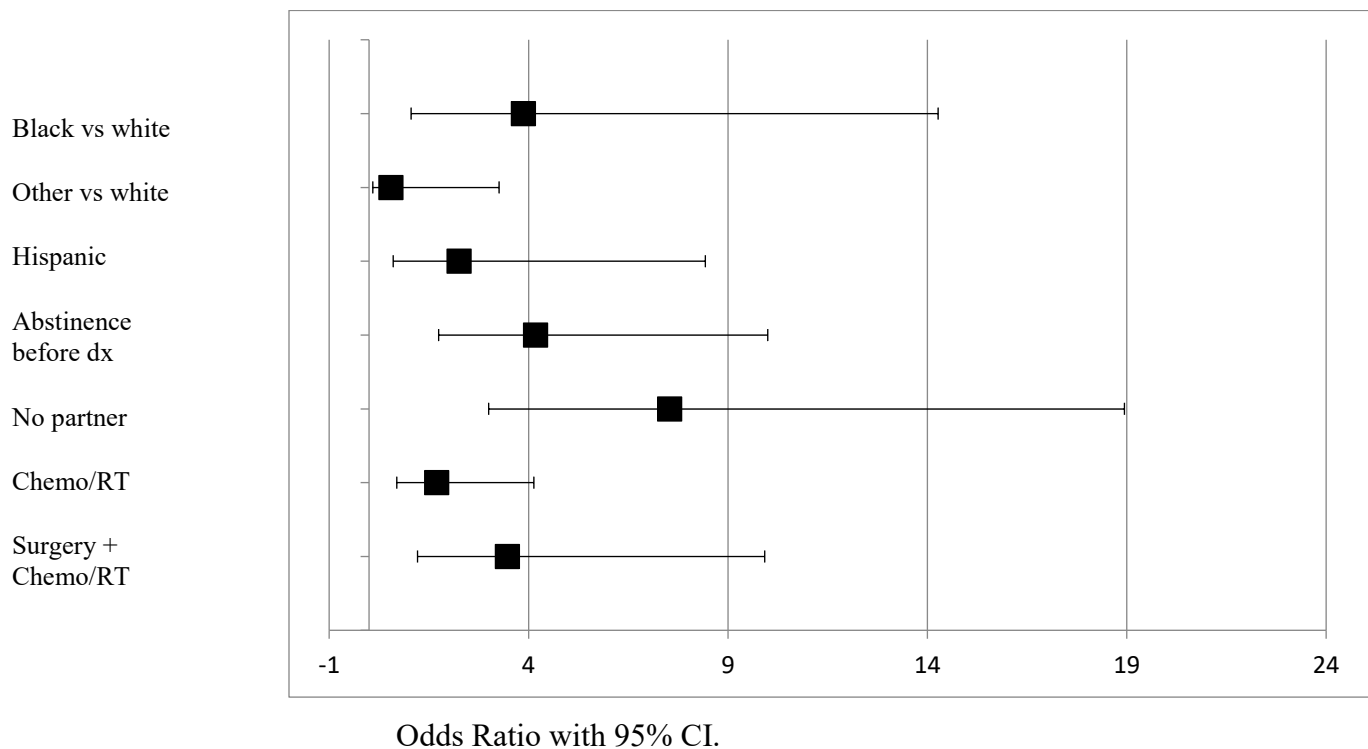


Fig. 1. Multivariate logistic regression model assessing predictors of sexual dysfunction.

308 - Poster Session

Disparities in cervical cancer screening by unmet basic needs: A randomized controlled trial comparing strategies for successful Pap referral

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Objective: Interventions to improve disparate rates of cervical cancer screening are critical. We aimed to assess need for Pap test among women with unmet basic need(s) and best approaches to facilitating referral.

Method: We analyzed data from women who enrolled from 2010 to 2012 in a randomized controlled trial of low-income callers to Missouri 2-1-1, a helpline providing referrals to local health/social services. Basic needs (safety, housing, family, financial) were assessed and were considered unmet if very unlikely or unlikely to be resolved in the next month. Need for cervical cancer screening was assessed. Callers were randomized to 1 of 3 arms to assist with Pap referral: verbal referral only, verbal referral and tailored print reminder, or verbal referral and navigator. Primary outcome was contact for cervical cancer screening referral 1 month postintervention. Data were analyzed using χ^2 tests.

Results: Among 933 women callers, 211 (23%) needed cervical screening. Mean age was 43.5 years; 50% were African-American; 56% had less than high school education; 45% were uninsured; and 187 (88%) rated their health as poor or fair. Most common basic needs included financial (838, 90%) and family needs like food, clothing, and household goods (654, 70%). Frequency of unmet basic needs was high: 438 (47%) had 3+, 313 (34%) had 2; 132 (14%) had 1; and 49 (5%) had no needs. Across these strata, women in the navigator arm had the highest rate of contacting a health referral for cervical screening. This benefit was most apparent among women with 1 need (navigator vs verbal referral, OR = 5.43, 95% CI 1.39–21; tailored reminder vs verbal referral, OR = 4.56, 95% CI 1.20–17.27). Women with 2 or 3+ needs were twice as likely to call a referral for cervical screening if exposed to the navigator compared to verbal referral or tailored reminder (Table 1). Likelihood of contacting a health referral for a Pap test was not influenced by age, race, education, insurance status, self-perception of health, or number of unmet basic need(s).

Conclusion: Low-income women who seek assistance with basic needs often lack cervical cancer screening. Navigator interventions or tailored reminders are effective strategies that can facilitate referral.

Table 1. Contacted referral for cervical cancer screening at 1-month follow-up by number of unmet basic needs among women eligible for a Pap test.

Unmet Basic Needs	Contacted a referral, n (%)					OR (95% CI)		
	All	Verbal Referral	Tailored Reminder	Navigator	χ^2 P value	Tailored Reminder vs. Verbal Referral	Navigator vs. Verbal Referral	Navigator vs. Tailored Reminder
1 unmet basic need (n = 132; 15%)	27 (21)	3 (7)	13 (26)	11 (29)	0.02	4.56 (1.20-17.27)	5.43 (1.39-21.31)	1.19 (0.46-3.06)
2 unmet basic needs (n = 313; 35%)	83 (27)	25 (23)	21 (21)	37 (36)	0.02	0.91 (0.48-1.76)	1.96 (1.07-3.57)	2.14 (1.14-4.01)
3+ unmet basic needs (n = 438; 50%)	111 (25)	26 (18)	35 (24)	50 (5)	<0.01	1.45 (0.82-2.57)	2.48 (1.44-4.28)	1.70 (1.02-2.84)

309 - Poster Session

Disparities in time to treatment among cervical cancer patients receiving primary radiation treatment: A National Cancer Data Base analysis

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Objective: In cervical cancer, treatment delays can lead to worse outcomes. In this study, we aim to identify sociodemographic variables that affect time to initiation of radiation therapy in patients with cervical cancer.

Method: The National Cancer Database includes 8,939 cases from 2004 to 2013 of cervical cancer patients primarily treated with radiation. Time to radiation (TTR) was defined as the interval between diagnosis and treatment initiation. Log rank tests were used to compare sociodemographic variables—race, income, and insurance—to look for differences in time to radiation. Cox proportional hazards models were fit to estimate the effect of race, income, and insurance type on survival, while controlling for age, facility type, location, stage, geographic region, distance, and Charlson-Deyo score.

Results: The median TTR among all patients was 1.12 months. In univariate analyses, race was significantly associated with time to radiation ($P < 0.001$) with Hispanic patients having longest TTR, followed by black patients, others, and white patients. Lower income ($< \$38,000$) was significantly associated with a longer TTR ($P = 0.04$). There was no impact of insurance type on time to radiation. In multivariable analyses, race continued to show an impact on TTR with Hispanic and black patients having significantly longer TTR than white patients ($P = 0.01$). Patients in the lowest income bracket ($< \$38,000$) had the longest TTR ($P = 0.007$), and patients with government insurance had significantly longer TTR than those with private insurance ($P = 0.01$). See Table 1.

Conclusion: Wait time to treatment initiation is emerging as a new health indicator. Race, lower income, and government insurance confer a longer wait time to initiation of radiation treatment in patients with cervical cancer. These findings could represent issues of access to care. The next step is to understand why patients in lower income brackets, patients with

government insurance, and Hispanic and black patients have longer wait times to radiation treatment in order to direct efforts at addressing these disparities to care.

Table 1. Adjusted hazard ratios for initiation of radiation therapy. Hazard ratios were estimated using Cox proportional hazards models adjusting for age, facility type, location, stage, geographic region, distance, and Charlson-Deyo score.

Parameter	Adjusted Hazard Ratio (HR)	95% CI	P Value
Insurance Type			
Government versus private	0.91	(0.85–0.97) ^a	0.0116
No insurance versus private	0.97	(0.87–1.07)	
Median Income Quartiles			0.0072
\$38,000–\$47,999 versus <\$38,000	1.01	(0.94–1.08)	
\$48,000–\$62,999 versus <\$38,000	1.12	(1.04–1.21) ^a	
>\$63,000 versus <\$38,000	1.09	(1.00–1.18) ^a	
Race			0.0100
Non-Hispanic black versus non-Hispanic white	0.91	(0.85–0.97) ^a	
Hispanic versus non-Hispanic white	0.89	(0.82–0.98) ^a	
Other versus non-Hispanic white	1.00	(0.88–1.13)	

^aConfidence interval does not include 1.

310 - Poster Session

Geographic information system (GIS) analysis of food deserts in the southern United States and endometrial cancer recurrence

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Objective: To evaluate the association between USDA "food deserts" and endometrial cancer recurrence.

Method: This was a retrospective cohort study of all women treated for endometrial cancer between 2009 and 2013 at a tertiary referral center. The primary exposure variable was living in a food desert with low income and low access to healthy food. Low income was defined as a poverty rate greater than 20% or median family income less than 80% of the local median. Low access was defined as living one-half mile for urban and 10 miles for rural communities from a supermarket or fresh-food purveyor ascertained using the USDA Economic Research Service (ERS) Food Access Research Atlas and 2010 Decennial Census data. Patient food desert status was evaluated by matching her address with food desert areas in a geographic information system (GIS) model. The primary outcome was endometrial cancer recurrence. Time to recurrence was evaluated using the Kaplan-Meier method with log rank test. A competing risks regression model was used to adjust for potential confounders.

Results: In total, 689 women were included in the study, 26.1% of whom were living in food deserts (Figure 1). Most had endometrioid adenocarcinoma (79.6%) and stage I disease (72.2%), and 27.7% were African-American. African-Americans were almost twice as likely (40.3%) to live in food deserts as non-African-Americans (20.6%). Median follow-up time was 47 (range 1–123) months. Within 24 months, 14.3% ($n = 99$) had recurrent cancer, of these 64.6% ($n = 64$) were living in food deserts. A total of 21.8% ($n = 150$) had recurrence, of these 36.0% ($n = 54$) lived in food deserts. In our cohort, living in food deserts was associated with shorter time to recurrence and a 50% increase in the risk of endometrial cancer recurrence in our patient population (sHR = 1.53, 95% CI 1.06–2.21, $P = 0.02$) when adjusting for age, BMI, cancer histology, and stage using a

competing risk model. When also adjusting for race, however, this association is no longer significant (HR = 1.41, 95% CI 0.97–2.05, $P = 0.07$), suggesting that the effect of living in a food desert is mediated by African-American race.

Conclusion: Living in food deserts is associated with increased risk of endometrial cancer recurrence in our regional patient population. Continuing efforts to address food disparities may improve endometrial cancer survival.

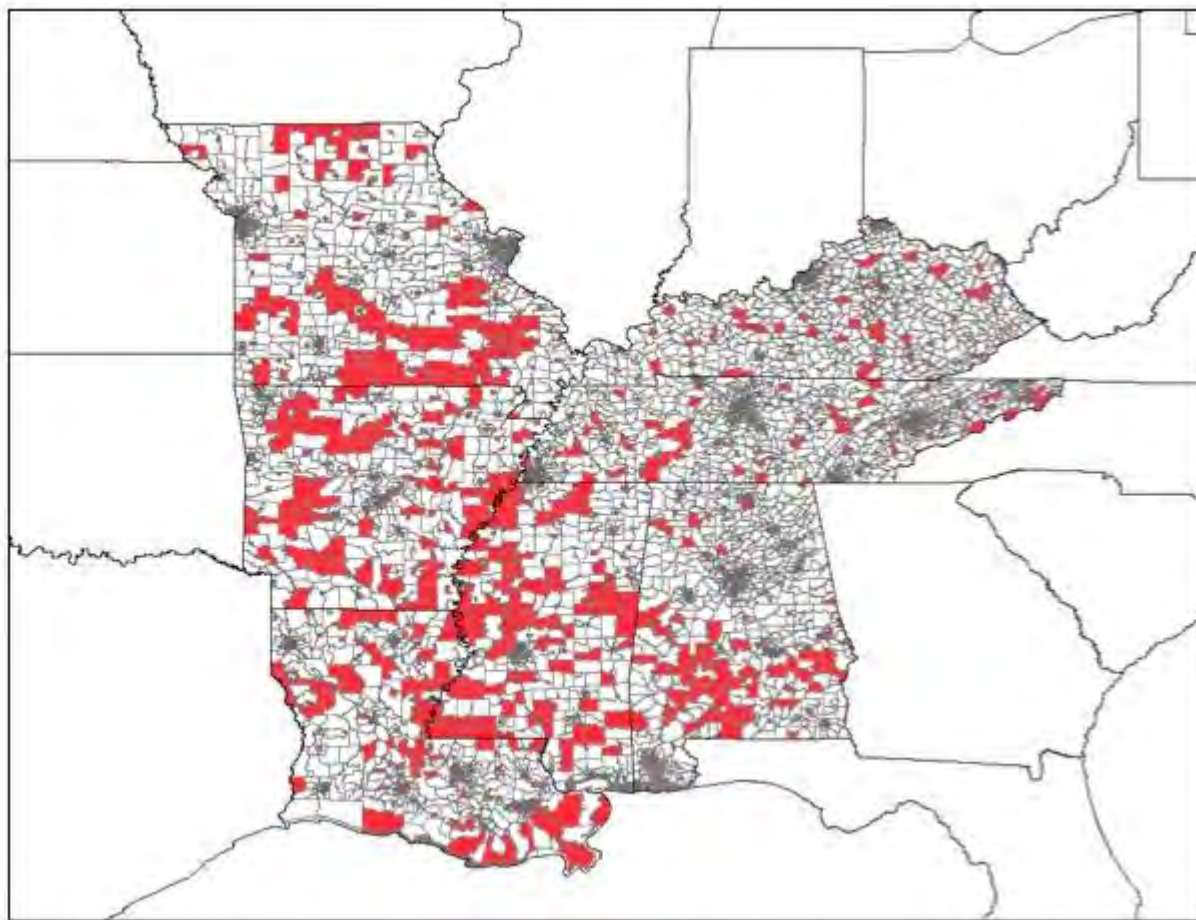


Fig. 1. Census tracts designated as Food Deserts by the USDA, with high poverty and limited access to healthy, affordable food.

311 - Poster Session

Age and race alter the risk of uterine serous carcinoma among breast cancer survivors

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Objective: To evaluate the influence of age and race on risk of uterine serous carcinoma (USC) among breast cancer survivors.

Method: The Surveillance, Epidemiology, and End Results (SEER-9) database was queried to identify women registered from 1973 to 2014 with breast and endometrial cancers. Multiple Primary-Standardized Incidence Rates were calculated and compared, and the influence of age and race was investigated.

Results: The study population consisted of 673,385 women with breast cancer and 144,542 women with endometrial cancer. The risk of subsequent endometrial cancer (all histologies) among breast cancer survivors was elevated compared to the general population (O/E = 2.78, 95% CI 2.69–2.87). Among the 77,322 endometrial cancer patients for whom cell type was known, 4,233 (7%) had serous histology. There were 508 women with USC who previously had breast cancer. The risk of USC in breast cancer survivors was elevated nearly 4 times compared to the general population (O/E = 3.7, 95% CI 3.4–4.1.)

Among breast cancer survivors developing USC, the average age at diagnosis of breast cancer was 61 years and the average age of diagnosis of USC was 72 years; the mean person-years at risk for the entire population was 10. Compared to the general population, the risk of USC among breast cancer survivors who were ≤ 51 years old at the time of breast cancer diagnosis was elevated nearly 5 times (O/E = 4.5, 95% CI 3.6–5.4), and the risk of USC among black patients was elevated nearly 7 times (O/E = 6.8, 95% CI 5.2–8.8). Among young, black breast cancer survivors, the risk of serous endometrial cancer was elevated more than 8-fold (O/E = 8.2, 95% CI 4.4–14.0).

Conclusion: This population-based study confirms previous reports of a disproportionately elevated risk of USC among breast cancer survivors. Moreover, we find that, individually and in combination, black race and younger age significantly further increase risk. Further investigations are warranted to better understand the mechanism of greatly increased predilection to this type II, nonestrogen-dependent, endometrial malignancy.

312 - Poster Session

Self-reported race is the greatest limitation in racial disparity research: A comprehensive genetic analysis in ovarian cancer patients

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Objective: Despite controlling for differences in clinical features, treatment, and environmental factors, a survival disadvantage remains in black patients with ovarian cancer. This project was performed to determine the effect of the definition of race on genetic analyses.

Method: Self-reported (SR) black and white patients with ovarian cancer (OC) were matched for age, stage, and survival. Racial genetic admixture (RGA) was performed using a custom panel of previously validated SNPs for estimation of ancestry from African, European, and American ancestry. A full genome RNA sequencing library was constructed and sequenced on Illumina HiSeq instrument. Differentially expressed genes were inferred by using DESeq2 software. Candidate gene sets of significantly regulated genes were used for pathway enrichment analyses.

Results: A total of 94 matched patients were included, SR 55% ($n = 52$) white and 45% ($n = 42$) black. SR black patients had mean African RGA of 0.83 (range 0.03–1.0), while SR white patients had mean European RGA of 0.89 (range 0.28–0.99). Survivals were similar between SR groups. However, survival differences were seen when proportion of African RGA was compared. Regardless of SR, patients >0.80 African RGA had lower median PFS than patients <0.80 African RGA (18 vs 23 months, $P = 0.03$). An OS difference of 40 versus 54 months was seen for >0.80 and <0.80 , respectively ($P = 0.008$). Genetic analyses were grouped based on SR, tertiles for African RGA, or continuous African RGA. A total of 4,392 genes demonstrated significant up/down expression across all racial cohorts. The top 40 genes with the greatest 20 upregulated and 20 downregulated log-fold expression for each genetic cohort demonstrated low concordance with only 7 of 120 (5.8%) genes found in all 3 genetic cohorts. In addition, each genetic cohort had 30% ($n = 12$), 47% ($n = 14$), and 63% ($n = 25$) sentinel genes found only in that specific racial cohort for SR, tertiles, and continuous groups, respectively. Subsequent pathway analyses based on gene expression demonstrated low concordance rates among racial cohorts as well. See Figure 1.

Conclusion: Racial genetic admixture for African descent was more predictive of disparate survival in ovarian cancer than self-designated race. In addition, how race was defined had significant differences in global gene expression levels and subsequent molecular pathway analyses. Collectively, these data support the incorporation of racial genetic admixture when evaluating biologic etiologies of racial disparities in cancer.

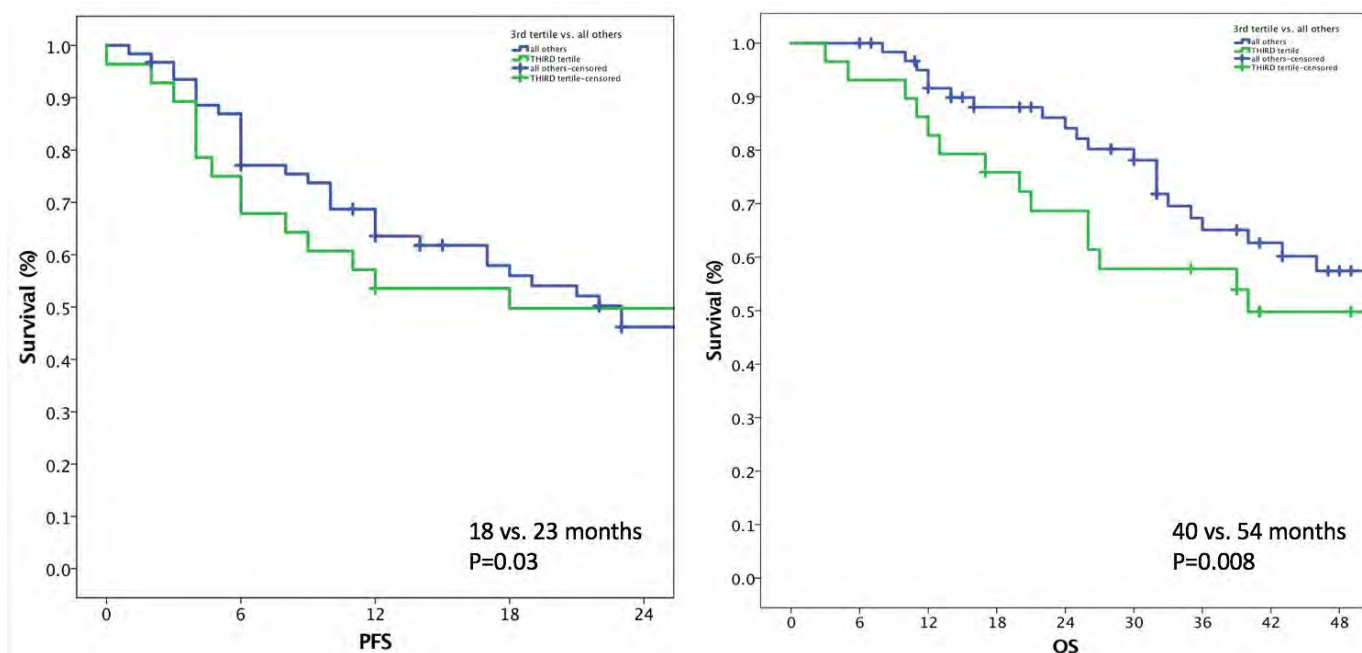


Fig. 1.

313 - Poster Session

Disparities in the use of fertility-sparing surgery among women with stage I ovarian cancer.

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Objective: To investigate the presence of disparities in the use of fertility-sparing surgery (FSS) among premenopausal women diagnosed with stage I ovarian cancer using a multiinstitutional cancer registry.

Method: The National Cancer Data Base was accessed to identify women younger than 40 years diagnosed with a malignant unilateral stage I ovarian tumor between 2004 and 2014. Based on site-specific surgery codes, those who underwent FSS (defined as unilateral salpingo-oophorectomy) and comprehensive (defined as hysterectomy and bilateral salpingo-oophorectomy) surgery were identified. An area-based measure of rurality and urban influence was assessed by using the typology published by the USDA Economic Research Service. Average hospital volume was assessed by dividing the number of eligible patients managed at each reporting site by the number of years with reported data. For analysis purposes, hospital volume was divided into tertiles. Univariate analysis was performed with the χ^2 and Mann-Whitney *U* tests, while multivariate analysis was performed with binary logistic regression.

Results: Among 2,344 patients who met the inclusion criteria, the rate of FSS was 76.3%. Women who underwent FSS were younger compared to those who did not (median age 26 vs 35 years, $P < 0.001$). By univariate analysis, higher rates of FSS were observed among those diagnosed with germ cell (90.2%) and sex-cord stromal (81%) tumors compared to epithelial (61.9%) tumors ($P < 0.001$). Moreover, women residing in areas with a population less than 1 million received FSS (78.5%) more frequently compared to other locations (73.3%) ($P = 0.004$). Higher rates of FSS were also observed among African-American (83.8%), Hispanic (80.2%), and Asian (79.3%) women compared to Caucasian women (73.2%) ($P < 0.001$). However, nonepithelial tumors were more prevalent among African-American (78.4%) and Hispanic women (59.9%) than in Asian (46%) and Caucasian women (48.2%) ($P < 0.001$). Receipt of FSS was not associated with hospital volume ($P = 0.81$), education level ($P = 0.42$), or insurance status ($P = 0.18$). Multivariate analysis identified histology, age, and location, but not race, as independent predictors of FSS receipt.

Conclusion: Premenopausal women with unilateral stage I ovarian cancer residing in large metropolitan areas have a higher likelihood of receiving FSS. Future studies should further explore the causes of this disparity.

314 - Poster Session

Obesity is associated with chemotherapy delay in ovarian cancer patients

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Objective: Ovarian cancer is the leading killer of women among those with gynecologic malignancies in the United States. Treatment often includes surgical debulking followed by platinum-based adjuvant chemotherapy. While there is no clear recommendation for the timing of chemotherapy, there is evidence that a shorter interval from surgery may improve outcomes. With the growing obesity epidemic, surgery has incurred additional risks, and postoperative courses have become more complicated. Our study aimed to determine whether obesity is associated with chemotherapy delay following surgery in patients with ovarian cancer.

Method: A retrospective chart review identified all women treated for ovarian cancer from 2015 to 2017. Demographic information and clinical factors were collected. Bivariate analyses were performed to determine the impact of various factors on the interval from surgery to chemotherapy. A multivariable analysis was performed to control for confounding variables.

Results: A total of 110 patients were included in the analyses; 39 (35.5%) received chemotherapy within 28 days (9–28 days), while 71 (64.5%) received chemotherapy after 28 days (29–97 days). The median BMI was 27 kg/m² (18–48 kg/m²). On bivariate analysis, increasing BMI was significantly associated with chemotherapy delay ($P < 0.005$). The rate of superficial wound infection trended to increase in obese patients (OR 3.5, 95% CI 0.83–14.8, $P = 0.06$). There was no relationship between route of surgery, complexity of surgery, or nutritional status and chemotherapy delay. When controlling for comorbid conditions, age, albumin, and smoking status, BMI remained significant with respect to chemotherapy delay.

Conclusion: Obesity is associated with a delay in the interval from surgery to first adjuvant chemotherapy. For every 2 point increase in BMI, chemotherapy was delayed by 1.2 days. The rate of superficial wound infection trended to be significant in patients with BMI >30, which could explain treatment delay in obese patients. It is imperative in obese patients who are high risk for wound complications to make efforts to modify that risk to prevent chemotherapy delay.

315 - Poster Session

Treat and release emergency department utilization by patients with gynecologic cancers: National estimates and trends

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Objective: While 17% of cancer patients use the emergency department (ED) annually, many are evaluated, treated, and discharged home. This study sought to describe the burden of "treat and release" ED utilization by patients with gynecologic cancers in order to identify targets for improved outpatient triage.

Method: The National Emergency Department Sample (NEDS) includes an annual sample of approximately 30 million ED visits. All patients with diagnosis of gynecologic cancer were identified among ED treat and release discharges from 2009 to 2013. Sample weights were utilized to generate national estimates. The Student t test, χ^2 test, and linear regression were used to analyze utilization and costs (2013 US\$).

Results: A total of 38,670 annual treat and release visits by patients with gynecologic cancers were identified between 2009 and 2013. Using sample weights, this extrapolated to a national estimate of 174,912 annual visits (95%CI 174,811–175,012) corresponding to over \$766 million in annual charges, with an average charge of \$4,380 per visit (95%CI \$4,357–4,404). Annual visits increased significantly over time during the 5 years under study. Of all visits by patients with gynecologic cancers, more were for patients with cervical cancer (44.3%) versus ovarian (27.4%) and uterine cancer (24.5%). Patients had a mean of 2.57 chronic conditions, and more chronic conditions were significantly associated with higher charges. The most common primary diagnoses were abdominal pain (10.4%), chest pain (6.1%), and urinary tract infection (5.2%). The most frequent diagnostics were bacterial culture, CT scan, and X-ray, and most frequent invasive procedures were incision/drainage/suture, transfusion, and paracentesis. Visits were no more frequent on weekends than weekdays, but had \$254 less in adjusted average charges. Medicare or Medicaid was the primary payer for 59.6% of charges.

Conclusion: Patients with gynecologic cancers are frequently evaluated and discharged from the ED, often with ambulatory issues, and the diagnostic tests and therapeutic procedures that are often used could be more cheaply provided in the clinic setting. The majority of these costs are borne by government payers. Although less prevalent overall, patients with ovarian and cervical cancer represent a higher proportion of these ED visits than patients with uterine cancer.

Table 1. National estimates¹ for treat and release Emergency Department visits for patients with gynecologic cancers, by cancer, 2009-2013.

	Ovarian ¹	Uterine	Cervical	Vulvar/Vaginal	Overall ²
Sample Frequency Visits	53,081	47,216	85,734	12,928	193,349
<i>Total</i>	239,461	214,608	387,170	58,800	874,560
<i>Annual</i>	47,892	42,921	77,434	11,760	174,912
Charges					
<i>Total</i>	\$1.10 billion	\$1.05 billion	\$1.53 billion	\$259 million	\$3.83 billion
<i>Annual</i>	\$220 million	\$210 million	\$306 million	\$51.8 million	\$766 million
<i>Mean per visit</i>	\$4,584	\$4,876	\$3,954	\$4,404	\$4,380
Patient Profile (mean)					
<i>Age</i>	56.3	61.5	45.0	60.4	53.1
<i>Comorbidities</i>	2.49	3.06	2.32	2.93	2.57
<i>Procedures</i>	6.83	6.85	6.33	6.66	6.62
Primary Diagnosis, by Overall Frequency (% , rank)					
<i>Abdominal Pain</i>	11.8%, #1	8.9%, #1	10.9%, #1	8.0%, #1	10.4%, #1
<i>Chest Pain</i>	5.9%, #2	7.3%, #2	5.6%, #3	6.0%, #2	6.1%, #2
<i>Urinary Tract Infection</i>	4.3%, #3	5.0%, #3	5.7%, #2	5.6%, #3	5.2%, #3
<i>Back/spine disorder</i>	3.3%, #6	3.7%, #4	4.3%, #4	3.4%, #4	3.8%, #4
<i>Headache</i>	3.3%, #5	2.7%, #6	4.1%, #5	2.6%, #11	2.6%, #5

¹ Includes fallopian tube and primary peritoneal cancers

² Not exact sum or mean of row due to patients with multiple primary cancers ($n = 384$, estimated 1,777 visits over 2009-2013)

316 - Poster Session

The potential for reporting bias in the upfront treatment of ovarian cancer and the continued case for 'denominator data': An MSK team ovary project

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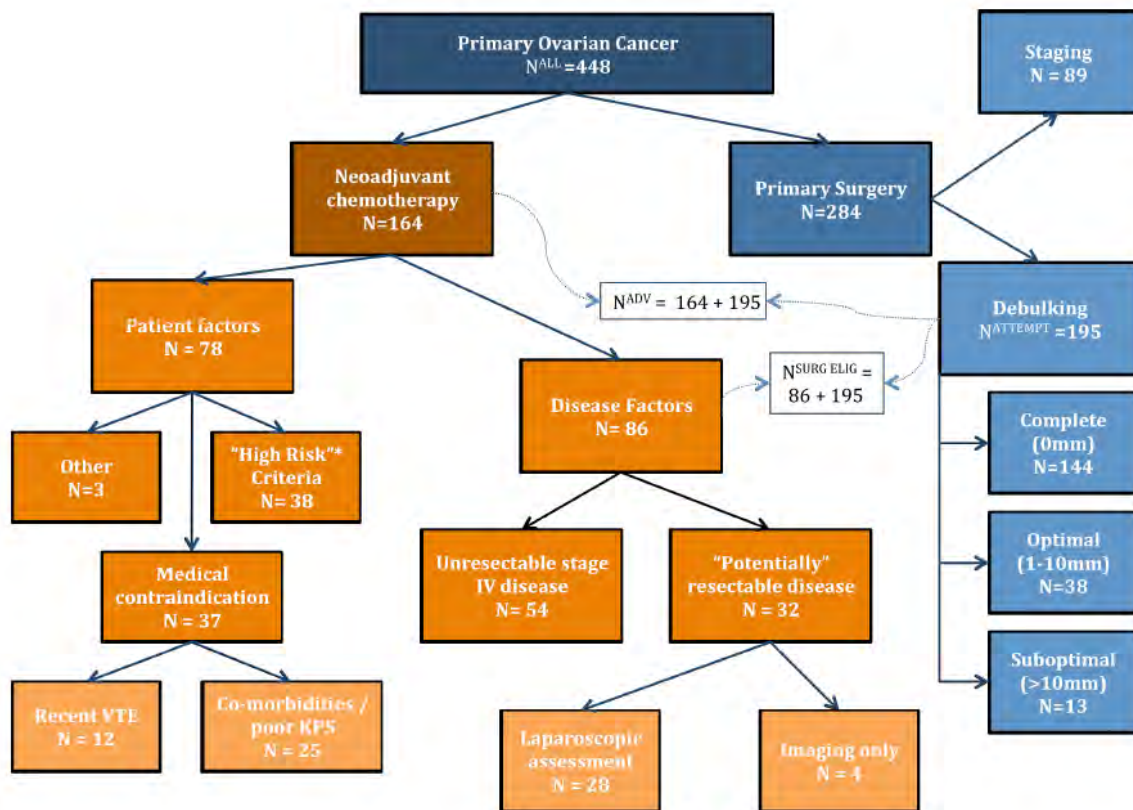
Objective: Published work has demonstrated the importance of reporting "denominator data" in ovarian cancer (OC) research. Our objective was to comprehensively characterize a cohort of patients with OC and evaluate the potential for reporting bias in neoadjuvant chemotherapy (NACT) rates and primary debulking surgery (PDS) outcomes.

Method: All new visits to the gynecology medical and surgical services were prospectively screened. All patients with ovarian-related complaints were categorized prospectively and followed through treatment. To determine NACT rates and PDS outcomes, patients were excluded if they sought a second opinion only, transferred care mid-treatment, or presented with recurrent OC. NACT rates were examined using 3 different denominators: all OC (^{ALL}), advanced OC (^{ADV}), and advanced OC with no medical contraindication to PDS (^{SURG ELIG}). Optimal (OPT) and complete gross resection (CGR) rates were examined using the above 3 denominators in addition to advanced OC with attempt at PDS (^{ATTEMPT}).

Results: From July 2015 to March 2017, 7,690 new visits were screened, and 2,966 patients were included. The patients included had suspected OC, 28%; recurrent OC, 13%; adnexal mass, 35%; hereditary cancer syndrome, 14%; endocrine

ablation, 8%; or other, 2%. In total, 811 patients had pathologically confirmed primary OC: second opinion, 229; transfer of care, 134; and complete care at our institution, 448. Denominators were as follows: N_{ALL} , 448; N_{ADV} , 359; $N_{SURG\ ELIG}$, 281; and $N_{ATTEMPT}$, 195. Rates of NACT were as follows: $NACT_{ALL}$, 36.8%; $NACT_{ADV}$, 45.7%; and $NACT_{SURG\ ELIG}$, 30.6%. Optimal debulking rates were as follows: OPT_{ALL} , 60.5%; OPT_{ADV} , 50.7%; $OPT_{SURG\ ELIG}$, 64.8%; and $OPT_{ATTEMPT}$, 93.3%. CGR rates were as follows: CGR_{ALL} , 32.1%; CGR_{ADV} , 40.1%; $CGR_{SURG\ ELIG}$, 51.2%; and $CGR_{ATTEMPT}$, 73.8%. See Figure 1.

Conclusion: Reported rates of NACT and outcomes of PDS are highly dependent on the denominator used in the calculation. Comprehensive reporting with clearly defined "denominator data" is crucial to interpretation of results and should be considered a quality benchmark in OC research.



^a"High Risk" Criteria = age > 75 years, serum Albumin ≤ 3 or ASA ≥ 3 , and evidence of extensive or stage IV disease.

Fig. 1.

317 - Poster Session

Disparities in the survival trends in epithelial ovarian cancer patients in the United States

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Objective: To identify disparities in the survival trends of ovarian cancer patients in the United States.

Method: Data from 2004 to 2013 were obtained from the National Cancer Database. χ^2 tests and Kaplan-Meier survival methods were employed for statistical analyses.

Results: Of 89,343 epithelial ovarian cancer patients (median age, 61 years, range 18–89 years). The majority were white (84.3%, $n = 75,274$), with 6,011 (6.7%) black, 2,658 (3.0%) Asian, and 4,465 (5.0%) Hispanic. Among the study group, 21,295 (23.8%), 8,490 (9.5%), 40,965 (45.9%), and 18,593 (20.8%) presented with stage I, II, III, and IV cancers, respectively. More than half of these women (50.8%, $n = 45,379$) had private insurance, 3,733 (4.2%) no insurance, 4,927 (5.5%) Medicaid, 3,2618 (36.5%) Medicare, and 2,686 (3.0%) other/unknown insurance. Black patients were more likely to present with more advanced stages at 72.4% compared to only 66.8% white, 54.2% Asian, and 64.6% Hispanics ($P < 0.0001$). Women with higher incomes of $>\$63,000$ were more likely to present with advanced cancers at 33.3% vs. 15.4% with incomes of $<\$38,000$, 22.6% $\$38,000$ – $\$47,999$, and 26.6% $\$48,000$ – $\$62,999$ ($P < 0.0001$). We divided the time into periods of 2004–2008 and 2009–2013 and found that the 5-year overall survival improved from 48.2% to 51.3% ($P < 0.0001$). The survival of younger patients improved from 66.0% to 69.3% and that of older patients, from 43.8% to 47.3%. Although survival improved for the white (48.8% to 50.8%, $P < 0.0001$), Hispanic (55.0% to 61.4%, $P = 0.0005$), and black (37.3% to 43.3%, $P < 0.0001$) patients, Asian patients had the most improvement at nearly 7% (59.9% to 66.6%, $P = 0.0014$) with highest overall survival. Of note, those with no insurance did not have a significant improvement in survival over time (53.7% to 56.4%, $P = 0.21$).

Conclusion: The survival of ovarian cancer patients improved over the 10 years. Black patients were more likely to present with advanced stages and had the least improvement in survival over time. Public health efforts should continue to address these disparities and direct resources to those who need it most.

318 - Poster Session

Gender differences in reasons for lack of HPV vaccination in 2015: Tailoring the cancer-prevention vaccine message

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Objective: HPV vaccination rates in the United States remain below the Healthy People 2020 goal and fall far behind those of other Westernized nations. National routine childhood vaccination recommendations include the HPV vaccine for both boys and girls; however, vaccination rates in boys have consistently been below those in girls. We sought to characterize the differences in reasons for lack of HPV vaccination in adolescent girls and boys living in the United States in 2015.

Method: Provider-verified data from the National Immunization Survey-Teen (NIS-Teen) 2015 were used to calculate survey-weighted prevalence estimates of HPV vaccine initiation among boys and girls aged 13–17 years. Prevalence estimates for parent-reported reasons for lack of initiation were calculated, and survey weighted χ^2 tests were used to compare reasons for lack of vaccination between parents of adolescent boys and girls.

Results: In 2015, 63% of girls had initiated HPV vaccination compared to 50% of boys ($P < 0.001$). The most common reason overall for lack of vaccine initiation was perceived lack of necessity (21% in girls, vs 22% in boys, $P = 0.6$). Both genders also reported lack of knowledge about the vaccine as a common reason (13% in girls, 14% in boys, $P = 0.5$). However, parents of boys were significantly more likely to cite lack of HPV vaccine recommendation from a provider as a reason (19% in boys, 10% in girls, $P < 0.001$), and were less likely to report concerns about safety and side effects (9% in boys, 14% in girls, $P < 0.01$). Only 3% of parents of boys cited gender as their reason for lack of vaccination. Parents of girls were more likely to cite the girls' lack of sexual activity as reason for lack of vaccination (15% in girls, 9% in boys, $P < 0.01$). See Figure 1.

Conclusion: Gender differences in lack of HPV vaccine initiation demonstrate that parents of boys are less likely to report concerns about safety and lack of sexual activity than parents of girls. In addition, parents of boys are more likely to report a lack of provider recommendation. The HPV vaccine message should continue to address the vaccine's necessity and parents' lack of knowledge, and the message should be tailored to address gender-specific parental concerns in order to promote HPV vaccine uptake.

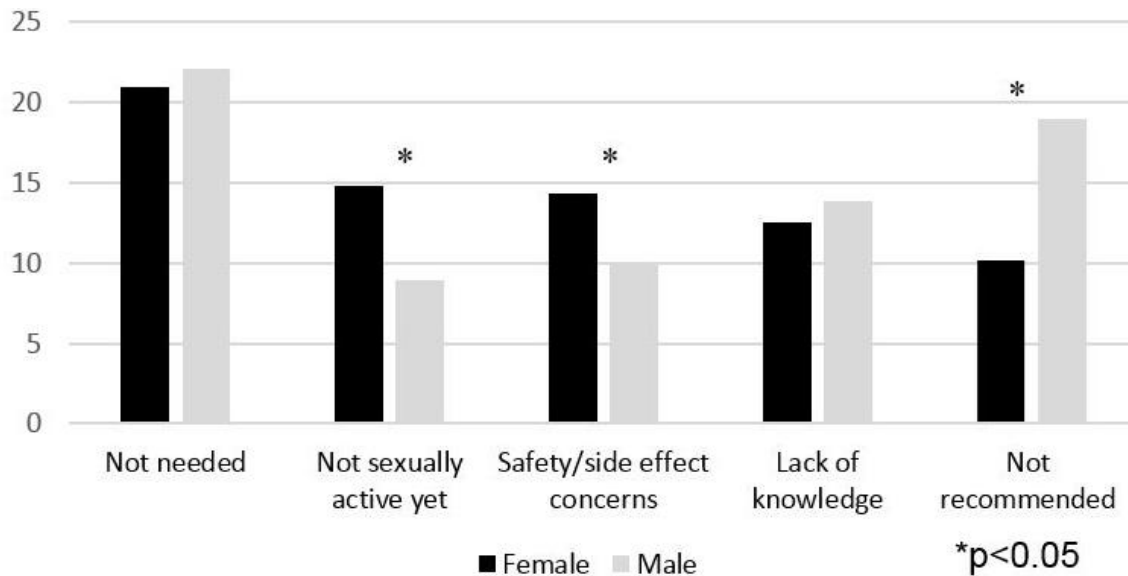


Fig. 1. Reasons for Lack of HPV Vaccine Initiation, 2015.

319 - Poster Session

Screening for Lynch syndrome in a medically underserved population

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Objective: Lynch syndrome (LS) is diagnosed in 2%–5% of endometrial and colon cancers. The American College of Obstetricians and Gynecologists and SGO recommend choosing one approach to consideration of genetic assessment for LS: universal screening, screening if diagnosed at an early age, or testing patients at risk by family history using Amsterdam II or modified Bethesda criteria. Patients with low socioeconomic resources have barriers to health care access. We sought to examine the efficacy of screening at-risk patients and to evaluate patient compliance within a hospital system caring for a medically underserved population.

Method: We reviewed patients with a diagnosis of endometrioid endometrial cancer from 2009 through June 2017. Clinical, pathologic, immunohistochemistry (IHC), and mutational analysis (MA) results were obtained. Reason for LS screening was recorded. We examined the family history of women who were not screened to determine whether they would have qualified for testing based on age, Amsterdam II criteria, or modified Bethesda criteria.

Results: A total of 479 women were studied; 201 patients met age criteria for screening. Of these, 138 were screened with IHC: 31 were abnormal, 7 tested positive for LS, and 107 were screened negative; 30 were referred for MA due to clinical suspicion, and none tested positive for LS. Of the 63 unscreened patients, 6 were referred for MA, and none tested positive for LS. There were 278 patients who did not meet age criteria. In 78 there was clinical suspicion for LS. Of these, 45 had IHC testing, 15 were abnormal, and 1 was positive for LS. Of the 30 with negative IHC, 14 were referred due to continued clinical suspicion, and none were diagnosed with LS. There were 33 patients in this group who did not have IHC but were referred, of which none tested positive for LS. In the remaining 200 unscreened patients not meeting age criteria, only 3 (1.5%) would have met Amsterdam II or modified Bethesda guidelines. There were 127 total patients referred for MA, and 91 (71.7%) attended their appointments. Of the 36 who did not go for testing, 23 did not follow up, 10 declined, and 3 rescheduled. The majority of these patients were white (54.6%) and English-speaking (84.8%). LS was diagnosed in a total of 8 patients (1.7%), all identified after screening due to age or family history.

Conclusion: We found that screening women with endometrioid endometrial cancer based on diagnosis at a younger age or family history identified the majority at risk. Follow-up was an impediment to genetic testing, underscoring the importance of patient education and awareness.

320 - Poster Session

Racial disparities in outcomes for patients with type II endometrial cancer: A California cancer registry study

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Objective: To examine factors affecting prognosis and survival among different racial groups diagnosed with type II endometrial cancer (EC) using the California Cancer Registry

Method: We identified all women diagnosed with type II EC from 1998 to 2009. A Charlson index was used as a measure of comorbidity. Time to treatment (TTT) was calculated in days from the date of diagnosis to date of definitive surgery, radiation, or chemotherapy, whichever was the earliest. TTT was categorized as 2 weeks or less, 2–4 weeks, and more than 4 weeks. The Kaplan-Meier method was used to describe overall survival (OS) and disease-specific survival (DSS). Survival by stage, race, and time to treatment category were compared using the log rank test.

Results: A total of 11,274 patients met the eligibility criteria. Median follow-up was 9.24 years for nondeceased patients. The majority of patients with type II EC were non-Hispanic white (64.2%), followed by Hispanic (15.8%), Asian (10.6%), and non-Hispanic black (9.4%). Non-Hispanic black women had higher incidence of certain aggressive histologic subtypes in comparison to non-Hispanic white women, including serous carcinomas (23.8% vs 15.4%) and carcinosarcoma (24.4% vs 15.1%), respectively. Non-Hispanic white patients were more likely to have stage I disease compared to non-Hispanic black women (44.4% vs 34.9%). Non-Hispanic black patients were more likely than non-Hispanic white patients to be treated more than 4 weeks after diagnosis (55.7% vs 43.9%). Non-Hispanic black patients had a worse 5-year DSS and OS when compared to other racial groups. Five-year OS for non-Hispanic black women was 42% (39%–45%) compared to non-Hispanic white women, 54% (52%–55%); Hispanic, 55% (53%–58%); and Asians 60% (57%–63%). This clear survival disadvantage of non-Hispanic black women persisted when evaluated by stage or time to treatment. After adjusting for age, histologic subtype, type of treatment, time to treatment, comorbidity, insurance status, socioeconomic status, marital status, NCI cancer center, and year of diagnosis, non-Hispanic black women still had an increased hazard of disease-specific death compared to non-Hispanic white women, both in early-stage (HR = 1.26, 95% CI 1.03–1.55) and late-stage disease (HR = 1.17, 95% CI 1.03–1.34).

Conclusion: Non-Hispanic black women have a higher incidence of more aggressive histologic subtypes, even among a cohort of type II EC patients, and have disproportionately worse DSS and OS. Non-Hispanic black women have a higher risk of disease-specific mortality than non-Hispanic white women even after controlling for potential confounders.

321 - Poster Session

Identifying barriers to faith-based human papillomavirus education in the mid-South

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Objective: To assess willingness of and barriers to faith-based education on human papillomavirus (HPV) screening and immunization in Memphis, TN.

Method: A total of 63 religious congregations in the Memphis, TN, area were identified for recruitment as sites of research on the effectiveness of faith-based HPV education on immunization uptake, screening utilization, and identification of barriers to vaccination and screening. Congregations were contacted by email and phone until a positive or negative response was given. Congregations were considered unwilling after 3 unreturned voicemails. Utilizing ARCGIS software (ESRI Atlanta, GA), demographic data were collected on the U.S. Census Tract in which each congregation resides. Racial makeup of a congregation was elicited from the contact person at each organization. Data were compared between congregations that were willing to participate and those that were not. Congregations that were unwilling to participate were asked to identify reasons for nonparticipation. The χ^2 test was used for discrete variables, and the Student t test was used for continuous variables using SPSS software.

Results: Fifty-nine of the 63 (93%) congregations responded to our inquiry; 14 agreed to participate and 49 declined (78%). We sought to evaluate demographics and barriers to faith-based HPV education given the unexpected number of negative responses. Congregations that declined to participate reside in Census tracts with lower median incomes (average \$4,0825 vs \$66,120, $P = 0.013$), have a lower percentage of residents with a bachelor's degree (19% vs 49%, $P < 0.001$), and spent less money on insurance annually per capita in 2016 (\$2,411 vs \$4,459, $P = 0.002$) (Table 1). There were no differences between the two groups in terms of distance from health care providers/facilities or level of poverty. Reasons given for nonparticipation are summarized in Table 2.

Conclusion: Congregations that elected not to participate in faith-based HPV education research were more likely to serve areas of socioeconomic disparity. Our initial outreach identified characteristics of congregations that may be less likely to participate in faith-based HPV education and will aid in finding solutions to improve disparities in health care education.

Table 1. Demographic Data by Congregational Location.

	Yes (n = 14)	No (n = 49)	P Value
Average Median Household Income	66120	40825	0.013
Located in Census Tract Below Poverty Level	3	11	0.19
Racial Predominance of Congregation			0.003
African American	2	32	
Caucasian	11	15	
Mixed	1	2	
2016 Average Annual Insurance Expenditure Per Capita (Dollars)	4459	2411	0.002
Average Distance from Federally Qualified Health Center (Miles)	2.36	2.85	0.392
Average Distance from Hospital (Miles)	2.1	2.8	0.217
Percentage of Residents with a Bachelor's Degree	49	19	<0.001

Table 2. Reasons for Non-Participation.

Not the right time	14
Not interested	13
No Reason	11
Not appropriate for church discussion	5
Not the right population	5
Have own health ministry	1

322 - Poster Session

Pilot of an international collaboration to build capacity to provide gynecologic oncology surgery in Botswana

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Objective: To increase capacity for gynecologic oncology surgery in Botswana. Gynecologic cancers are the leading cause of cancer death among women in Botswana. Cervical cancer accounts for 25% of all female cancer cases, followed by vulvar, ovarian, and endometrial cancer. The epidemiology of gynecologic cancers is affected by Botswana's high HIV prevalence

(22%); 60% of women with gynecologic cancers are HIV-infected. Chemotherapy and radiation are available, but there are no trained gynecologic oncologists to provide advanced surgery. Since 25% of cervical cancer cases present at a stage that could be cured by surgery alone, a model for delivering gynecologic oncology services is a priority.

Method: Under Ministry of Health guidance, a model was developed to provide 8 weeks/year of gynecologic oncology services in Botswana, in 4 2-week blocks, delivered by United States-based gynecologic oncologists. A gynecologic oncology campaign was planned, and all essential equipment, medications, and staffing were prepared. Eligible patients were identified through the gynecologic oncology multidisciplinary clinic at Botswana's tertiary referral hospital. All patients had preoperative evaluations by a general gynecologist and were screened by the operating gynecologic oncologist prior to surgery. Local gynecologists and surgeons were invited to participate in gynecologic oncology surgeries to build local surgical capacity.

Results: One United States-based gynecologic oncologist and two gynecologists and two surgeons working locally participated in the pilot campaign. A total of 16 operations were performed over 8 days. Indications included cervical cancer (4), ovarian cancer (3), vulvar cancer (1), complex atypical hyperplasia (1), preinvasive cervical disease (2), and benign disease (3), as well as 2 obstetric emergencies. The only gynecologic oncologic complication was a case of bleeding requiring transfusion and postoperative ICU care.

Conclusion: Periodic gynecologic oncology campaigns in settings otherwise lacking local capacity to perform advanced gynecologic cancer surgery are a feasible model to create access and build local capacity. Strong local collaboration is essential. The time lag between diagnosis of a gynecologic cancer and the next surgical campaign remains a challenge. Future plans include recruiting more gynecologic oncologist faculty to increase campaign frequency, enabling gynecologic oncology surgical planning to be incorporated into routine clinical services, and increased local participation.

323 - Poster Session

Racial and ethnic disparities in place of death among gynecologic cancer patients in the United States

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Objective: Helping patients achieve their goals of care, including their preferred place of death, is a key aspect of palliative care for advanced cancer patients. Patients who are racial minorities are less likely to receive palliative services, which may increase their likelihood of dying in a hospital. This study tested for such racial disparities in place of death among all patients who recently died from gynecologic cancers in the United States.

Method: Using death certificate data from the Mortality Multiple Cause-of-Death Public Use Data Files, we identified all women who died from gynecologic cancers from 2010 to 2015. Regression analyses with ordinary least-squares linear probability modeling were used to test for differences in location of death by race and Hispanic ethnicity, controlling for age, marital status, education status, year, and cause of death. Regression analysis was also used to test for differences in racial disparities between gynecologic cancer patients and women who died from breast, lung, and colorectal cancers.

Results: Gynecologic cancer was the cause of death for 178,001 patients who died between 2010 and 2015. The plurality of gynecologic cancer patients were white (82.9%), had ovarian cancer (48.2%), and died at home/hospice (54.7%). In unadjusted analyses, the rate of death at home/hospice was 56.1% for white, 47.3% for black, 52.8% for Asian/Pacific Islander, and 50.7% for Native Americans patients. For Hispanic patients, 57.8% died at home/hospice, compared to 54.5% of non-Hispanic patients. In adjusted analyses, white patients were more likely to die at home/hospice than black, Asian/Pacific Islander, and Native American patients by 6.5 ($P < 0.001$), 4.8 ($P = 0.003$), and 4.6 ($P < 0.001$) percentage points, respectively. There was no statistically significant difference in rates of dying at home/hospice between Hispanic and non-Hispanic patients. There were no significant differences in racial disparities in place of death between patients who died from gynecologic cancers and patients who died from nongynecologic cancers.

Conclusion: White gynecologic cancer patients are significantly more likely than black, Asian/Pacific Islander, and Native American patients to die at home/hospice. Earlier palliative and hospice care referral, as well as improved advanced care planning discussions, may improve this disparity.

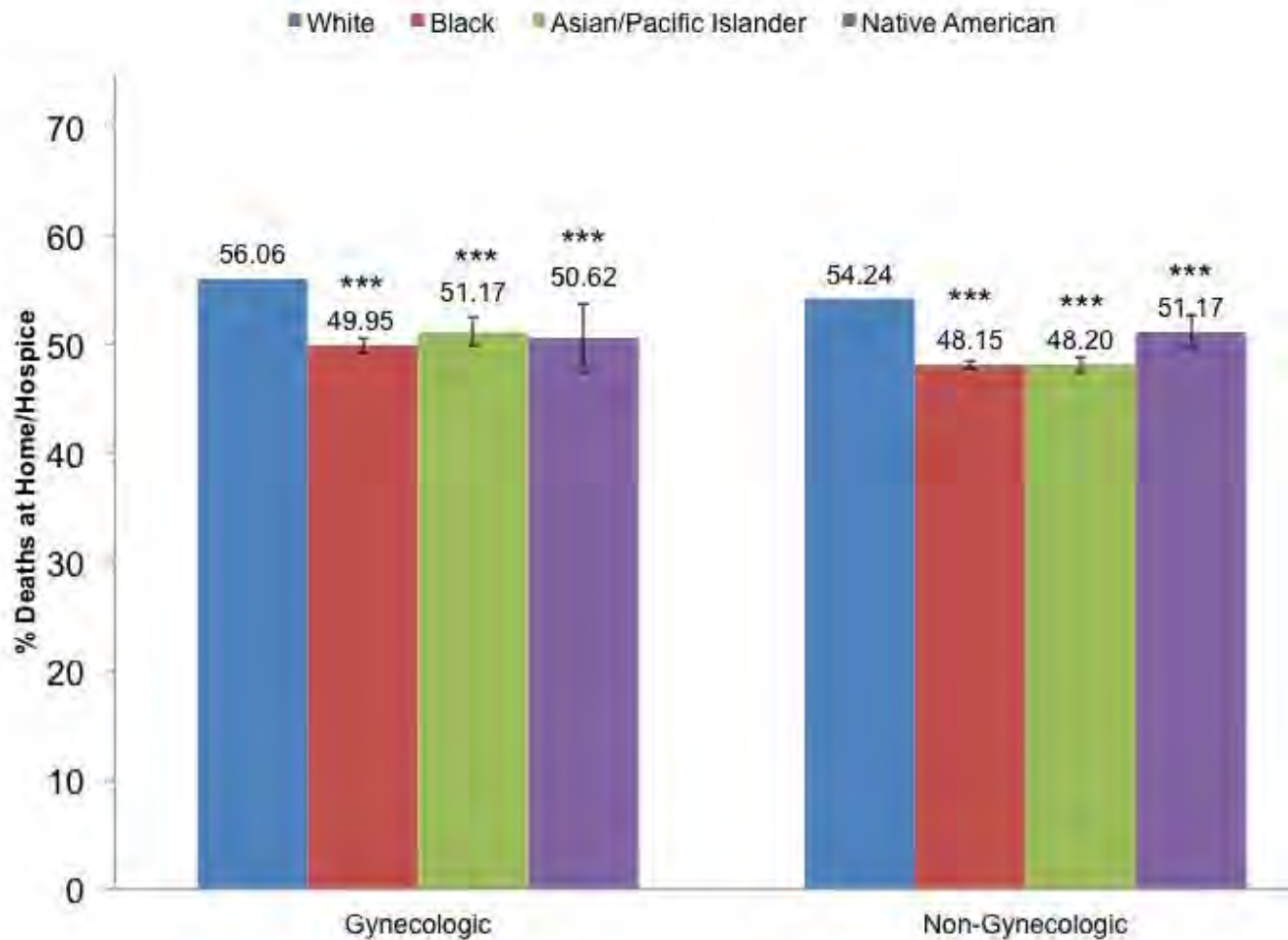


Fig. 1. Adjusted Rates of Cancer Deaths at Home/Hospice by Race.

324 - Poster Session

Increased prevalence of psychological distress among women with a gynecologic cancer: An underreported disparity driven by low socioeconomic status

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Objective: Distress related to a cancer diagnosis likely persists throughout a woman's cancer journey. We aim to evaluate whether differences in distress exist based on socioeconomic status among gynecologic oncology patients.

Method: As a quality improvement project, we initiated the National Comprehensive Cancer Network distress thermometer screening throughout all gynecologic oncology clinics at a high-volume institution between June 2017 and September 2017. Distress scores (scale 0–10, ≥ 5 = high) at initial visit were excluded because of uncertainty of cancer diagnosis, but were subsequently recorded by visit type. Primary outcome was a distress score ≥ 5 . Secondary outcome was attended referral to free psycho-oncology counseling. Univariate and multivariate logistic regression were used.

Results: Among 1,085 women screened for distress, 20% self-reported a score ≥ 5 . As a surrogate marker of low socioeconomic status, having no insurance or Medicaid was the predominant factor that best predicted distress ($P < 0.001$). Analyzed per visit ($n = 1423$), median distress score among women with no insurance or Medicaid versus private insurance or Medicare was 4 versus 0, respectively ($P < 0.001$). Black women were 1.8 times more likely to report high distress than white women (OR = 1.76, 95% CI 1.16–2.66). Those who were widowed or marked "other" (e.g., not single or separated) were also more likely to report high distress than married women (OR = 1.85, 95% CI 1.16–2.94). Distress scores ≥ 5 were most

commonly reported at time of an established visit (64%), followed by a chemotherapy (25%) and postoperative visit (11%) ($P = 0.038$). After adjusting for age, race, and relationship status, women with no insurance or Medicaid were 3 times more likely to have high distress than women with private insurance or Medicare (adjusted OR = 3.35, 95% CI 1.87–5.98) (Table 1). Of 29 patients who received free psycho-oncology counseling, there were no differences in median distress score immediately preceding referral, nor differences in number of counseling appointments based on insurance status.

Conclusion: High distress is a common symptom among women receiving care by a gynecologic oncologist. Future studies are needed to evaluate effective strategies for reducing distress scores and optimizing integration of psycho-oncology care into gynecologic oncology outpatient visits.

Table 1. Predictors of high distress (NCCN Distress score of ≥ 5).

Risk factor	Crude OR (95% CI)	Adjusted OR (95% CI)
Insurance		
Private or Medicare	Reference	Reference
No insurance or Medicaid	4.01 (2.31-6.96)	3.35 (1.87-5.98)
Age	0.99 (0.98-1.00)	0.99 (0.98-1.01)
Race		
Black	1.76 (1.16-2.66)	1.53 (0.98-2.40)
White	Reference	Reference
Other	1.19 (0.51-2.78)	1.00 (0.42-2.42)
Marital status		
Single	1.39 (0.93-2.09)	1.05 (0.67-1.64)
Divorced	1.36 (0.86-2.15)	1.21 (0.76-1.94)
Married	Reference	Reference
Widowed or other	1.85 (1.16-2.94)	1.69 (1.03-2.78)

325 - Poster Session

Primary treatment of ovarian cancer with weekly carboplatin and paclitaxel vs. conventional 3 weekly administration: A retrospective chart review

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Objective: To retrospectively compare primary treatment of advanced epithelial ovarian cancer (EOC) with the standard treatment of paclitaxel 175 mg/m² and carboplatin AUC 6 (PC-3W), every 3 weeks versus weekly paclitaxel 80 mg/m² and carboplatin AUC 2 on days 1, 8, and 15 in a 28-day cycle (PC-W).

Method: Medical records of 750 consecutive EOC, tubal carcinoma, and primary peritoneal carcinoma patients were reviewed; 440 of them were treated with carboplatin-paclitaxel combinations. Those charts were reviewed for age, tumor information (stage, histological features, CA-125 level at diagnosis), effectiveness of treatment (progression-free survival [PFS], overall survival [OS]), and toxicity profile.

Results: A third of the patients (146/440, 33.2%) were treated with PC-W, and 66.8% (294/440) were treated with PC-3W. Patients in the PC-W group were older than patients in the PC-3W group ($P = 0.01$), but other baseline characteristics (stage of disease, histology, CA-125 at the diagnosis, and BRCA carrier) were similar. Median OS and PFS of the PC-W group (63 and 17 months, respectively) were higher but not statistically significantly different from the median OS and PFS of the PC-3W group (54 months and 14.2 months, $P = 0.312$ and 0.106 , respectively). Survival analysis using the Cox regression hazard model adjusted for age, disease stage, BRCA status, and platinum sensitivity showed that patients in the PC-3W group were at a

significantly higher risk of death than those in the PC-W group (HR 1.357, 95% CI 1.037–1.775, $P = 0.026$). The patient's age at diagnosis, stage of disease at baseline, and platinum insensitivity were also found to contribute significantly to the risk of death (HR 1.02, 2.39, and 1.82 respectively; $P < 0.05$ for all factors). The toxicity profile showed lower incidence of thrombocytopenia (grade 3 2.3% vs 0%), neuropathy (grade 3 toxicity 4.8% vs 1.5%), and hair loss (grade 2 91.2% vs 44.8%) ($P < 0.01$, $P = 0.023$, and $P < 0.005$, respectively) in the PC-W group and similar rates of anemia ($P = 0.158$) in both treatment regimens.

Conclusion: Our retrospective study suggests that weekly treatment with carboplatin and paclitaxel administered in a 28-day cycle as primary chemotherapy for EOC has similar efficacy and better tolerability than the standard 3-week treatment and should be considered for specific populations. Further investigation is warranted.

326 - Poster Session

Innovative simulation models for cervical cancer training in low-resource settings

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Objective: Cervical cancer is the leading cause of cancer death among women living in low- and middle-income countries. Moreover, the incidence of cervical cancer is higher for women in underserved settings of the United States. Screening for preinvasive lesions is an effective cervical cancer prevention tool; however, many low-resource settings lack providers trained to provide comprehensive cervical cancer screening services. To address this need, Rice University developed a low-cost (<\$100), anatomical model to train providers in low-resource areas to learn and practice the skills of cervical cancer screening and prevention including VIA, colposcopy, cervical biopsy, cryotherapy, and loop electrosurgical excision procedure (LEEP); see Figure 1.

Method: The model includes a low-cost pelvic frame that allows the trainee to perform a gynecologic examination; the frame can easily incorporate different models of the cervix that depict the visible differences between a normal cervix, benign changes, low- and high-grade dysplasia, and cervical cancer. These models are interactive with “white lesions” appearing after the application of hot water, simulating a positive VIA or colposcopy result for precancer and/or cancer. The models are made to scale with a diameter of 3 cm, making them good targets for colposcopy training. Cervix models made from ballistic gel have also been developed to allow training in cervical biopsy, cryotherapy, and LEEP. For cervical biopsy training, the ballistic gel models contain small black beads that trainees remove using cervical biopsy forceps. The ballistic gel models can also be ablated/cut during cryotherapy and LEEP training.

Result: The models have been used in two colposcopy/LEEP training courses held in the Rio Grande Valley along the Texas–Mexico border. During these courses, trainees used the models to simulate and practice colposcopy, performing cervical biopsies and LEEP. The courses were each led by 5–7 physicians who indicated that the models were easy to use and helpful in teaching the skills discussed during the morning lectures.

Conclusion: These models will be formally evaluated in cervical cancer screening and prevention courses set to take place in underserved areas of Texas and low- and middle-income countries.

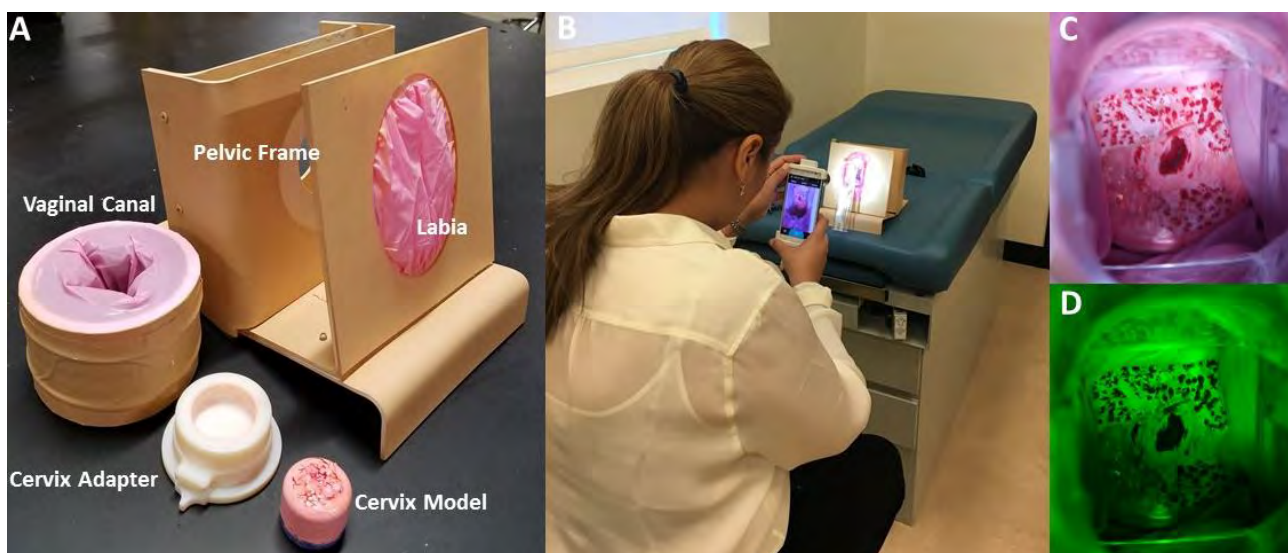


Fig. 1. A) Labeled image showing the different parts of the cervical cancer training model. B) Image of assembled model being used for colposcopy training. C) Colposcopic image of 3D printed cervix model and D) colposcopic image of the cervix model using a green filter. Red marks on the cervix model symbolizing blood vessels appear darker under the green light.

327 - Poster Session

Are gynecology oncology fellows ready for independent attending practice?

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Objective: With the recent transition of gynecologic oncology fellowships to the Accreditation Council for Graduate Medical Education (ACGME), assessing and demonstrating clinical competence on behalf of graduating fellows will now be an integral part of continued accreditation. Little is known about fellows' perceptions regarding the adequacy of their training. Thus in this study we sought to determine the perspectives of recently graduated fellows regarding their preparedness for autonomous clinical practice

Method: The SGO database was used to identify contact information for gynecologic oncology fellows who graduated from an accredited program within the past 3 years (2015–2017). An online survey software and questionnaire tool was used to create, disseminate, and collect responses to a 33-question survey gauging the perspectives of recent graduates regarding their surgical and medical preparedness for independent practice.

Results: Seventy-two (53.3%) of the 135 previous gynecologic oncology fellows with up-to-date contact information completed the questionnaire. The majority of respondents were female (79.2%), were between the ages of 31 and 35 years (52.1%), and practiced in the university hospital setting (54.9%). Most respondents reported "agree" (54.9%) or "strongly agree" (42.3%) that they were adequately trained for their role as an attending. Fellows reported didactic lectures (91.3%) and journal clubs (84.1%) as the most integral teaching tools for their fellowship training. Recently trained fellows reported a perceived lack of proficiency in performing pelvic exenterations (29.2%), radical trachelectomy (43.1%), and complex urologic procedures (56.9%). Recently trained fellows had "strong" agreement in competence in chemotherapeutic decision making (41.5%), management of critically ill patients (47.7%), and palliative/end-of-life management (55.4%).

Conclusion: Most recently trained gynecologic oncology fellows feel very well prepared for independent practice upon graduation. Perceived deficiencies were expressed regarding rare and complex surgical procedures. Given limited exposure and infrequent training opportunities, exenterations, urologic reconstruction, and other rare procedures should not be included in the assessment of graduating fellows, but instead should be considered procedures of interest.

328 - Poster Session

Impact of histological grade on patients with clinical stage I endometrial carcinoma who received primary radiation therapy

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Objective: This study aims to determine the impact of histological grade on overall survival in patients with clinical stage I endometrioid endometrial adenocarcinoma who receive radiation therapy as primary definitive treatment.

Method: A retrospective analysis of patients with endometrioid endometrial adenocarcinoma patients was conducted using the National Cancer Database. Patients with stage I disease treated with primary, definitive radiation therapy (i.e., brachytherapy +/- external beam radiation therapy) and did not undergo surgery or chemotherapy between 2004 and 2104 were identified. Survival for each stage was analyzed by using Kaplan-Meier univariate analysis. Multivariable analyses were performed utilizing Cox proportional hazard regression for overall survival to identify factors affecting survival.

Results: A total of 1,139 patients were identified. Grade 1, 2, and 3 accounted for 48.6%, 23.9%, and 10.6%, respectively, with 16.9% having unknown grade. Patients with grade 1 tumors had a median overall survival of 62 months (95% CI 53.8–70.1), which decreased to 48.5 months for grade 2 (95% CI 38.2–58.8) and 33.45 months for grade 3 (95% CI 23.1–43.8). There was no difference in Charlson-Deyo comorbidity score based on histologic grade. Grade 3 tumors were more likely to be associated with older age and treated with brachytherapy plus external beam radiation therapy, although in univariate analysis, only grade ($P < 0.001$), insurance status ($P < 0.001$), and age ($P < 0.001$) were significantly associated with survival. In multivariable analysis, all 3 of the identified factors remained independently associated with overall survival.

Conclusion: This is the largest dataset to examine the impact of grade when radiation therapy is used as definitive treatment in clinical stage I endometrial cancer. The survival outcome of primary definitive radiotherapy in women diagnosed with grade 2 endometrioid adenocarcinoma is similar to that of those with grade I disease. However, women with grade 3 histology had a significantly lower survival rate. This suggests that histologic grade should be carefully considered and factored into treatment planning in patients diagnosed with endometrioid cancer who are not surgical candidates.

329 - Poster Session

After the cervical cancer diagnosis, who's talking about why?

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Objective: HPV vaccination is an important part of routine preventive care for adolescents and young women. Current efforts focusing largely on educating parents about the importance of HPV vaccination for their children have had limited success. Our aim was to evaluate the willingness and ability of cervical cancer patients to promote HPV vaccination.

Method: Patients with a diagnosis of malignant neoplasm of the cervix who had received care at Geisinger Medical Center were identified. Four hundred and fifty patients were randomly selected to receive a survey evaluating their understanding of the relationship between HPV infection and their disease, barriers to HPV vaccination, other prevention measures, and the role of their physician and gynecologic oncologist.

Results: A total of 113 (25%) surveys were returned. Women who responded were between the ages of 28 and 99 years with an average age of 57 years; most (94%) were white; and 55% reported annual household income less than \$35,000. Eighty-four (82%) patients had spoken to at least 1 family member about their diagnosis. Among those who had conversations, 74% ($n = 62$) had spoken with females in the next generation, while only 45% had spoken with males in the next generation about the kind of cancer. Sixty-nine (63%) patients received information regarding HPV vaccination from television, and 81% reported receiving information from at least 1 media source. Forty-seven women reported receiving information from their oncologist, and 69% of women received information from any health care provider. In general, women expressed a willingness to have prevention conversations with family, including 74% on the importance of Pap smear, 68% on the importance of flu vaccine, and 61% on the importance of the HPV vaccine.

Conclusion: There appears to be a willingness among cervical cancer patients to discuss HPV with family members. Given the finding that patients are receiving a great deal of information from media, it is imperative that the information be accurate. Should cervical cancer patients be enlisted as health advocates or educators to promote prevention strategies including HPV vaccination, it will be important to ensure that a training program be developed that provides accurate information and a

succinct message.

330 - Poster Session

The state of women in academic gynecologic oncology programs

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Objective: Prior studies have demonstrated that women are less likely to be full professors than men even after adjusting for age and research productivity. According to data from the Association of American Medical Colleges (AAMC), in 2013 women accounted for 82.6% of all residents in obstetrics and gynecology, up from 74.1% in 2003. In 2014, women also accounted for 55% of all obstetrics/gynecology faculty, but only 27% of full professors. In this study, we aimed to identify gender differences in academic rank among gynecologic oncologists at major academic institutions in the United States.

Method: We examined institutional websites of the 2016–2017 American Board of Obstetrics and Gynecology (ABOG)-accredited gynecologic oncology fellowship programs to conduct a cross-sectional analysis identifying the number of men and women at each academic rank.

Results: We identified 45 ABOG-accredited programs associated with academic centers. Of the 45 institutions, 24.4% had female division directors and 33.3% had female fellowship program directors ($P < 0.0001$ and $P = 0.0029$, respectively). A total of 307 faculty of all academic ranks were identified, with 163 (53%) male faculty members and 144 (47%) female faculty members. There were a total 105 full professors, with 76 male professors and 29 female professors ($P < 0.001$). There was no statistical difference between the number of male or female associate professors ($P = 0.3657$). However, there were significantly more female assistant professors (81/122) compared to male assistant professors (41/122) ($P < 0.001$).

Conclusion: Despite accounting for a majority of residents in obstetrics and gynecology over the past 13 years and roughly half of all gynecologic oncology faculty, women are still underrepresented among leadership positions and full professors in academic gynecologic oncology programs. Encouragingly, more women are currently assistant professors suggesting that this trend may change in the future.

331 - Poster Session

Comprehensive serum glycopeptide spectra analysis might be a new tool for the early detection of ovarian cancer

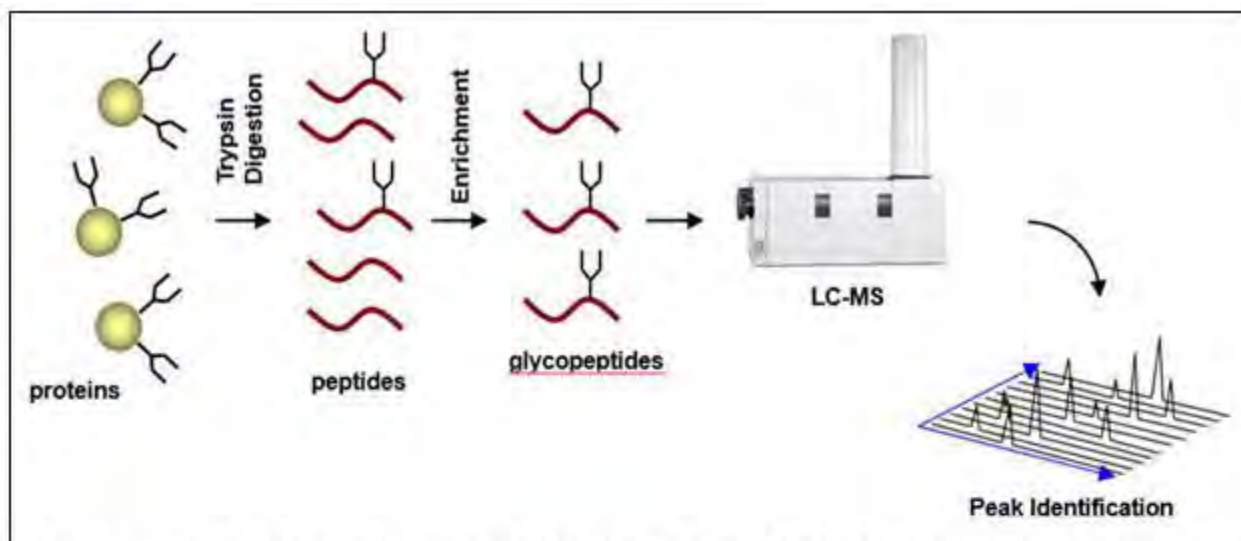
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Objective: New techniques for early diagnosis of epithelial ovarian cancer (EOC) could have a major effect on women's health. However, current methods have a relatively poor positive predictive success rate of just 10–20%. In this study, comprehensive glycopeptide spectra of blood serum were investigated as potential indicators of pathological changes in the ovaries.

Method: More than 100,000 glycopeptide peaks digested from serum glycoproteins of 39 EOC patients and 45 noncancer control women (including 18 with endometriomas) were obtained by liquid chromatography/mass spectrometry (LC/MS). We assessed how well these glycopeptide peak spectra can discriminate between women with EOC and benign controls by applying chemometric techniques of OPLS and PLS discriminant analysis (Figure 1).

Results: The OPLS-DA model was constructed using the first and second orthogonal component (Figure 2, left). The quality of the models was described by the cross-validation parameters R^2 and Q^2 , which represented the total variation for the X matrix. In OPLS-DA score plots of serum sample, a significant distinction between early-stage EOC patients and controls was identified with $R^2 = 0.84$ and $Q^2 = 0.60$. Based on the PLS-DA models for serum samples (Figure 2, right), early-stage EOC patients and controls were discriminated with an R^2Y of 0.84 and a Q^2 of 0.47. In addition, women with early-stage clear cell carcinoma and those with endometriomas could be distinguished by this method.

Conclusion: Generation of the LC/MS spectra used in this study requires just a small sample of blood serum that can be obtained with a pin prick. This highlights the potential of comprehensive serum glycoprotein analysis as a screening tool for diseases such as ovarian cancer in the general population, which could lead to a quantum leap in quality of life.



Chemometric techniques of OPLS and PLS Discriminant Analysis.

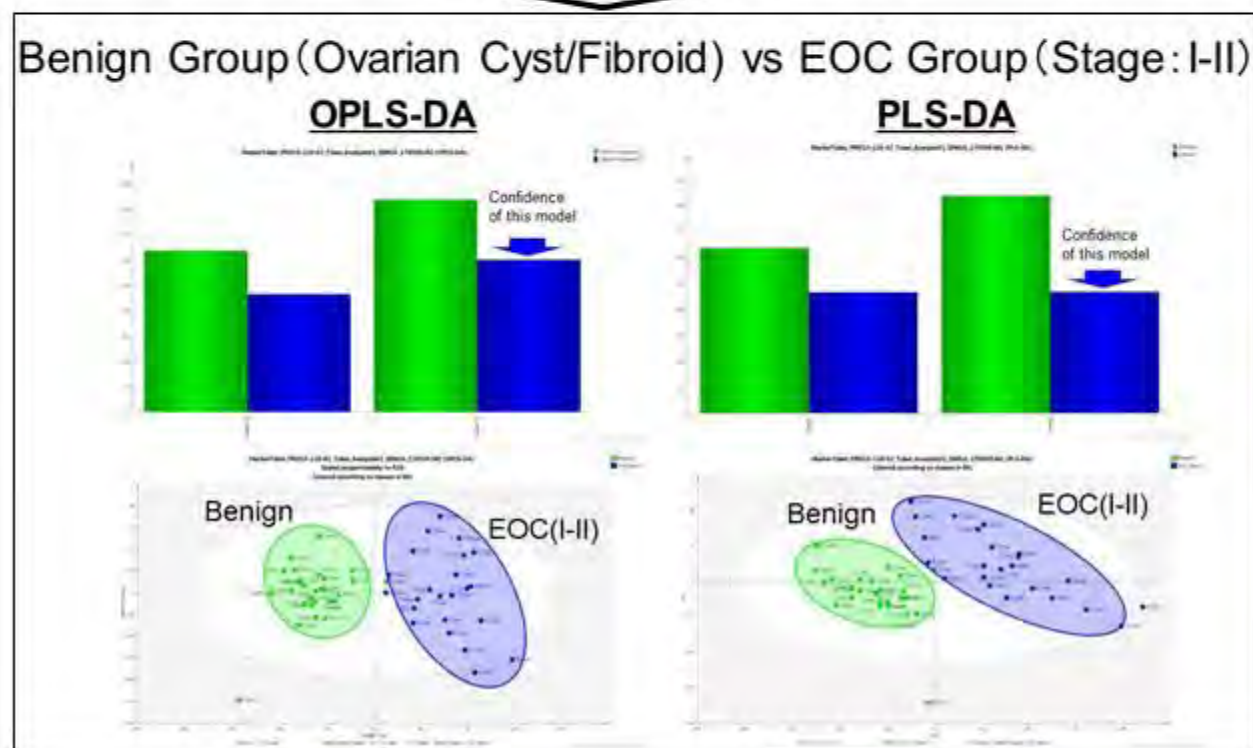


Fig. 1.

332 - Poster Session

Provider volume and guideline compliance in ovarian cancer patients receiving front-line chemotherapy

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Objective: Vast literature shows that ovarian cancer surgery by high-volume surgeons is associated with improved outcomes in advanced-stage disease. This has not been studied for front-line chemotherapy. We sought to evaluate the association of provider volume with chemotherapy guideline compliance, and the impact of chemotherapy guideline compliance on overall survival (OS) in patients with newly diagnosed advanced ovarian cancer.

Method: We queried the SEER-Medicare database for patients 65 years of age and older who underwent primary debulking surgery within three months of diagnosis and received chemotherapy within seven months of surgery for FIGO stage III-IV epithelial ovarian cancer from 2004 to 2013. We assigned provider volume using the average volume of ovarian cancer patients (all stages) in the years that patients were seen. Study outcomes were National Comprehensive Cancer Network guideline compliance, which was defined as receiving six or more cycles of a platinum-containing doublet, and OS. Rates of guideline compliance were compared by volume quartiles using the χ^2 test, and by increments of provider volume using logistic regression. OS was estimated using the Kaplan-Meier method and compared by guideline compliance using the log-rank test.

Results: A total of 1,416 patients met inclusion criteria. There were no significant differences in the rate of guideline compliance across provider-volume quartiles in either univariate or multivariable logistic regression analysis (Table 1, in which adjusted OR for an increase of 1 patient in annualized volume = 1.00, 95% CI 0.97–1.03). For stage III patients, median OS was 48 months (95% CI 45–53) in those who received guideline-compliant chemotherapy and 36 months (95% CI 29–40) in those who did not ($P < 0.01$). For stage IV patients, median OS was 43 months (95% CI 36–50) in those who received guideline-compliant chemotherapy and 19 months (95% CI 16–24) in those who did not ($P < 0.01$).

Conclusion: Chemotherapy-specific guideline compliance was associated with improved OS in patients with advanced ovarian cancer. However, increased provider volume was not associated with a change in rates of guideline compliance. The focus of this study was limited to front-line chemotherapy for elderly patients; additional research is needed to determine whether provider volume is associated with differences in other groups and later lines of therapy.

Table 1. Adjusted odds ratios and 95% confidence intervals for compliance with NCCN guidelines.

Characteristics*	Adjusted Odds Ratio (95% Confidence Interval)
Provider volume	
1 patient increase	1.00 (0.97–1.03)
2 patient increase	1.00 (0.94–1.07)
5 patient increase	1.01 (0.87–1.18)
Age at diagnosis (years)	
66–69	1.00 (Reference)
70–74	1.34 (0.97–1.85)
75–79	1.02 (0.73–1.42)
80–84	0.68 (0.46–0.99)
85+	0.42 (0.23– 0.79)
Geographic region	
Midwest	1.00 (Reference)
Northeast	1.09 (0.69–1.72)
South	1.69 (1.09– 2.60)
West	1.05 (0.70– 1.57)
Charlson comorbidity index	
0	1.00 (Reference)
1	0.76 (0.56– .04)
2+	0.68 (0.46–1.00)

*FIGO stage, histology, grade, provider specialty, census tract median income, residence (metro/nonmetro), race, and marital status were included in the model and not significant.

333 - Poster Session

Identifying causes of postoperative urinary retention in gynecologic oncology patients and implementation of a novel voiding management protocol

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Objective: To determine the rate of and risk factors associated with postoperative urinary retention. To implement a standardized postoperative voiding management protocol to reduce unnecessary recatheterization.

Method: A new postoperative voiding management protocol was designed and implemented that was predicated on several principles based on literature review: (1) Foley removal at 6 hours postoperatively, (2) universal bladder scan after first void, and (3) limiting recatheterization to patients with bladder scan volumes greater than 150 cc. Data were abstracted for a range of parameters: demographics, diagnosis, stage, medical comorbidity, preoperative bacteriuria, surgical and anesthesia characteristics, and performance of postoperative recatheterization. A threshold of 150 cc was used to classify recatheterization as “necessary” or “unnecessary.” A total of 70 patients were assessed preprotocol and 116 postprotocol. χ^2 and Student t tests were performed, with a *P* value of 0.05 considered significant for all comparisons.

Results: Gynecologic oncology patients have a baseline rate of postoperative urinary retention of 19.3%. Risk factors associated with urinary retention include diabetes (*P* = 0.038), anticholinergic medications (*P* = 0.002), preexisting urinary dysfunction (*P* = 0.024), and performance of paraaortic lymphadenectomy (*P* = 0.012). Preoperative bacteriuria was present in 8.1% of cases, but it was not associated with urinary retention (*P* = 0.204). The new voiding management protocol reduced the rate of unnecessary recatheterization significantly (10.0% vs 1.7%, *P* = 0.027) without overlooking retention (21.4% vs 18.1%, *P* = 0.578). Finally, for patients undergoing laparoscopic or robotic hysterectomy, this protocol significantly increased hospital-defined early discharges (4% vs 22%, *P* = 0.022).

Conclusion: Postoperative urinary retention is a substantial problem in gynecologic oncology patients with a baseline rate of 19.3%. In addition to the expected medical comorbidity, patients undergoing paraaortic lymphadenectomy are significantly more likely to experience retention. A new voiding management protocol reduced unnecessary recatheterization and increased early discharges in minimally invasive hysterectomy patients.

334 - Poster Session

Does age-adjusted Charlson comorbidity score skew survival endpoints in women with FIGO-stage III endometrial cancer?

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Objective: Most women with endometrial carcinoma (EC) are elderly with significant comorbid conditions that may have a negative impact on their tolerance to treatment as well as their survival. We sought to evaluate the impact of Age-Adjusted Charlson Comorbidity index (AACCI) score on survival endpoints for women with 2009 FIGO stage III EC.

Method: We identified 238 patients with stage III EC who underwent surgical staging between January 1990 and June 2016 at our institution. AACCI score was calculated at the time of hysterectomy for all patients, and three groups were created accordingly: group 1 with a score of 0–2 (*n* = 63), group 2 with score 3–4 (*n* = 94), and group 3 with score ≥ 5 (*n* = 81). Kaplan–Meier and log-rank test methods and univariate and multivariate modeling with Cox regression analysis were used to determine significant predictors of recurrence-free (RFS), disease-specific (DSS), and overall survival (OS).

Results: Median follow-up time for the study cohort was 54 months, and median age was 65 years. Stage IIIC was the most common stage (69%), and endometrioid EC was the most common histological type (57%). The three groups were well-balanced in clinicopathological, surgical, and adjuvant therapies except for less utilization of adjuvant chemotherapy in group 3 (*P* = 0.01). The 5-year OS in group 3 was significantly lower than those in groups 1 and 2 (23% vs 65% and 51%, respectively) (*P* = 0.002). Similarly, 5-year RFS was 54%, 41%, and 33% (*P* = 0.04), and DSS was 65%, 54%, and 35% (*P* = 0.03) for AACCI groups 1, 2, and 3, respectively. On multivariate analyses for the entire cohort, AACCI group 3, cervical stromal involvement, positive peritoneal cytology, and higher tumor grade were predictors for shorter OS (*P* < 0.01). Cervical stromal involvement and higher grade were independent predictors for worse RFS and DSS (*P* < 0.05). In addition, positive cytology, lymphovascular space invasion, and stage IIIC2 were significantly detrimental for RFS (*P* < 0.05).

Conclusion: Our study suggests that comorbidity burden as measured by AACCI score is an independent strong predictor of worse OS in women with FIGO stage III EC. Women with higher AACCI are less likely to receive adjuvant chemotherapy.

Comorbidity score can skew survival endpoints for women with advanced EC and thus should be considered in the design of future prospective studies.

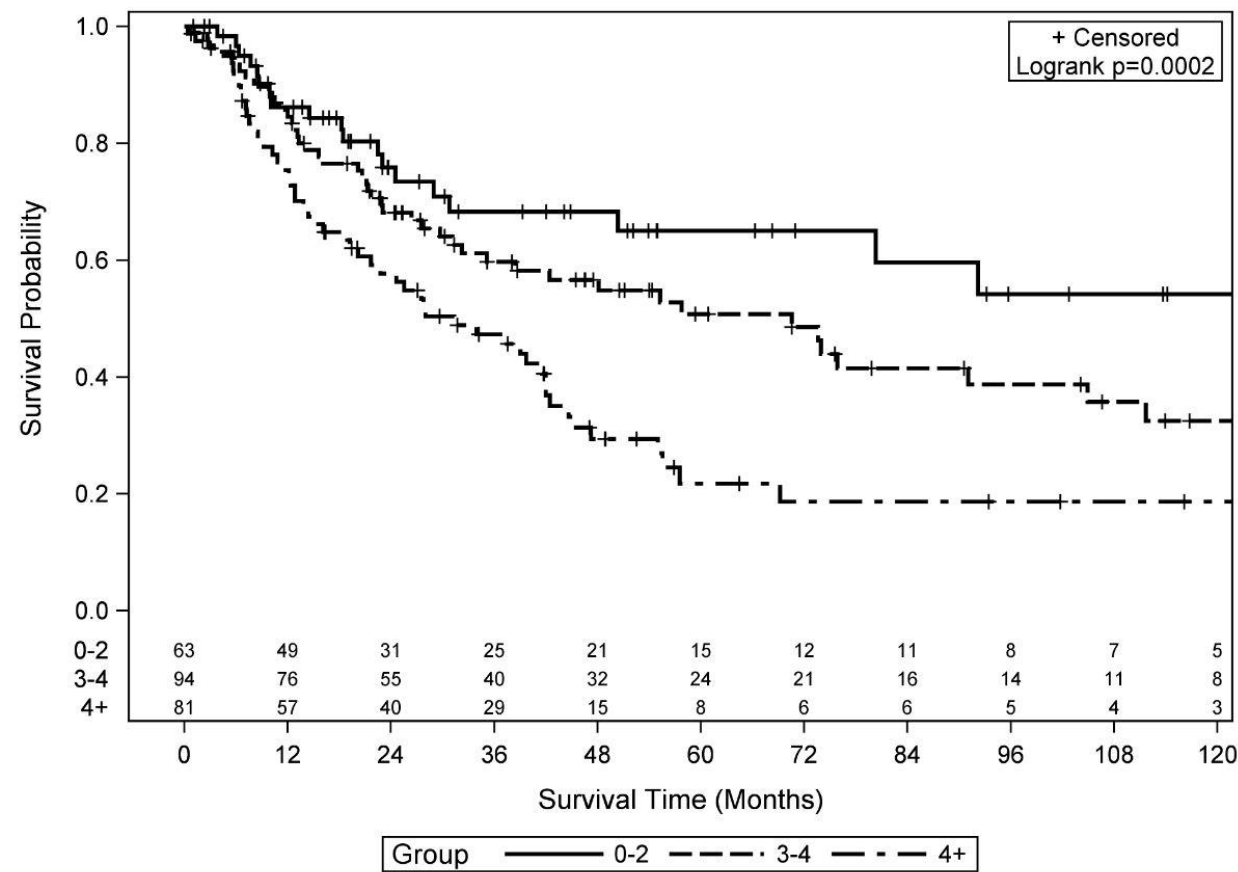


Fig. 1.

335 - Poster Session

Should ovaries be conserved in low-risk endometrial cancer?

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Objective: Cardiovascular disease is the leading cause of death in women with endometrial cancer. Removal of the ovaries prior to the age of 65 increases the risk of cardiovascular death. Should we consider retention of the ovaries in women with endometrial cancer as a strategy to improve overall survival?

Method: We performed a review of all cases of uterine cancer at our institution between January 2007 and May 2017. Pathology reports on all patients were reviewed. Data collected included patient age and BMI, procedure performed, grade and depth of invasion of uterine cancer, histology, adnexal involvement, lymphatic involvement, and any other evidence of metastatic disease.

Results: A total of 779 underwent removal of the uterus, tubes, and ovaries. Of these, 435 (56%) had lymphadenectomy. The mean age was 59.4 years (23–89); 59% of tumors were grade 1, 16% grade 2, and 25% grade 3. Tumor histology was 82% endometrioid, 9% serous, 5.4% carcinosarcoma, 3% clear cell, and less than 1% undifferentiated, mucinous, or adenosquamous cancer. Adnexal involvement with uterine cancer was found in 99 women (12.7%). Of these, 58 (7.4% of total) had ovarian involvement. In 35/58 (60%) the ovaries were grossly involved. In 23/58 (40%) only microscopic disease was identified. If Mayo criteria for avoidance of lymphadenectomy (G1,2 <50% invasion) were applied to oophorectomy, the incidence of microscopic ovarian metastases was 3/779 women (0.4%). This is comparable to the rate of lymph node metastasis with the same criteria (0.8%).

Conclusion: These data suggest that ovarian preservation with bilateral salpingectomy may be a reasonable option for women with low-risk uterine cancer and grossly normal appearing ovaries. Such a strategy may reduce all-cause mortality for these women.

Table 1. Pathology of 23 cases with only microscopic ovarian involvement.

Carcinosarcoma		7	30.4%
Serous		5	21.7%
Clear cell		2	8.6%
Endometrioid		9	39.1%
	Grade 1	5	55.5%
	Grade 2	1	11.1%
	Grade 3	3	33.3%
	Invasion >50%	5	55.5%

336 - Poster Session

Uptake of sentinel lymph node procedures in women with vulvar cancer over time in population-based study

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Objective: To evaluate the increase in sentinel lymph node (SLN) procedures over time and the associated factors in women with vulvar cancer.

Method: This retrospective population-based cohort study includes women diagnosed with invasive squamous cell cancer of the vulva identified in the provincial cancer registry between 2007 and 2016. Patients who underwent an SLN procedure were compared to those who had complete groin node dissection (GND). Multivariable analysis was used to identify factors associated with having an SLN procedure.

Results: A total of 1,385 patients with vulvar cancer were identified. Among the 1,079 patients who had a surgical procedure, the rate of groin node assessment was 68% ($n = 732$). SLN was done in 52% vs GND in 48%. Mean age was 66 years ($SD \pm 14.6$), 50% had associated comorbid conditions, and 92% had their procedures by gynecologic oncologists (GYNONC) at high-volume gynecologic cancer centers. When comparing those who had SLN versus GND, the rate of SLNs was significantly different by year of diagnosis ($P < 0.001$), associated comorbidity ($P < 0.001$), and by institution ($P < 0.0001$). The rate of SLNs by institution with GYNONC were variable and ranged from 32% to 79% among 9 centers. There were no differences in age, income quintile, and urban/rural residence. Over the study period, the proportion of SLN procedures increased from 30.1% (95% CI 18.9–45.6) in 2008 to 65.2% (95% CI 36.5–107.6) in 2016 ($P < 0.001$). On multivariate analysis, factors significantly associated with having an SLN procedure were more recent year of diagnosis (OR 7.9, 95% CI 2.7–23.5, $P < 0.001$) associated comorbid conditions (OR 2.7, 95% CI 1.5–5.0, $P = 0.002$), and institution. When compared to the institution with the lowest rate of SLNs, only two centers had a significant increased association with having an SLN procedure (OR 12.3, 95% CI 5.6–26.8, $P < 0.0001$ and OR 3.7, 95% CI 1.7–8.5, $P < 0.0001$). Age and income quintile were not significant.

Conclusion: Overall, the proportion of SLN procedures in women with vulvar cancer has increased over time. Factors significantly associated with having an SLN procedure include year of diagnosis, associated comorbid conditions, and institution. Although SLN is becoming the standard of care in vulvar cancer, the uptake of SLNs is not uniform as demonstrated by the wide variability in SLN rates per institution. Research into explanations and methods to counteract these are needed.

337 - Poster Session

Stratified follow-up for endometrial cancer according to characteristics of the tumor

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Objective: As the number of women who survive endometrial cancer rises, we explore the role and cost-effectiveness of stratified follow-up. Tumour characteristics can be used to individualise patient follow-up.

Method: This was a retrospective analysis of all women diagnosed with endometrial cancer 2005–2015 ($n = 459$). The Cox regression model was used to evaluate any independent prognostic factors associated with relative survival and recurrence. The cost of a routine follow-up visit was £104.

Results: A total of 411 cases were analysed. Overall survival at five years was 79%; 7.3% (30) women had a recurrence, and 90% of recurrences occurred within 3 years, 43% in the first year. The rate of recurrence in stage 1 endometrial cancer was 5.9%, comparable to other studies. Pelvic recurrent disease was diagnosed in 11 women. Eight women with recurrence had salvageable disease that was amenable to surgery or radiotherapy; two of these women had no symptoms. A total of 2,545 appointments were carried out for women with stage 1 and 2 cancers during the study period. Only 5 (1.2%) asymptomatic recurrences were detected at these appointments. Routine follow-up identified one woman with an asymptomatic recurrence for every 509 appointments with a cost of £52,936 for every recurrence detected. Multivariate analyses showed that the risk of death and recurrence was increased by two- and fourfold in high-grade cancers (HR 2.87, 1.48–5.53, $P = 0.002$; HR 4.48, 1.76–11.44, $P = 0.002$), respectively. The absence of lymphovascular space invasion was associated with a statistically significant reduction in the risk of death in women with recurrence (HR 0.03, 0.002–0.53, $P = 0.016$). High-grade disease was also associated with a fivefold increase in death in women who had recurrence, although this failed to reach statistical significance probably because of the small subgroup of patients (HR 5.49, 0.62–48.56, $P = 0.126$).

Conclusion: A risk-stratified pathway of posttreatment management is necessary to release resources to diagnosing more new patients and supporting those with metastatic and complex disease. Grade 3 disease, presence of lymphovascular space invasion, and a tumour-free distance from the serosa of <1.75 mm may be risk factors for death and recurrence of endometrial cancer that can help to stratify women for follow-up. Women with stage 1 or 2 endometrial cancer and these characteristics may benefit from follow-up, whilst others would be suitable for self-management.

338 - Poster Session

The trend, feasibility, and safety of salpingectomy as a form of permanent sterilization

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Objective: The study objective was to assess the change in rate of laparoscopic salpingectomy for sterilization after the release of the November 2013 Society of Gynecologic Oncology (SGO) Clinical Practice Statement and the January 2015 American College of Obstetricians and Gynecologists (ACOG) Committee Opinion: Salpingectomy for Ovarian Cancer Prevention. It was hypothesized that there would be an increase in salpingectomy as a percentage of total laparoscopic sterilizations performed without an increase in complications when compared to conventional bilateral tubal ligation (BTL).

Method: A retrospective cohort chart review was performed at two university-affiliated hospitals using procedure codes to identify all women 21 years or older who underwent laparoscopic permanent sterilization by either salpingectomy or BTL between April 2013 and September 2016. Pertinent medical and surgical histories and demographic data were collected. Method of sterilization, surgical times, estimated blood loss (EBL), and complication rates were also reviewed. Exclusions included postpartum sterilizations; sterilizations at time of other surgical procedure; women with breast, uterine, or ovarian cancer; or known BRCA mutation carriers. Differences in medical and surgical characteristics and demographics were examined using the Student t test or Wilcoxon rank sum test for continuous variables and the χ^2 test or Fisher exact test for categorical variables.

Results: There were 390 sterilization procedures identified: 62% were BTLs, while 38% were salpingectomies. Salpingectomies dramatically increased from 5% to 7% in 2013–2014 to 80% by 2016. There was no significant difference when intraoperative or postoperative complications or EBL were compared. Mean procedure time was 54 minutes for salpingectomy compared to 43 minutes for BTL ($P < 0.0001$). Salpingectomy was more likely to require three ports compared to two ports for BTL ($P < 0.0001$). The only significant demographic difference was that more Hispanic women selected BTL than salpingectomy ($P = 0.03$).

Conclusion: The support of SGO and ACOG of salpingectomy for ovarian cancer prevention increased its utilization for sterilization. Based on this study, laparoscopic salpingectomy is a safe method of sterilization.

339 - Poster Session

Duration of exposure to select DNA-damaging therapy and the risk of secondary myelodysplastic syndrome and acute

myeloid leukemia in patients with ovarian or breast cancer in a real-world setting in the United States

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Objective: To evaluate the impact of exposure to select DNA-damaging therapies on the risk of secondary myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) among patients with ovarian cancer (OC) or breast cancer (BC) in the United States.

Method: Adult females with OC or BC between January 1, 2000, and June 30, 2014 (first observed diagnosis of OC or BC = index date) were identified from the MarketScan® Commercial and Medicare claims databases. Patients had ≥12 months of pre-index and ≥1 month of post-index continuous health plan enrollment. The incidence of MDS and AML per 1,000 person-years was assessed using International Classification of Diseases (ICD-9) codes over a variable-length follow-up period for each cancer cohort and separately for patients exposed to select DNA-damaging therapies. Alkylating agents, antimetabolites, platinum-based antineoplastics, or topoisomerase inhibitors were included as DNA-damaging therapies. The association between duration of exposure to these therapies and secondary MDS or AML during follow-up was assessed using Poisson regression.

Results: The study identified 23,862 OC patients (mean [standard deviation, SD] length of follow-up 35.8 [31.4] months), and 281,473 BC patients (mean [SD] length of follow-up 46.0 [37.2] months). During follow-up, 56.6% of OC patients utilized DNA-damaging therapy, with a mean (SD) exposure duration of 116.9 (115) days. Within the BC cohort, 28.1% of patients utilized a DNA-damaging therapy, with a mean (SD) exposure duration of 84.2 (168) days. The incidence of MDS or AML among patients with OC or BC was 2.77 and 1.44 per 1,000 person-years, respectively. Within both cohorts, the incidence of MDS and AML was significantly higher among patients exposed to DNA-damaging therapy than in those not exposed. Increased duration of exposure to DNA-damaging therapy was associated with significantly increased risk of developing MDS or AML during follow-up among patients with OC or BC compared to those with no exposure (see Table 1).

Conclusion: Within this U.S. commercially insured population, patients with OC or BC who were exposed to select DNA-damaging therapies had increased risk of developing secondary MDS or AML.

Table 1. MDS/AML incidence rate ratios by duration of exposure to DNA-damaging therapy^a.

Duration of Exposure to DNA-Damaging Therapy	Incidence Rate Ratio for MDS/AML (95% CI) ^b	P Value versus 0 days
Patients with OC (n = 23,862)		
0 days	1.00	
1–180 days	2.10 (1.20–3.69)	0.010
181+ days	2.27 (1.13–4.53)	0.021
Patients with BC (n = 281,473)		
0 days	1.00	
1–180 days	2.62 (2.22–3.09)	<0.001
181+ days	1.86 (1.47–2.36)	<0.001

^a Model estimated was a generalized linear model with Poisson error distribution, log link, and log of exposure as an offset. Additional model covariates: class of DNA-damaging therapy, radiation treatment, National Cancer Institute modification of the Charlson Comorbidity Index, number of unique medications filled, age, health plan type, and geographic region.

^b Per 1,000 person-years.

340 – Poster Session

Factors associated with rates of venous thromboembolism in patients with advanced stage ovarian cancer undergoing neoadjuvant chemotherapy and the relationship with patient overall survival

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Objective: Rates of utilization of neoadjuvant chemotherapy (NACT) are increasing in advanced-stage ovarian cancer. Studies have shown a decrease in venous thromboembolism (VTE) in patients who receive thromboprophylaxis with solid tumors while undergoing ambulatory chemotherapy. This study determines the rate and risk factors associated with VTE and the impact of VTE on survival in the NACT population.

Method: Patient demographics and survival data were collected on all patients with stage IIIC or stage IV ovarian cancer who completed NACT and an interval cytoreductive surgery at two academic institutions between January 2010 and June 2015. Clinical variables were correlated using χ^2 and Student t tests for bivariate analyses. Multivariable regression analysis was conducted to test for the effect of the clinical variables on development of a VTE. Overall survival and progression-free survival (PFS) hazard ratios were calculated using log rank tests.

Results: There were 295 total patients who completed NACT and had a subsequent interval cytoreduction. The majority, 165 (55.93%), had stage IIIC disease. Of these patients, 13 (4.41%) had a VTE at time of cancer diagnosis or within the prior year. Of the 282 remaining patients, 21 (7.46%) had a VTE while undergoing NACT. Patients were diagnosed with deep venous thrombosis (46%), pulmonary embolism (45%), or both (9%). In bivariate analyses age, non-white race, and low preoperative albumin were all significantly associated with a VTE event while undergoing NACT. In multivariate analyses non-white race and low preoperative albumin were significantly associated with a VTE event while undergoing NACT. Kaplan-Meier curves showed no difference in PFS between those who had a VTE and those who did not while undergoing NACT. There was no difference in PFS or OS when comparing patients who did and did not develop a VTE while undergoing NACT.

Conclusion: There is a growing population of patients undergoing NACT prior to surgical intervention for advanced-stage ovarian cancer who are at risk of VTE. This study suggests that VTEs are common in this population and potentially predicts a worse OS. These patients may benefit from VTE prophylaxis while undergoing NACT.

341 - Poster Session

Predicting thromboembolism after total abdominal hysterectomy in gynecologic oncology patients using machine learning: A national database study

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Objective: Current practice guidelines and preoperative deep vein thrombosis (DVT) risk scores for DVT prophylaxis have not been specifically developed for gynecologic oncology patients. The purpose of this study was to determine risk factors and create a machine learning model to predict in-hospital DVT after total abdominal hysterectomy (TAH) in patients with endometrial, ovarian, and cervical cancer utilizing a large, publicly available, national database.

Method: The HCUP Nationwide Inpatient Sample (NIS) was evaluated for the years 2002 to 2014. Patients who received TAH for endometrial, ovarian, or cervical cancer were identified by ICD-9 CM codes. These data were used to train and validate a DVT prediction model using a random forest (RF) model. Logistic regression was used to determine the relationship of demographic risk factors and DVT. Statistical significance was set at $P < 0.05$.

Results: A total of 615,476 patients were included, of which 7,590 (1.2%) developed postoperative DVT. Patients who developed DVT were significantly older (62.0 vs 57.7 years, $P < 0.0001$) and had greater Charlson Comorbidity Index (5.5 vs 3.3, $P < 0.0001$). The DVT rate was similar between white and non-white patients (1.26% vs 1.12%, $P = 0.4010$). Concurrent lymph node dissection was not associated with increased DVT rate (1.4% vs 1.2%, $P = 0.4899$). DVT was associated with increased length of stay (13.9 vs 4.1 days, $P < 0.0001$), total hospital charges (\$115,942 vs \$36,898, $P < 0.0001$), and in-hospital mortality rate (4.4% vs 0.4%, $P < 0.0001$). Using a threshold of 13% predicted DVT risk to separate high- and low-risk patients, the RF model correctly classified 50% of postoperative DVT patients as high risk and 84.2% of patients who did not develop DVT as low risk. The model has an AUROC (c-statistic) of 0.74 in predicting DVT.

Conclusion: This study represents the highest reported accuracy for DVT prediction and the first model developed specifically for gynecologic oncology patients. Further, this study identifies demographic risk factors for in-hospital DVT and describes the

adverse hospital outcomes of DVT patients. More accurate DVT risk prediction will better inform clinicians which patients require aggressive DVT prophylaxis, reducing morbidity and mortality in gynecologic oncology patients through better targeted use of long-term anticoagulation.

342 - Poster Session

Performance of hysterectomy by very low-volume surgeons and their outcomes

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Objective: There is a moderate association between surgeon procedural volume and outcomes for hysterectomy. However, little is known about the outcomes of patients treated by surgeons who perform a very low number of surgeries. We examined performance of hysterectomy by very-low-volume (VLV) surgeons (1 case per year) and their outcomes.

Method: All women who underwent hysterectomy (abdominal, robotic-assisted, laparoscopic, or vaginal) in New York state between 2000 and 2014 were captured in the New York Statewide Planning and Research Cooperative System. Surgeons were classified based on the average annual procedural volume for each modality of hysterectomy separately. A VLV surgeon was defined as a physician performing 1 procedure per year. Multivariable models were used to examine the association between VLV surgeon status and intraoperative, surgical site, and medical complications as well as prolonged length of stay and excessive charges (>75th percentile for each).

Results: A total of 441,660 patients were identified. Among surgeons performing hysterectomies, VLV surgeons accounted for 41.0% of the abdominal, 43.4% of the robotic-assisted, 43.6% of the laparoscopic, and 39.9% of the vaginal surgeries. The overall complication rate was higher for VLV surgeons compared to higher volume surgeons for each route of hysterectomy: abdominal (RR = 2.04, 95% CI 1.93–2.15), robotic-assisted (RR = 2.52, 95% CI 1.95–3.25), laparoscopic (RR = 1.90, 95% CI 1.64–2.19), vaginal (RR = 1.26, 95% CI 1.07–1.47) (Table 1). The findings were similar when intraoperative, surgical site, and medical complications were analyzed separately. Similarly, the mortality rates were higher for VLV surgeons compared to higher volume surgeons for each route of hysterectomy: abdominal (RR = 4.33, 95% CI 3.51–5.34), robotic-assisted (RR = 6.74, 95% CI 1.30–34.80), laparoscopic (RR = 8.25, 95% CI 2.92–23.31), and vaginal (RR = 6.12, 95% CI 1.84–20.34) hysterectomies. Transfusion rates, excessive charges, and prolonged length of stay were also significantly higher in VLV versus higher volume surgeons.

Conclusion: A substantial number of hysterectomies are performed by VLV surgeons. Performance of hysterectomy by VLV surgeons is associated with increased complication rates, mortality, and resource utilization.

Table 1. Outcomes per hysterectomy type at physician level.

Outcomes/ Complication	Risk Ratio for Each Outcome for Very-Low-Volume Surgeons Compared to Surgeons Performing More Than 1 Hysterectomy per Year			
	Abdominal <i>n</i> = 1	Robotic-Assisted <i>n</i> = 1	Laparoscopic <i>n</i> = 1	Vaginal <i>n</i> = 1
Mortality	4.33 (3.51–5.34)	6.74 (1.30–34.80)	8.25 (2.92–23.31)	6.12 (1.84–20.34)
Intraoperative complications ^a	2.44 (2.22–2.67)	3.11 (2.19–4.43)	1.96 (1.56–2.46)	1.22 (0.93–1.60)
Surgical site complications ^b	2.11 (1.95–2.29)	3.63 (2.43–5.43)	2.11 (1.65–2.69)	1.25 (0.92–1.71)
Medical complications ^c	2.26 (2.10–2.43)	2.80 (1.97–3.96)	2.17 (1.76–2.67)	1.43 (1.15–1.76)
Any complication ^d	2.04 (1.93–2.15)	2.52 (1.95–3.25)	1.90 (1.64–2.19)	1.26 (1.07–1.47)
Transfusion	2.02 (1.92–2.12)	3.11 (2.37–4.09)	1.68 (1.46–1.94)	1.55 (1.35–1.79)

Excessive charges ^e	2.11 (2.01–2.21)	1.72 (1.44–2.06)	1.43 (1.31–1.56)	1.31 (1.21–1.42)
Prolonged length of stay ^e	2.41 (2.29–2.53)	1.63 (1.37–1.93)	2.05 (1.86–2.26)	1.34 (1.23–1.45)

^a Intraoperative injury: bladder, ureteral, intestinal or vascular injury.

^b Surgical site complications: hemorrhage, wound infection, abscess, GI complication.

^c Medical complications: DVT, PE, shock, MI, CVA, renal or respiratory failure, stroke, sepsis, pneumonia.

^d Any complication: intraoperative, surgical site, or medical complication.

^e Changes of length of stay above the 75th percentile.

343 - Poster Session

Decision aids in gynecologic oncology: An initial survey

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Objective: Randomized controlled trials have shown that decision aids increase patient comprehension and decisional participation, improve quality and efficiency of decision making, and decrease decisional conflict. Unfortunately, high-quality decision aids are rare in gynecologic oncology. We sought input from practicing gynecologic oncologists to prioritize high-impact clinical decisions with potential benefit from a decision aid.

Method: Using international Delphi consensus process guidelines, we identified and developed a scoping statement for 5 common scenarios for clinical decision-making: (1) CA-125 in ovarian cancer surveillance, (2) clinical trial enrollment with advanced disease, (3) hysterectomy in *BRCA1* patients, (4) dose-dense neoadjuvant chemotherapy, and (5) bilateral salpingo-oophorectomy in premenopausal grade 1 endometrial cancer. We designed a 22-item web-based questionnaire for gynecologic oncologists practicing in the southeastern United States. Participation was voluntary, and the study was given institutional review board exemption.

Results: We received 32 responses from 140 surveyed (23%). Seventy percent of respondents identified their practice as academic and 30% as nonacademic. Most reported practicing for 11–20 years (41%), while 26% and 33% reported practicing 1–10 years and more than 20 years, respectively. When considering whether women with advanced gynecologic malignancies should participate in clinical trials, 41% of respondents were “very interested” in using a decision aid for this scenario (all scenario range 11%–41%). Eighty-nine percent responded that a decision aid would be “somewhat” or “very” useful in promoting good decisions in this scenario (all scenario range 57%–89%). Most (72%) thought a decision aid for this scenario was “likely” or “very likely” to increase clinical trial enrollment. And when asked to rank all 5 scenarios, 37% of respondents ranked this scenario as highest priority (all scenario range 4%–37%).

Conclusion: For these 5 clinical scenarios, a decision aid involving clinical trial enrollment was deemed most interesting, most useful, and highest ranked according to gynecologic oncologists who participated in our study. This work serves as foundation for the ongoing development of a high-quality decision aid regarding clinical trial enrollment in gynecologic oncology patients.

344 - Poster Session

Significance of malignant and atypical cells in peritoneal cytology on survival of women with stage I-II endometrioid endometrial cancer

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Objective: To examine survival outcome of women with stage I–II endometrioid endometrial cancer whose peritoneal cytology showed malignant or atypical cells.

Method: This is a multicenter retrospective study examining 1,668 women with stage I–II endometrioid endometrial cancer who underwent primary hysterectomy-based surgery with available peritoneal cytology results between 2000 and 2015. Results of peritoneal cytology were correlated to clinicopathological characteristics and oncological outcome.

Results: Malignant and atypical cells on peritoneal cytology were seen in 125 (7.5%) and 58 (3.5%) patients, respectively, significantly correlated to race and lymphovascular space invasion (LVSI) (both, $P < 0.001$). On multivariate analysis, presence of malignant cells on peritoneal cytology was independently associated with decreased disease-free survival (5-year rate 87.4% vs 93.8%, HR 3.40, 95% CI 1.77–6.53, $P < 0.001$), whereas atypical cells had a marginal significance (87.7% vs 93.8%, HR 2.30, 95% CI 0.97–5.43, $P = 0.059$). Presence of malignant or atypical cells on peritoneal cytology was associated with an increased risk of distant recurrence (5-year rate, 9.1%, 8.2%, and 3.6%, $P = 0.001$) but not local recurrence ($P = 0.31$) compared to those without atypical or malignant cells. Among cases with malignant or atypical cells on peritoneal cytology but no LVSI, postoperative chemotherapy use was associated with decreased distant recurrence compared to no chemotherapy treatment (5-year rate, 0% vs 11.9%, $P = 0.022$).

Conclusion: Our study suggests that presence of malignant or atypical cells in peritoneal cytology may be a prognostic factor for decreased survival in women with stage I–II endometrioid endometrial cancer. Efficacy of adjuvant chemotherapy in this population warrants further investigation.

345 - Poster Session

Venous thromboembolism (VTE) in ovarian cancer during neoadjuvant chemotherapy: Is it time to start prophylaxis?

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Objective: To assess clinical characteristics and timing of venous thromboembolism (VTE) in patients with ovarian, fallopian tube, or primary peritoneal cancer undergoing neoadjuvant chemotherapy (NACT) and effects on survival outcomes.

Methods: A retrospective cohort study was performed from January 2013 to September 2017 at our institution. Patients with advanced disease were triaged by laparoscopic scoring assessment to determine primary resectability at tumor reductive surgery. Patients with medically inoperable or distant metastatic disease received neoadjuvant chemotherapy (NACT). Clinical and demographic data were correlated with occurrence of VTE. The diagnosis and timing of VTE (pretreatment or during NACT events) were evaluated and correlated with OS and PFS. Prognostic factors were compared by using χ^2 or Fisher exact tests ($P \leq 0.05$). PFS and OS were estimated using the Kaplan-Meier method.

Results: A total of 354 patients who received at least 3 cycles of NACT were included in this analysis, 88% with serous histology and 12% with other histologies. A total of 44 (12.4%) patients were diagnosed with VTE, 18 (40%) prior to treatment and 26 (60%) during NACT. Patients 65 years and older were at a greater risk of VTE (OR = 2.01, 95% CI 1.03–3.94, $P = 0.042$). When correlated with timing of VTE, age was associated with presence of VTE before start of treatment ($P = 0.017$) but not during NACT ($P = 0.27$). The occurrence of VTE was associated with a significantly worse PFS of 10 versus 12.7 months (HR = 2.18, 95% CI 1.41–3.37, $P = 0.001$). The occurrence of VTE was also associated with a significantly worse OS of 28.4 versus 42.5 months (HR = 2.38, 95% CI 1.39–4.05, $P = 0.002$). The correlation with timing of VTE revealed that diagnosis during NACT had a worse impact on PFS ($P < 0.001$), although not before treatment ($P = 0.205$). A worse OS was also correlated with VTE diagnosed during NACT ($P < 0.001$) but not prior to treatment ($P = 0.434$).

Conclusion: The occurrence of VTE was a poor prognostic factor in patients with advanced ovarian cancer undergoing NACT and led to worse survival outcomes. These findings have implications for considering thromboembolic prophylaxis during chemotherapy.

346 - Poster Session

AJCC versus FIGO staging of cervical cancer to predict disease severity

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Objective: Disease staging is a clinically based measure of severity that uses objective criteria to assess the stages of disease progression. Recent studies demonstrate that disease stage explains significant variations in resource utilization and cost. This

study compares the effectiveness of FIGO versus American Joint Committee on Cancer (AJCC) staging of locally advanced cervical cancer in predicting progression-free survival (PFS) and disease severity.

Method: We identified all women treated for FIGO stage II–IVA cervical cancer from 2008 to 2016. Stage was assigned retrospectively based on examination, pathology, and imaging reports prior to treatment initiation. Kaplan-Meier survival curves, log rank tests, and hazards ratios were calculated with $P < 0.05$ considered significant.

Results: A total of 265 eligible women were identified. Median age was 48 years (range 21–85 years); 82% were squamous cell histology versus 11% adenocarcinoma. In the FIGO system, 163 (62%) were stage II, 80 (30%) stage III, and 22 (8%) stage IVA. In the AJCC system, 77 (29%) were stage II, 114 (43%) stage III, and 74 (28%) stage IV. One-fifth of the patients were AJCC stage IVB due to paraaortic lymph node metastases: 17% of FIGO stage II, 31% of FIGO stage III, and 27% of FIGO stage IVA. Primary treatment was uniform across stages: 78% chemo-radiation, 16% chemo-radiation with adjuvant chemotherapy, and 5% radiation alone; 31% received extended field radiation. With a median follow-up of 19 months, median PFS was 17 months (FIGO stage II), 8 months (III), and 9 months (IVA). Both FIGO ($P = 0.0109$) and AJCC ($P = 0.0061$) stage were predictors of PFS, although FIGO lost significance when stratified by substage ($P = 0.0509$). Age, race, histology, and BMI did not correlate significantly with PFS. Positive paraaortic nodes correlated with PFS for FIGO stage II (HR = 2.6, 95% CI 1.19–5.80, $P = 0.0174$) but not stage III or IVA patients. When stratifying tumors by volume, we found that the base 10 logarithm was significantly correlated to survival ($P < 0.001$). See Figure 1.

Conclusion: AJCC staging is a better predictor of PFS than FIGO and would result in upstaging of one-third of the patients. In our study cohort, 22% were upstaged to stage IVB. Incorporation of paraaortic lymph node status is urgently needed to improve outcomes for women with cervical cancer.

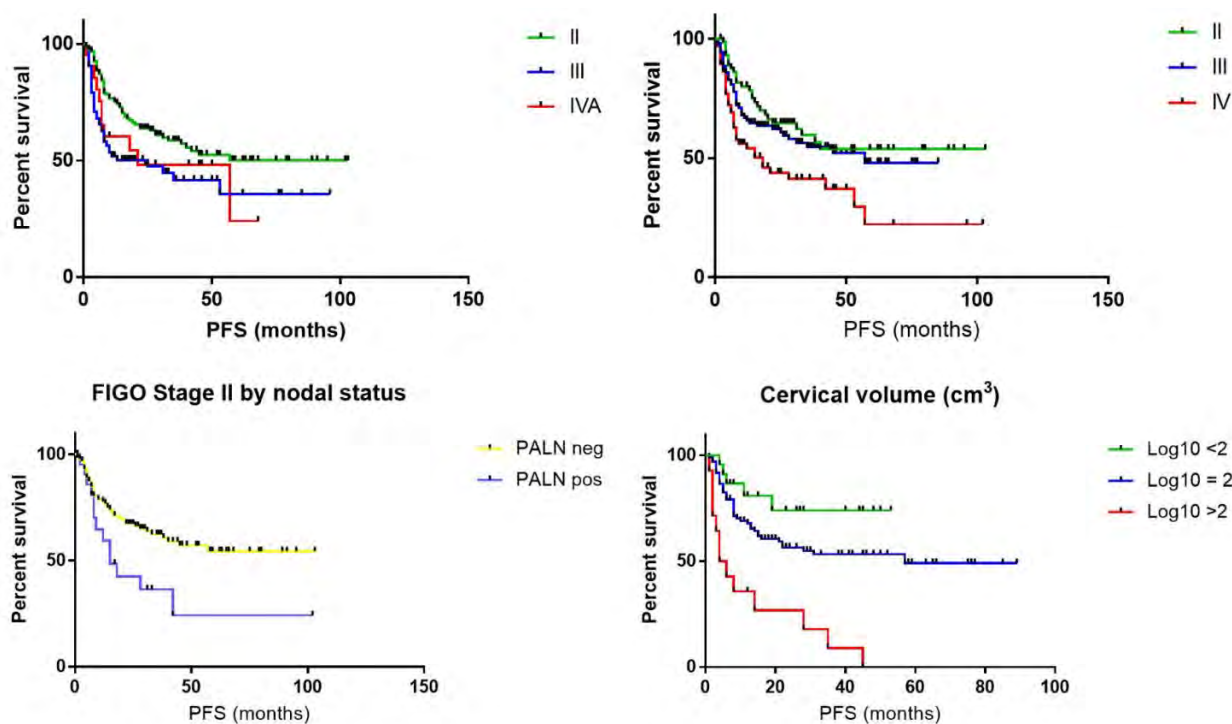


Fig. 1.

347 - Poster Session

National patterns of adjuvant treatment for stage I uterine serous carcinoma: A SEER-Medicare analysis

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Objective: To determine national patterns of care in the delivery of adjuvant chemotherapy (CT) and radiation therapy (RT) for stage I uterine serous carcinoma (USC).

Method: Stage I USC patients older than 65 years treated with hysterectomy between the years 1999 and 2011 were identified from the SEER–Medicare database. Demographic, clinical, and pathologic data were collected. Descriptive statistics were performed, and the effect of treatment modality on survival was analyzed using Kaplan–Meier estimates.

Results: A total of 682 cases of stage I USC were identified; 44.3% ($n = 302$) received no adjuvant treatment, including 30.1% of those with stage IB disease; 18.9% received RT alone; and 22.7% received CT alone. The remainder received a combination of CT/RT, most commonly concurrent CT/RT (7%), and then CT followed by RT (5.4%). Rates of adjuvant treatment differed significantly by age ($P = 0.0003$), and 56.9% of patients older than 80 years received no treatment. As age increased, the frequency of the utilization of RT alone increased and CT alone decreased. There was no difference in treatment rates by marital status, race, or Charlson comorbidity score. Utilization of RT alone decreased between 1999 and 2008 and between 2009 and 2011 (23.9% vs 8.29%, respectively), while CT alone (18.5% vs 31.8%) and combination CT/RT increased (11.6 vs 19.4%, respectively) ($P < 0.001$). Patients residing in the Northeast ($P = 0.0035$) and with a higher socioeconomic status ($P = 0.001$) were more likely to receive treatment. There was an association between an increased number of lymph nodes removed at lymphadenectomy and a decreased frequency of utilization of adjuvant treatment ($P = 0.0026$). In the unadjusted model, both CT only and concurrent CT/RT had improved survival compared to no treatment (HR = 0.62, 95% CI 0.44–0.86 and HR = 0.55, 95% CI 0.31–0.97, respectively). After adjusting for age, year of diagnosis, nodes examined, SES, and region, only CT alone compared to no treatment was significant (HR = 0.70, 95% CI 0.50–0.98). See Figure 1.

Conclusion: There is variability in national practice patterns of adjuvant treatment for stage I USC, including 44.3% of patients in this cohort not receiving any adjuvant treatment. Older patients, a lower socioeconomic status, geographical location, and patients with increased number of lymph nodes evaluated were less likely to receive treatment. CT has increased in frequency in the more recent decade, while the use of RT alone has decreased. Survival is improved with the addition of CT.

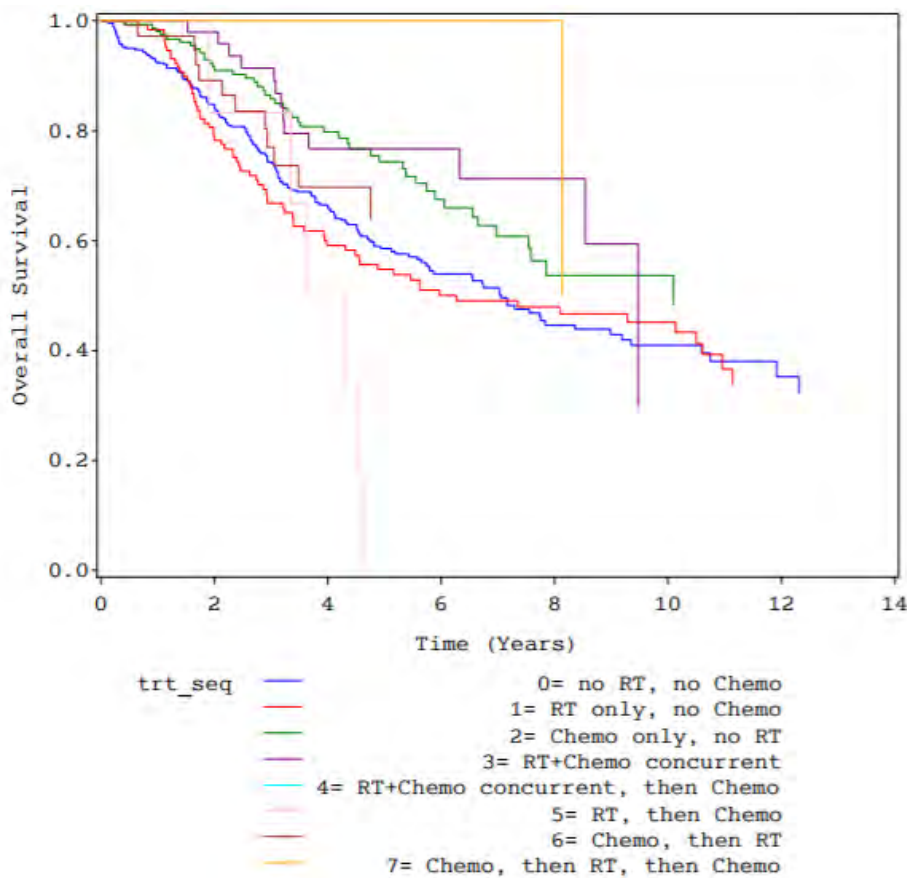


Fig. 1. Overall Survival and Type of Adjuvant Treatment for Stage I USC.

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Objective: Surgical site infections (SSIs) delay recovery and increase costs. Characterizing pathogens associated with SSI can guide perioperative infection prophylaxis. We present patterns in hysterectomy-related SSI microbiology before and after implementation of a bundled SSI prevention intervention.

Method: A perioperative infection prevention bundle was implemented January 19, 2016. Charts for patients who underwent hysterectomy from January 19, 2016, to January 18, 2017, were retrospectively reviewed. Patients with surgery prior to implementation (pre-bundle) were compared to those with surgery after implementation (post-bundle). All SSIs were identified, and culture results were reviewed. The Fisher exact test was used for analysis.

Results: We identified 178 pre-bundle and 180 post-bundle patients. A total of 20 SSIs occurred with a lower incidence in the post-bundle group (14/178 pre- vs 6/180 post-bundle, $P = 0.05$). Infections were polymicrobial in 9/20 (45%) and monomicrobial in 7/20 (35%). No growth occurred in 2 cultures. A higher rate of monomicrobial infections occurred in the pre- versus post-bundle group (53.8% vs 0%, $P = 0.04$). We identified 23 infectious species in 14 pre-bundle SSI cultures and 13 species in 6 post-bundle cultures. Gram-positive bacteria were present in 11/23 (47.8%) pre- and 9/13 (69.2%) post-bundle cultures. Gram-negative bacteria were present in 8/23 (34.7%) pre- and 3/13 (23%) post-bundle cultures. Anaerobic bacteria were present in 11/23 (47.8%) pre- and 9/13 (69.2%) post-bundle cultures. Regarding preoperative antibiotic prophylaxis, a single agent (cefazolin, cefoxitin, or clindamycin) was used in 154/178 (86.5%) pre-bundle cases. In the post-bundle group, a multiagent regimen (cefazolin with metronidazole) was used in 162/180 (90%). Multiagent antibiotic prophylaxis was used more frequently in the SSI post-bundle group (5/6) than in the pre-bundle group (1/14) ($P = 0.002$). See Table 1.

Conclusion: Many SSIs following hysterectomy at a cancer center are polymicrobial. Anaerobic bacteria are an important cause of SSI after hysterectomy and should be considered in the development perioperative prophylaxis regimens. Addition of metronidazole to the intervention group may contribute to the observed decrease in SSI rates through improved anaerobic coverage. Perioperative antibiotics may exert selective pressure on SSI pathogens over time.

Table 1. Pathogen characteristics and prevalence in surgical site infection (SSI) cultures before and after surgical site infection prevention bundle ($n = 36$ cultures collected from 20 SSIs).

Pathogen	G+	G-	An	PRE	POST	Total
Enterococcus faecalis	x			2	1	3
Enterococcus faecium	x			0	1	1
Methicillin Sensitive Staph Aureus	x			2	1	3
Coagulase negative staphylococcus	x			2	1	3
Streptococcus agalactiae	x		x	1	1	2
Streptococcus viridans	x			0	2	2
Peptostreptococcus magnus	x		x	1	0	1
Eggerthella lenta - formerly Eubacterium lentum	x		x	2	0	2
Diphtheroid	x			0	1	1
Propionibacterium granulosum	x		x	0	1	1
Mixed gram positive	x			1	0	1
Bacteroides fragilis		x	x	3	0	3
Pseudomonas aeruginosa		x		2	0	2
Escherichia coli		x	x	1	1	2
Bacteroides vulgatus		x	x	1	0	1
Bacteroides thetaiotaomicron		x	x	0	1	1
Proteus mirabilis		x	x	1	0	1
Enterobacter cloacae		x	x	0	1	1
Mixed anaerobic			x	1	1	2
Candida Galbrata				1	0	1

Abbreviations: G+ (Gram positive), G- (Gram negative), An (Anaerobe), PRE (pre-bundle group), POST (post-bundle group)

349 - Poster Session

Prevention of surgical site infection after hysterectomy at a cancer center

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Objective: Surgical site infections (SSIs) are linked to increased morbidity, mortality, cost, readmission, and extended hospital stay. We evaluate the outcome of a bundled intervention to reduce the incidence of SSI after hysterectomy at a cancer center.

Method: A perioperative intervention bundle was implemented on January 19, 2016. Prior established practices included patient education, 4% chlorhexidine gluconate (CHG) shower before surgery, preoperative antibiotics, 2% CHG and 70% isopropyl alcohol coverage of incisional area, and povidone iodine vaginal preparation. New interventions included universal MRSA screening, 4% CHG skin wipes on day of surgery, change to 4% CHG vaginal preparation, standardized antibiotic regimen (metronidazole IV once, cefazolin IV redosed at 4-hour intervals), glove change with separate sterile instruments for surgical closure, and CHG showers postoperative day 1 and after discharge. SSI rates were determined retrospectively in consecutive hysterectomy patients 6 months before and after bundled intervention implementation. Statistical significance was assessed by the Fisher exact test and Kruskal-Wallis test.

Results: From January 18, 2016, to January 18, 2017, we identified a cohort of 178 pre-intervention and 180 post-intervention patients. Median BMI was 31 in both groups. Mode of hysterectomy included laparoscopic (38% pre, 41% post), robotic (15% pre, 23% post), and abdominal (47% pre, 36% post) ($P = 0.052$). A colorectal procedure was performed in 3.9% pre and 8.3% post surgeries ($P = 0.122$). The incidence of SSI was 14/178 (7.9%) pre and 6/180 (3.3%) post ($P = 0.0499$). Superficial SSI rates were 6/178 (3.4%) pre and 4/180 (2.2%) post ($P = 0.54$), whereas organ space SSI rates were 8/178 (4.5%) pre and 1/180 (0.6%) post ($P = 0.019$). There was no difference in deep SSI rates (1/178 pre and 1/180 post). Mean length of stay was 3.24 (\pm SD 3.03) days pre and 2.67 (\pm SD 2.44) days post ($P = 0.053$). Readmissions decreased from 12/178 (6.7%) pre to 4/180 (2.2%) post ($P = 0.043$).

Conclusion: A bundled perioperative intervention significantly reduces SSI after hysterectomy and is associated with significantly reduced readmission and a trend toward reduced length of stay. Unique aspects of our intervention, including a CHG vaginal preparation and IV metronidazole, may improve prevention of vaginal cuff cellulitis and pelvic abscess in the deep and organ space compartments.

350 - Poster Session

Role of hyperthermic intraperitoneal chemotherapy in the management of recurrent ovarian, fallopian and peritoneal cancer

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Objective: We aimed to evaluate morbidity and mortality outcomes of hyperthermic intraperitoneal chemotherapy (HIPEC) in recurrent ovarian, fallopian tube, or primary peritoneal cancer (EOC) at a single institution.

Method: We performed a retrospective single-institution chart review evaluating patients who received HIPEC for recurrent EOC between January 2013 and June 2017. Standard statistical analysis was used.

Results: We identified 35 patients with a median age of 61 (range 33–79) years. The most common histology was high-grade serious ovarian cancer (29, 82.9%), followed by low-grade serious (2, 5.7%). The median CA-125 at time of HIPEC was 59.5 (range 4–769). The majority (24, 68.6%) had an Eastern Cooperative Oncology Group performance status of 0. Some patients had previously been treated with primary adjuvant intraperitoneal chemotherapy (7, 20%), but the majority received intravenous chemotherapy (28, 80%). HIPEC was the first regimen used after recurrence in the majority (26, 74.9%) of patients. Median operating room time was 260 minutes (range 150–780 minutes), and median estimated blood loss 300 mL (range 50–2,200 mL). Oxaliplatin was used in 31 (88.6%) cases and cisplatin in 4 (11.4%). Bowel resection (including appendectomy) was performed on 17 (48.6%) patients at the time of HIPEC surgery. More than half (18, 51.4%) received a

blood transfusion during their hospitalization. Postoperative complications included pneumonia (9, 25.7%), urinary tract infection (5, 14.3%), venous thromboembolism (2, 5.7%), and postoperative ileus (5, 14.3%). Median length of stay was 9 days (range 5–54 days). Ten patients (28.6%) were readmitted within 90 days of discharge. There were no mortalities within 90 days. The median time to outpatient chemotherapy was 49.5 days (range 25–132 days). Median progression-free survival (PFS) after HIPEC was 10.0 months with an overall survival (OS) of 19.5 months. There were no significant differences between PFS and OS in relation to platinum sensitivity, number of previous treatment regimens, and length of surgery. At time of follow-up, 10 patients were alive with disease, 13 have no evidence of disease, and 12 have died of their disease.

Conclusion: These data support that HIPEC is a reasonable treatment modality for recurrent EOC, and further studies are needed to clarify the optimal patient population and treatment regimen.

351 - Poster Session

Prospective comprehensive geriatric assessment in surgically versus non-surgically treated elderly ovarian cancer patients

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Objective: Comprehensive geriatric assessment (CGA), a set of tests that assess the physical, mental, and social well-being of the elderly patient, can assist tailoring suitable treatment for the elderly ovarian cancer patient. The aim of our study was to investigate whether CGA could differentiate between patients deemed unfit to undergo surgery and patients treated with surgery and chemotherapy.

Method: Between April 2011 and May 2017, all primary ovarian cancer patients older than 70 years had prospective CGA before treatment. CGA consisted of seven tests that assessed patients' general health, medications, activity level, cognitive function, depression, and nutrition status. CGA scores were compared between patients deemed unfit to have surgery and thus treated with chemotherapy only and patients treated with a combination of surgery and chemotherapy.

Results: Altogether, 150 elderly patients had prospective CGA. Of those, 67 patients had primary ovarian cancer. No difference between groups was found in age, stage, number of comorbid conditions, BMI, or albumin levels. Chemotherapy-only group patients scored significantly lower in mini mental test (20.5 vs 23.3, $P < 0.01$), nutrition assessment (17.9 vs 21, $P < 0.01$), geriatric depression assessment (6 vs 3.9, $P < 0.05$), and overall geriatric assessment score calculated from all tests together (76 vs 82, $P < 0.01$). Overall survival was significantly lower among patients treated with chemotherapy alone in both univariate and multivariate analysis (23 vs 36 months, $P < 0.05$).

Conclusion: Surgery has a significant positive effect on overall survival in elderly ovarian cancer patients. Mini mental test, nutrition assessment, and geriatric depression scale are objective CGA tests that can be used to assess elderly ovarian cancer patients and support clinical decisions while planning oncological treatment for these patients.

352 - Poster Session

Optimal tumor size for predicting prognosis of early-stage cervical cancer: MRI versus pathology versus colposcopy

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Objective: To evaluate the optimal modalities of tumor size predicting prognosis among magnetic resonance imaging (MRI), colposcopic, and pathologic findings.

Method: Patients with FIGO stage 1B1–2A2 cervical cancer who underwent primary surgical treatment between 2000 and 2015 were enrolled. Through the medical records review, we evaluated tumor size and stages by colposcopy, MRI, and pathologic reports. Eventually, we compared disease-free survival (DFS), overall survival (OS), and pathologic prognostic factors with the 3 parameters.

Results: Of 894 patients, 248 met eligibility criteria. Among the appraisal models, only the longest diameter MRI-FIGO stage reflected recurrences as the sequential increases of stage significantly ($P = 0.028$). As the longest diameter MRI FIGO stage increased, the incidence of lymphovascular space invasion, parametrial invasion, lymph node invasion, and paraaortic lymph

node invasion also increased significantly ($P < 0.05$). In the logistic regression analysis, the factors correlating with recurrence were the longest diameter MRI stage and MRI volume ($P < 0.05$). However, none of the models reflected OS significantly ($P < 0.05$).

Conclusions: In patients with FIGO stage 1B1–2A2 cervical cancer, recurrence can be predicted by preoperative MRI evaluations. Further studies are warranted to support our findings.

353 - Poster Session

Lymphovascular space invasion is an independent predictor of overall survival in risk-adjusted patients with endometrioid endometrial carcinoma: A National Cancer Data Base analysis

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Objective: Lymphovascular space invasion (LVSI) is an important adverse prognostic factor in endometrial cancer (EC); it is an independent predictor of lymph node metastasis and distant recurrence. This study evaluates the prevalence of LVSI and its impact on overall survival (OS) in endometrioid EC.

Method: Data on the presence or absence of LVSI began to be collected through the National Cancer Data Base (NCDB) in 2010. The database was queried to identify patients with endometrioid EC between 2010 and 2013. The prevalence of LVSI over time was evaluated, and the correlation between age, stage, and grade of EC was assessed. Recursive partitioning was used to classify patients into low-, intermediate-, and high-risk groups based on stage, age, and grade. OS was measured from date of diagnosis and summarized using the Kaplan-Meier method. Survival was analyzed using the log rank test and Cox proportional hazards model.

Results: A total of 102,962 women with endometrioid EC had LVSI data recorded between 2010 and 2013. The overall prevalence of LVSI was 17.3% (17,763/102,962) and was constant over time. On multivariate analysis, LVSI was an independent prognostic factor for survival (HR = 1.64, 95% CI 1.54–1.74, $P < 0.0001$). OS for patients with LVSI was 61% \pm 2% versus 85% \pm 1.3% for those without it ($P < 0.001$). Within each stage, 5-year OS in patients with a given grade who had LVSI was generally similar to OS in patients with the next higher grade but no LVSI. Among low-, intermediate-, and high-risk groups, the prevalence of LVSI was 5.8% versus 18.8% versus 57.3%, respectively (Table 1). Within these risks groups, as prevalence of LVSI increased, 5-year OS significantly decreased.

Conclusion: The presence of LVSI has a detrimental effect on OS when stage, age, and grade are accounted for. A tripling in the prevalence of LVSI is associated with a 20% decrease in 5-year OS among patients stratified into low-, intermediate-, and high-risk groups by stage, age, and grade. This information can aid in counseling and decision making regarding adjuvant therapy.

Table 1. Prevalence of LVSI and 5-year overall survival in low, intermediate and high risk groups.

Prevalence Group	Description	n (%)	Prevalence of LVSI	5-year survival
Low	Stage I/grade 1/any age or Stage I/grade 2 and age<50	41,682 (50%)	2423 (5.8%)	92%
Intermediate	Stage I/grade 2/age>50 or Stage II/grade 1 or 2/any age	41,682 (50%)	5658 (18.8%)	79%
High	Stage II/grade 3/any age or Stage III/IV/any grade/any age	41,682 (50%)	6505 (57.3%)	58%

354 - Poster Session

Higher levels of resilience and flourishing are associated with lower burnout scores in members of the Society of Gynecologic Oncology

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Objective: Much of the research on physician well-being focuses on burnout and its associated factors. There is little information on factors and skills protective against burnout in physicians. Resilience and flourishing have been identified in other populations as malleable characteristics that have an impact on psychological well-being. In this study, we sought to determine whether performance on validated psychometrics measuring resilience and flourishing were related to burnout among physician members of the Society of Gynecologic Oncology.

Method: In this cross-sectional study, members of SGO were sent an electronic survey consisting of several inventories to measure both burnout and well-being. Demographics including age, gender, marital status, parental status, and religious affiliation were collected. Burnout was measured by using an abbreviated version of the Maslach Burnout Inventory. Resilience and flourishing scores were determined by using the Brief Resilience Scale and Flourishing/PERMA inventory.

Results: Of 1,745 members, 373 responded (response rate 21.4%). Overall, 23% of members were identified as meeting the criteria for burnout—scoring high on measures of either emotional exhaustion (16.9%) or depersonalization (14.8%). This is an improvement from a 2013 study in which 32% of SGO members met the cutoff for clinical burnout. Low personal achievement scores were measured in 15% of respondents, compared to 11% in 2013. Respondents who reported high levels of burnout scored significantly lower on both the resilience and flourishing inventories compared to those not meeting criteria for burnout ($P < 0.0001$). Several possible protective factors were identified. Married participants reported higher flourishing ($P = 0.026$), and parents reported higher resilience scores ($P = 0.023$). Religious affiliation and age were not associated with scores on any inventories.

Conclusion: SGO members with high levels of resilience and flourishing reported low levels of burnout. There are a number of evidence-based positive interventions that had been shown to build both resilience and flourishing including cognitive strategies, mental agility training, anxiety management, and relationship enhancement skills. Therefore, physician wellness programs aimed at decreasing burnout should be comprehensive and include positive psychology interventions.

355 - Poster Session

Assisted reproductive technology use among female gynecologic oncologists

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Objective: To compare the use of assisted reproductive technology among female gynecologic oncologists and other subspecialists within obstetrics and gynecology.

Method: A cross-sectional survey was conducted of female physician members of the Society of Gynecologic Oncology (SGO), the American Society for Reproductive Medicine (ASRM), the Society for Maternal-Fetal Medicine (SMFM) and the American Urogynecologic Society (AUGS). The survey was administered electronically (DatStat Illume) in February 2015. There were 75 fixed-response questions in 4 domains: demographics, mentoring issues, work-life balance, and caregiving responsibilities. Data were analyzed using Stata 10 (StataCorp, College Station, TX) with χ^2 or Fisher exact tests.

Results: A total of 468 women completed the survey; 172 SGO members, 79 ASRM members, 48 SMFM members, and 169 AUGS members. Twenty-two percent of respondents were age 35 years or younger; 43% were age 36–45 years; 22% were age 46–55 years; and 13% were older than 55 years. Among female gynecologic oncologists, 19% have used assisted reproductive technology (ART) and 7% have used egg or embryo cryopreservation. Forty-three percent of gynecologic oncologists would consider using cryopreservation. Among those who used cryopreservation, 33% did so because they desired to delay childbearing. The use of ART was 19% among gynecologic oncologists, 33% of reproductive endocrinology and infertility (REI) respondents, 19% of maternal-fetal medicine (MFM) respondents, and 28% of urogynecologists ($P = 0.023$). Gynecologic oncologists (47%) and urogynecologists (38%) used ART later, more often between ages 36 and 40 years, than their MFM and

REI counterparts, 0% and 12%, respectively ($P < 0.001$). Thirty-five percent of gynecologic oncologists did not have children at the time of the survey compared to the other subspecialties: REI (17%), MFM (30%), and urogynecology (25%) ($P = 0.003$).

Conclusion: Female gynecologic oncologists use assisted reproductive technology, and many consider utilizing cryopreservation in order to delay childbearing. We observed that gynecologic oncologists delay becoming a parent compared to the other obstetric/gynecologic subspecialties and used ART later suggesting that training may play a role in the timing of becoming a parent.

356 - Poster Session

Role of serum CA-125 in monitoring ovarian cancer patients on checkpoint blockade immunotherapy

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Objective: This study aims to evaluate whether serum cancer antigen-125 (CA-125) levels have utility in monitoring patients on checkpoint blockade immunotherapy.

Method: A retrospective analysis was conducted on patients diagnosed with epithelial ovarian, primary peritoneal, and fallopian tube cancer treated with checkpoint blockade immunotherapy at Memorial Sloan Kettering Cancer Center from January 2006 to May 2017. CA-125 levels (pre-, on-, and post-treatment) were recorded from the electronic medical record. CA-125 measurements were not uniform or per protocol but were conducted at the discretion of the treating physician. The CA-125 measurement window was from 0 to 42 days before treatment start date and after treatment end date for pre- and post-treatment values, respectively. Patients whose treatment was discontinued prior to 12 weeks for clinical and/or radiographic progression were considered to have undergone early discontinuation. Means and medians of CA-125 in patients with early versus late discontinuation were analyzed. Wilcoxon rank sum tests were performed.

Results: Of 115 identified patients, 12 (10%) were excluded due to early discontinuation for toxicity. Of the remaining 72 patients who had baseline CA-125 measurement (median time of measurement 5 days before treatment start date, range 0–39 days before treatment start date) (Figure 1), 51 (50%) had at least one CA-125 value on therapy, measured within 8 weeks of start (median time of measurement 42 days after treatment start date, range 7–56 days). Of these, 22 (43%) had early treatment discontinuation; 19 patients (86%) had increased CA-125 on therapy; however, in 3 patients (14%), CA-125 declined. Conversely, in the 29 patients who did not experience early treatment discontinuation, 8 patients (28%) had CA-125 decline and in 21 patients (72%) it increased. There was no statistically significant difference in the percentage change of CA-125 from baseline in the group who had early treatment discontinuation compared with those who did not (Wilcoxon rank sum test $P = 0.117$)

Conclusion: Our analysis fails to distinguish a difference in the trend of CA-125 levels among patients who discontinue early versus patients who discontinue late on immunotherapy. The data suggest that physicians should apply caution when using CA-125 data to guide treatment decisions for patients on checkpoint blockade immunotherapy.

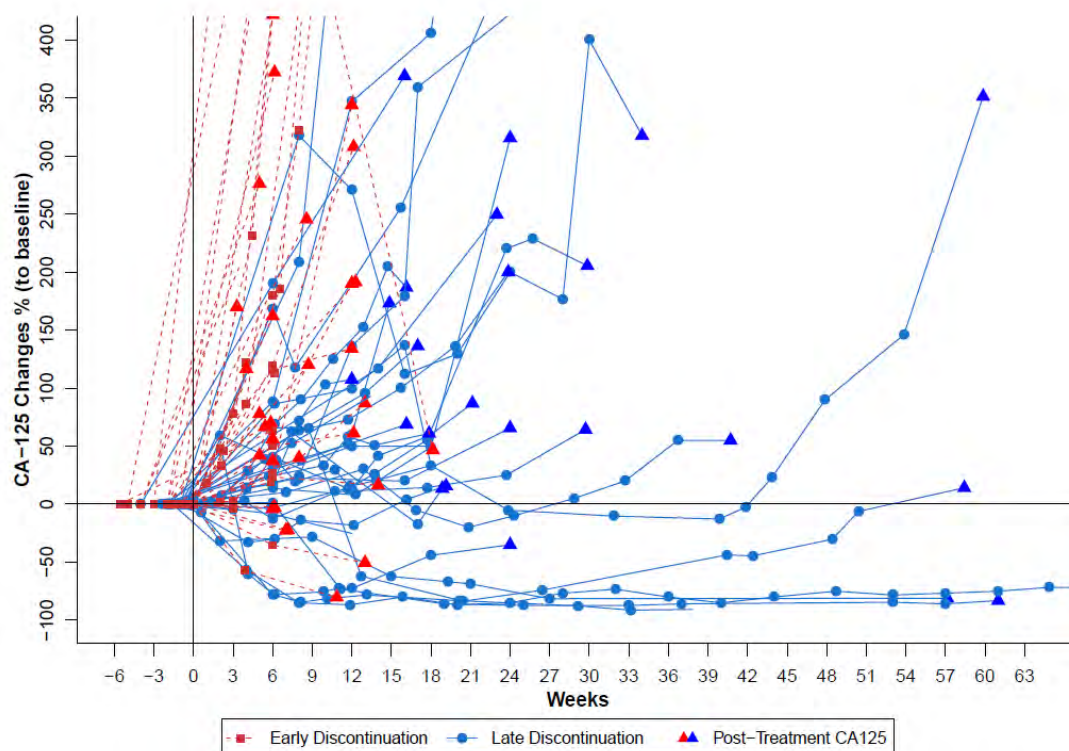


Fig. 1.

357 - Poster Session

Magnetic resonance imaging during definitive chemoradiotherapy can predict tumor recurrence and patient survival in locally advanced cervical cancer: A multi-institutional retrospective analysis of krog 16-01

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Objective: Definitive chemoradiotherapy (CRT) followed by brachytherapy is a standard treatment for locally advanced cervical cancer. During CRT, marked reduction of cervical tumor is often observed in magnetic resonance imaging (MRI). The primary aim of this study was to assess the association between tumor response in MRI using FIGO classification and clinical outcomes.

Method: Multiinstitutional data were retrospectively reviewed to identify the significance of MR tumor response on tumor recurrence and patient survival. A total of 225 patients with histologically confirmed squamous-cell carcinoma of the cervix, staged as FIGO Ib2-IVa on initial pelvic MRI, were included. Post-CRT MRI was performed median 35 days after the beginning of CRT and before brachytherapy. A median 54 Gy of external radiation was given with weekly cisplatin during CRT.

Results: A total of 112 (49.7%) of the 225 patients showed a positive response in post-CRT MRI and were named the responsive arm. After a median follow-up time of 36.2 months, the responsive arm had significantly lower paraaortic recurrence (7.5% vs 12.4%, $P = 0.04$) and distant metastasis (13.2% vs 27.6%, $P = 0.03$) rates than did the nonresponsive arm (Figure 1). The responsive arm had significantly higher 3-year cause-specific survival rate (94.6% vs 81.1%, $P < 0.01$) than did the nonresponsive arm. In the multivariate analysis, tumor size (HR = 1.91, 95% CI 1.07–3.43, $P = 0.028$) and positive MR response (HR = 1.75, 95% CI 1.06–2.27, $P = 0.045$) were significant factors for recurrence-free survival.

Conclusion: Early tumor response evaluation with MRI using FIGO classification effectively predicted distant tumor metastasis and disease-specific survival in locally advanced cervical cancer.

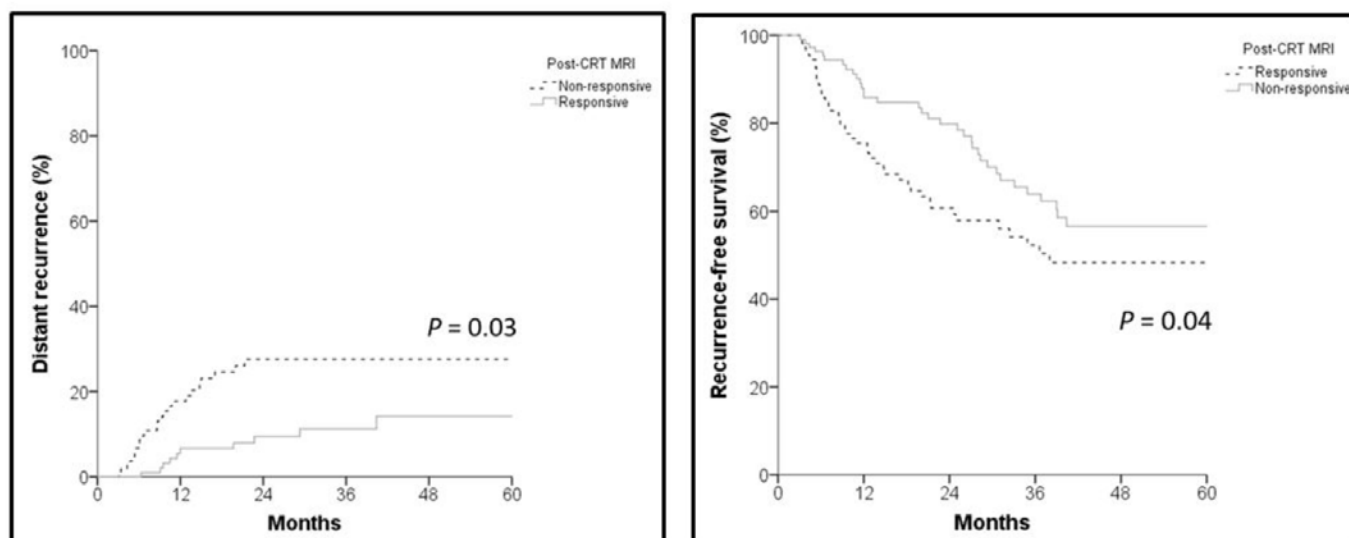


Fig. 1.

358 - Poster Session

Impact of increased utilization of neoadjuvant chemotherapy on survival in patients with advanced ovarian cancer: Experience from a comprehensive cancer center

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Objective: To determine the impact on survival of a programmatic change in neoadjuvant strategy to advanced-stage ovarian cancer.

Methods: We retrospectively investigated the clinical course of 437 patients with ovarian, tubal, and peritoneal carcinoma (FIGO stage III and IV) treated in the past 9 years (2006–2014) at Yonsei Cancer Hospital. We classified the patients into 2 groups. Group A, the control group, consisted of 217 patients who had been diagnosed from 2006 to 2010 and most of whom (83.9 %) underwent primary debulking surgery (PDS). Group B, the study group, consisted of 220 patients who had been diagnosed from 2011 to 2014, during which time more NAC followed by interval debulking surgery (IDS) was performed.

Results: There were no differences between the groups in age, BMI, histology, or tumor grade. Patients in group B versus group A more frequently underwent NAC followed by IDS procedures as upfront treatment (48.6% vs 16.1%, respectively, $P < 0.001$) and cytoreduction surgery to no residual disease (19.5% vs 9.7%, respectively, $P = 0.012$). Disease-unrelated death and morbidity from surgery were significantly decreased in group B. Kaplan-Meier analysis showed no difference in either progression-free survival or overall survival between the 2 groups ($P = 0.417$ and $P = 0.543$, respectively).

Conclusions: The incorporation of NAC did not affect PFS or OS, but increased no gross residual rates and decreased morbidity and mortality from cytoreduction surgery. Further large-scale studies such as comparative effectiveness research are required to answer the results as a paradigm shift toward NAC.

359 - Poster Session

Trends in uterine cancer incidence in the United States and Asian countries: A population analysis of 576,558 of women

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Objective: To evaluate the trends in uterine cancer incidence in United States and Asian countries (Japan and Taiwan) using population-based data.

Method: Cancer incidence data were obtained from 2002 to 2012 using population registries from the CDC's National Program of Cancer Registries (NPCR) and the NCI's Surveillance, Epidemiology and End Results registry (SEER) ($n = 454,187$), Cancer Information Service, National Cancer Center in Japan ($n = 108,342$), and the Taiwan Cancer Registry in Taiwan ($n = 14,029$) adjusted by World (WHO 2000–2025) Standard Million (18 age groups). Using SEER*Stat 8.3.4 and Joinpoint regression program 4.5.0.1, we evaluated the trends in age-adjusted uterine cancer (ICD-10 = C54) incidence expressed per 100,000 women.

Results: From 2002 to 2012, uterine cancer incidence increased with an annual percentage change (APC) of +1.2% (95% CI 1.0–1.5) in the United States, +8.2% (95% CI 6.5–9.8) in Japan, and +7.2% (95% CI 6.2–8.3) in Taiwan. With respect to age group, 16.3% of the increase in incidence was in the 60–64 age group in the United States, 17.97% in the 55–59 age group in Japan, and 21.0% in the 50–54 age group in Taiwan. In fact, the age-specific incidence peaked at 94.6 in the 65–69 age group in the United States compared with 37.4 in the 55–59 age group in Japan and 28.8 in the 55–59 age group in Taiwan. In a race-based subgroup analysis of U.S. data, the age-specific incidence peaked at 96.8 for 65–69 age group for whites, 106.7 for the 65–69 age group for blacks, 74.1 for the 65–69 age group for Hispanics, and 52.5 for the 60–64 age group for Asians. Interestingly, the U.S. Asian and Pacific Islander groups had an APC of +2.3% compared with +8.2% for native Japanese and +7.2% for native Taiwanese.

Conclusion: An increased trend in uterine cancer incidence was seen in the United States and two Asian countries, with the largest rise in native Asians. The peak incidence age appears to be younger in the native and U.S. Asians compared with whites and blacks.

360 - Poster Session

Feasibility study and dosimetric evaluation of real time CT-guided intracavitary plus interstitial cervical implantation in an outpatient setting for locally advanced cervical cancer patients

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Objective: The EMBRACE protocol requires blind intraoperative interstitial needle placement under general anaesthesia, an MRI planning scan, and overnight hospital stays. Benefits of an outpatient-based procedure would eliminate such access problems and improve the efficiency of the workflow. Our study objective was to evaluate workflow and dosimetric feasibility of real-time outpatient CT-guided intracavitary plus interstitial cervical implantation using moderate sedation in such patients.

Method: FIGO stage IB2–IIB4A cervical cancer patients with residual disease on prebrachytherapy MRI were eligible. Primary endpoints include time taken for the overall insertion procedure (from start of paracervical block to the completion of the final CT scan), time taken for the entire overall treatment (from start of paracervical block to the removal of the intrauterine applicator and interstitial catheters), pain score during insertion and after treatment using the Pain Visual Analog Scale (VAS), and any procedural-related complications. Secondary endpoints include comparing the primary endpoints and dosimetric plan with a similar cohort treated using the blind inpatient operating room/MRI approach. Prescription brachytherapy dose was 28 Gy in 4 fractions to the HRCTV. Plan evaluation parameters were cumulative EQD2 HR CTVD90, Rectal D2cc, and Bladder D2cc.

Results: A total of 88 insertions were done in 22 patients. Mean interstitial needles per patient was 8 (4–16). Mean insertion time was 28 minutes (20–35 minutes). Mean entire treatment time was 106 minutes (90–140 minutes). Mean pain score during insertion, before brachytherapy treatment, and at discharge was 0 (0), 1 (0–2), and 0 (0–1), respectively. There were no cases of postprocedural bleeding or infection. Dosimetric cumulative mean endpoints for HRCTV were 89.4 Gy (87–92 Gy), rectal 72.8 Gy (70.1–74.2 Gy), and bladder 86.7 Gy (87.3–90.1 Gy). When comparing inpatient cohort, only mean catheters (8 vs 12), mean insertion time (28 vs 76 minutes), mean time to complete entire treatment (106 vs 410 minutes), and cumulative HRCTV (89.4 vs 80.1 Gy) were statistically significant. See Figure 1.

Conclusion: Outpatient real-time CT guided interstitial implantation under regional anaesthesia is significantly shorter and well tolerated, can be safely performed in an ambulatory setting with superior dosimetric outcomes, and can be considered as an attractive alternative especially for departments that are resource poor or have difficult access to operating room facilities.

Workflow

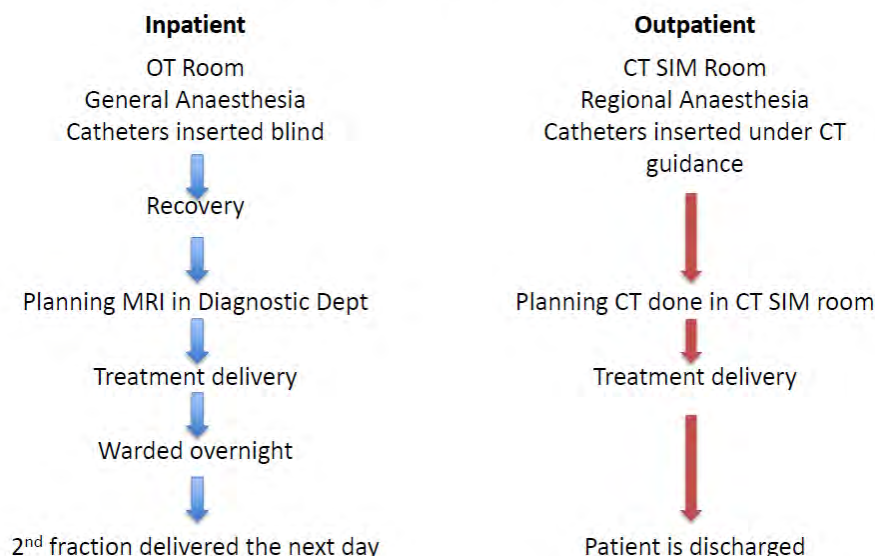


Fig. 1.

361 - Poster Session

Single-dose fosaprepitant for the prevention of chemotherapy-induced nausea and vomiting in patients with gynecologic cancers receiving moderately emetogenic chemotherapy regimens

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Objective: To explore effects of a single-day triple-antiemetic fosaprepitant (FA) regimen for preventing chemotherapy-induced nausea and vomiting (CINV) in a subgroup of patients with gynecologic cancers receiving moderately emetogenic chemotherapy (MEC).

Method: In a global, randomized, double-blind, parallel-group, phase 3 study (ClinicalTrials.gov, NCT01594749), adult subjects scheduled to receive an intravenous (IV) dose of ≥ 1 MEC (not including AC regimens) on the first day of treatment were eligible. Subjects were randomly assigned (1:1) to a control or FA regimen. The control regimen included 8 mg oral ondansetron, 20 mg dexamethasone, and IV saline as placebo before the first dose of MEC (day 1), and 8 mg oral ondansetron 8 hours after the first dose and every 12 hours on days 2 and 3. The FA regimen had the same dose of oral ondansetron on day 1, with 12 mg dexamethasone and a single dose of IV FA 150 mg before the first dose of MEC (day 1) and no additional prophylactic antiemetic beyond day 1. Primary endpoint was complete response (no vomiting or rescue medication) in the delayed phase (25–120 hours after chemotherapy initiation). A post hoc analysis of subjects with gynecologic cancers was explored.

Results: Overall, 1,000 subjects were included in the intention-to-treat population (FA, $n = 502$; control, $n = 498$); the primary endpoint was met ($P < 0.001$, FA vs control). In a subset of 152 female subjects with gynecologic cancers, 81 received the FA regimen and 71 control. Median age of the subjects was 56 years (range 24–88 years). All but 2 subjects received single-day MEC regimens, and most received carboplatin-based chemotherapy (76 subjects in the FA group and 66 in the control group). Complete response in the delayed phase was achieved by 74% of subjects in the FA group and 52% in the control group (difference 22%, $P = 0.005$), and 80% of the subjects in the FA group and 55% in the control group had no vomiting episodes in the overall phase (hours 0–120) (difference 25%, $P < 0.001$). Adverse events were similar between groups: treatment-related adverse events occurred in 7% and 10% of subjects in the FA and control groups, respectively. One subject in the FA group died (not considered drug related).

Conclusion: A single-day IV FA regimen may be more effective than the standard 3-day antiemetic regimen for preventing CINV in patients with gynecologic cancers receiving MEC.

362 - Poster Session

Is there a role for neoadjuvant chemotherapy in stage IV endometrial cancer?

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Objective: To describe outcomes in patients with stage IV endometrial cancer treated with neoadjuvant chemotherapy (NACT) and compare them to patients treated with upfront surgery.

Method: We performed a retrospective chart review for all patients diagnosed with stage IV endometrial cancer from January 1, 2000, to December 31, 2015. We abstracted relevant demographic and clinical data, including medical comorbid conditions, ECOG performance status, grade, histology, and treatment course. χ^2 , Fisher exact, and Wilcoxon rank sum tests were used as appropriate. Kaplan-Meier analysis was used to create survival curves; the Cox proportional hazards regression model was used to identify prognostic factors.

Results: Fifty-eight patients met inclusion criteria; the median age was 64.5 years. Thirty-two patients received NACT and 24 primary cytoreductive surgery. For the entire group, median progression free survival (PFS) was 11.7 months (1.8–89.4 months), and median overall survival (OS) was 12.4 months (0.9–169.5 months). The NACT group had a significantly higher BMI (31.0 vs 35.3, $P = 0.04$) and was more likely to have a diagnosis of diabetes (46.9% vs 19.2%, $P = 0.02$). Those in the NACT group were significantly less likely to have undergone surgery ($P < 0.0001$). Neither PFS (NACT 10.7 months vs surgery 11.7 months, $P = 0.83$) or OS (NACT 10.7 months vs surgery 12.7 months, $P = 0.14$) was significantly different between groups. After multivariable analysis, cardiac disease ($P = 0.04$), having a nonendometrioid histology ($P = 0.002$), and having grade 3 disease ($P = 0.03$) were independently associated with worse survival. Among patients who had surgery, more radical surgery was associated with worse survival ($P = 0.0018$). Primary treatment was not found to be independently prognostic of survival ($P = 0.37$).

Conclusion: For advanced-stage endometrial cancer patients, NACT may offer a reasonable treatment alternative to upfront surgery without significantly worse PFS or OS. While a prospective clinical trial would be ideal to answer this question, such a trial would not be feasible given the small number of patients and comorbid conditions.

363 - Poster Session

Characteristics of women with endometrial cancer and stress urinary incontinence (SUI) that desire concurrent cancer and SUI surgery: Cancer of the uterus and treatment of incontinence (CUTI) study

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Objective: To compare the characteristics of women with endometrial intraepithelial neoplasia (EIN) or clinical stage I–II endometrial cancer and stress urinary incontinence (SUI) who chose to have concurrent surgery (cancer + SUI surgery) compared to women who chose cancer surgery alone.

Method: We conducted a multicenter, prospective cohort study across 8 sites. Women diagnosed with EIN or clinical stage I–II endometrial cancer were screened for SUI. Those who screened positive were eligible to participate and offered a preoperative referral to a urogynecologist. Those diagnosed with SUI were offered all treatment options, including concurrent surgery. Baseline data between groups including demographics, quality of life, SUI symptom severity, life orientation, and clinical measures were analyzed using χ^2 and Fisher exact tests or Student t test.

Results: Of 917 screened women, 485 (52.3%) screened positive for SUI. Sixty women declined participation; 40 were ineligible. Of the 385 women enrolled, 29 subjects have not completed surgery and are not included in this analysis. Seventy-seven (21.6%) women had EIN, 276 (77.5%), and 3 (0.8%) clinical stage I and clinical stage II endometrial cancer, respectively. Two-hundred and fifteen had grade I/II endometrioid adenocarcinoma; 52 had serous, clear cell carcinosarcoma or grade 3 endometrioid adenocarcinoma; and 12 had mixed histology types. One-hundred and forty-five (40.7%) women opted for referral to urogynecology preoperatively, and 74 (20.8%) then opted for concurrent surgery. A higher proportion of women choosing concurrent surgery compared to cancer surgery alone were Hispanic (7% vs 2%, $P = 0.06$) and/or Caucasian (96% vs 84%, $P = 0.007$), and a lower proportion were African-American (3% vs 12%, $P = 0.017$). Women choosing concurrent surgery had higher SUI severity and bother scores ($P < 0.0001$). There were no differences in baseline quality of life scores, tumor characteristics, BMI, medical comorbid conditions, or optimism scores.

Conclusion: Half of all women undergoing surgery for endometrial cancer had symptoms of SUI, and among those, almost half opted for referral to urogynecology prior to their cancer surgery. Women choosing concurrent surgery reported more severe and bothersome SUI symptoms, but tumor characteristics were not associated with a woman's decision to have concurrent surgery.

364 - Poster Session

Predictors of severely compromised renal function to aid decision-making for placement of a percutaneous nephrostomy tube(s) or ureteral stent(s) in gynecologic oncology patients

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Objective: The majority of gynecologic oncology patients are exposed to treatments that have potential to compromise renal function (RF). Diuretic renography with radiotracers has been used successfully to diagnose genitourinary obstructions, measure the drainage time from the renal pelvis, and assess the relative contribution of each kidney to overall renal function. We aim to identify predictors of renal function (RF) $<20\%$ and determine clinical outcomes with and without placement of percutaneous nephrostomy (PCN) tube(s) or ureteral stent(s).

Method: We performed a single-institution case control study of gynecologic oncology patients who underwent diuretic renography between January 2007 and June 2017. Primary outcome was RF $<20\%$ (threshold for kidney salvageability) diagnosed by diuretic renography. Acute kidney injury was defined as serum creatinine 1.5 times above baseline or urine output <0.5 ml/kg/hour. Univariate and multivariate logistic regression with stepwise selection were used to assess predictors of RF $<20\%$.

Results: Among 273 gynecologic oncology patients who underwent diuretic renography, 15% had RF $<20\%$. Mean age was 58 years; 15% had diabetes; 12% chronic kidney disease; and 44% recurrent cancer with the most common primary site being cervix (41%), endometrial (24%), ovarian/fallopian/primary peritoneal (27%), or other (5%). Prior pelvic radiation (53% vs 38%, $P = 0.07$) and current chemotherapy (38% vs 28%, $P = 0.1$) were suggested risk factors for diminished RF, but not statistically significant at the cutoff of $<20\%$. The most common indication for diuretic renography was hydronephrosis/hydroureter (82%). Computerized tomography (CT) scan was routinely ordered a mean of 2 days prior to diuretic renography, and multivariate analysis revealed that renal atrophy significantly predicted RF $<20\%$ (adjusted OR = 8.7, 95% CI 1.88–40.33). All 6 patients with renal atrophy and RF $<20\%$ did not undergo intervention. Overall there were no differences in PCN or ureteral stent placement, outcomes of AKI, need for dialysis, or hospital length of stay between women with $<20\%$ versus $\geq 20\%$ RF.

Conclusions: Renal atrophy diagnosed by CT scan is a significant predictor of RF $<20\%$ and should be considered in the decision-making process whether to recommend ureteral stent(s) or PCN(s).

Table 1. Renal Lasix scan results ($n = 273$)^a.

Characteristic	<20% Renal Function ($n = 41$)	≥20% Renal Function ($n = 232$)	<i>P</i>
Indication for diuretic renography			
Acute kidney injury	4 (9.8)	34 (14.7)	0.40
Hydronephrosis/hydronephrosis	37 (90.2)	186 (80.2)	0.12
Elevated creatinine/suspected acute kidney injury	13 (31.7)	67 (28.9)	0.71
Other	3 (7.3)	14 (6.0)	0.75
Kidney function, % (mean ± SD)			
Left	37.4 (±37.2)	50.6 (±13.4)	<0.01
Right	62.6 (±37.2)	49.6 (±13.8)	<0.01
CT scan performed prior to renal lasix scan, median days (IQR)	2 (1-5)	2 (1-5)	0.78
Renal atrophy	6 (14.6)	4 (1.7)	0.02
Cortical thinning of kidney(s)	2 (4.9)	3 (1.3)	0.17
Hydronephrosis	28 (68.3)	147 (63.4)	0.37
Percutaneous nephrostomy tube placement			0.22
Unilateral	7 (17.1)	29 (12.5)	
Bilateral	3 (7.3)	30 (12.9)	
Time interval from diuretic renography to percutaneous nephrostomy tube placement, median days (IQR)	1 (1-2)	1 (1-2)	0.99
Ureteral stent(s) placed			0.08
Unilateral	13 (31.7)	49 (21.1)	
Bilateral	2 (4.9)	28 (12.1)	
Time interval from diuretic renography to stent, median days (IQR)	1 (1-3)	1 (1-2)	0.38

^aSD = standard deviation; CY = computerized tomography; IQR = interquartile range.

365 - Poster Session

SGO practice patterns regarding the timing of port flushes

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Objective: Following chemotherapy, our policy is to perform port flushes every 4–8 weeks. This is consistent with manufacturer guidelines; however, in clinical practice we extend the port flush interval to every 3–6 months to coincide with surveillance visits with seemingly few complications. The objective of this study was to assess the practice patterns of providers regarding the timing of port flushes.

Method: An anonymous 10-item multiple-choice questionnaire was emailed on 3 separate occasions to all U.S. member categories of the SGO with the exception of residents. Variables collected include SGO membership type, years since graduating fellowship, institution type, National Comprehensive Cancer Network (NCCN) membership, whether there is a hospital policy regarding flush timing, policy recommendations, and the provider practice pattern. An alpha of 0.05 was considered significant. Univariate and multivariate analyses were performed.

Results: The response rate was 14.1% ($n = 239/1,697$); 69% were in practice >6 years; and 64% recommended port flush intervals of every 4–8 weeks, 19% 9–12 weeks, and 10.5% 13–16 weeks. Only 60% of responders stated that there was an institutional policy regarding the interval. Of these, 80% were compliant with the policy and 76% had a policy of 4–8 weeks. Providers were more likely to be noncompliant when the port flush policy interval was longer than every 4–8 weeks ($P < 0.001$). This was significant after controlling for confounders (OR = 0.03, 95% CI 0.01–0.11). Although univariate analysis revealed that community institutions were less likely to have a port flush policy ($P = 0.033$) than academic or mixed

community/academic institutions, this was not significant on multivariate analysis (OR = 0.51, 95% CI 0.24– 1.09). NCCN institutions were more likely to have a 4–8 weeks policy compared to non-NCCN institutions (OR = 1.80, 95% CI 1.02–3.20).

Conclusion: Although extending the port flush interval to 3 months is safe in several studies, surprisingly, the majority of respondents support their institutions' policy of 4–8 weeks. Furthermore, when the policy interval was longer than 4–8 weeks, respondents continued to recommend shorter intervals. Extending the interval to coincide with surveillance visits may also prevent wasted time and cost for the patient and the institution.

366 - Poster Session

Utility of HE4 and CA-125 as predictive and prognostic factors in preoperative assessment of endometrial cancer

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Objective: The objective of this study was to evaluate the prognostic value of preoperative serum HE4 and CA-125 and to establish whether the serum levels of HE4 and CA-125 could be a good predictor for lymphadenectomy.

Method: Preoperative serum HE4 and CA-125 were measured in 145 patients treated surgically. The relation between serum levels and histopathological results of surgical staging, recurrence, and death were analyzed by Mann-Whitney *U* test. The ROC curves were generated to determine the optimal cutoff values of HE4 and CA-125 levels with optimum sensitivity and specificity for the prediction of lymphadenectomy.

Results: We enrolled patients from stage IA–IVB with a average follow-up period of 40.68 months (range 5–100 months). HE4 levels were significantly higher in patients who had deep myometrial invasion ($P < 0.001$), ovary metastasis ($P = 0.026$), and paraaortic lymph node metastasis ($P = 0.009$). CA-125 levels were significantly higher in patients who had deep myometrial invasion ($P = 0.008$), lymphovascular space involvement ($P < 0.001$), and paraaortic lymph node metastasis ($P = 0.048$). HE4 levels were higher in patients with recurrence and death ($P = 0.001$ and $P = 0.027$, respectively). Based on ROC curve, we found that the HE4 value of 62 pmol/l is the best cutoff to identify deep myometrial invasion with the sensitivity of 80.0% and the specificity of 69.1%. The AUC equals 0.786 (95% CI, 0.700–0.872). The HE4 value of 62 pmol/l is also the best cutoff to identify paraaortic lymph node metastasis with the sensitivity of 87.5% and the specificity of 59.9%. The AUC equals 0.768 (95% CI, 0.565–0.972).

Conclusion: HE4 and CA-125 are significantly correlated with prognostic factors and, in addition, may be successful in detection of high-risk subsets before surgery. Our findings indicate that HE4 could serve as a preoperative tool for helping to identify patients who may require lymphadenectomy including paraaortic lymph node.

367 - Poster Session

Targeting novel signaling pathways in endometrioid tumor via reducing self-renewal and cisplatin chemoresistance in cisplatin-resistant endometrioid tumors

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Objective: CD55 is a membrane complement protein expressed on endometrioid tumors that activates two nonoverlapping intracellular signaling pathways to maintain cancer stem cells (CSC) in a pluripotent and chemoresistant state. The goal of this study is to test the efficacy of inhibitors of CD55-dependent intracellular signaling as new therapeutic strategies to disrupt self-renewal and sensitize cisplatin-resistant tumors to cisplatin in endometrioid cancer.

Method: The current studies using endometrioid tumor-derived cancer cells utilize pharmacological reagents to inhibit c-Jun N-terminal kinase (JNK) and lymphocyte-specific protein tyrosine kinase (LCK) and determine their impact on self-renewal and cisplatin sensitivity, respectively. To assess the intracellular pathways, western blots were used to test pathway activation and functional in vitro assays of cancer stem cell maintenance after treatment without or with the JNK inhibitor SP600125. In vitro cisplatin sensitivity was tested using cell proliferation and apoptosis in LCK-silenced cells or cisplatin-resistant cells treated without or with the LCK inhibitor saracatinib. In vivo studies were performed for cisplatin sensitivity in mice injected with cisplatin-resistant endometrioid cancer cells and treated with saracatinib with and without cisplatin.

Results: Findings indicate that inhibition of CD55-dependent signaling is sufficient to disrupt endometrioid cancer cell maintenance and sensitize the cells to cisplatin. JNK inhibitor disrupts CSC maintenance via inhibition in activation of JNK and

attenuation in expression of the pluripotency gene NANOG. Moreover, the JNK inhibitor is able to block CD55-induced CSC self-renewal. In parallel, it was determined that disrupting LCK signaling with saracatinib is sufficient to sensitize cisplatin-resistant endometrioid cancer cells to cisplatin. In previous studies, saracatinib was shown to attenuate expression of DNA repair enzymes, and subsequently tumors derived from saracatinib-treated mice were also found to express lower levels of DNA repair enzymes compared to vehicle-treated mice.

Conclusion: Collectively, these studies provide proof of concept that targeting JNK and LCK signaling pathways is sufficient to inhibit self-renewal and cisplatin chemoresistance in cisplatin-resistant endometrioid tumors.

368 - Poster Session

Changes in DNA damage response markers with treatment in advanced ovarian cancer

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Objective: Ovarian cancer (OC) is sensitive to first-line chemotherapy, likely attributable to frequent defects in the DNA damage response (DDR) via homologous recombination. Unfortunately, most patients eventually relapse. How DDR competency evolves under the selection pressure of treatment is poorly described. Changes in DDR effectors beyond homologous recombination may be relevant to platinum and/or PARP inhibitor sensitivity. We sought to describe changes in DDR markers in a large cohort of OC samples obtained at diagnosis, after neoadjuvant chemotherapy (NACT) and relapse, and evaluate their impact on outcome.

Method: Sequential OC samples from 147 patients (pre-NACT $n = 132$, post-NACT $n = 105$, relapse $n = 22$) were analyzed for PAR, PARP-1, ATM, TP53BP1, RAD51, FANCD2 by IHC on TMAs using an H-score (0–300) where $H \leq 10$ defined negative. Expression of DDR markers was correlated to PFS and OS using Kaplan-Meier and log-rank tests.

Results: Before NACT a significant number of cases lacked expression of DDR markers: 60%, 59%, 23%, 20%, and 14% were PAR, FANCD2, RAD51, ATM, or TP53BP1 negative, respectively. Under NACT all six markers showed a decrease, which was significant for PAR, PARP-1, and RAD51 ($P < 0.01$). At relapse DDR markers were significantly increased for PAR and PARP-1 ($P < 0.05$) compared to post-NACT values. At diagnosis, PAR negativity was associated with improved PFS (HR 0.55, $P = 0.016$), while TP53BP1 negativity predicted worst PFS (HR 3.97, $P < 0.0001$). Post-NACT, ATM loss was associated with worst progression-free survival (PFS) and overall survival (OS) (HR 2.12, $P = 0.003$; HR 2.17, $P = 0.013$, respectively). Investigating combined markers, at diagnosis TP53BP1-/ATM+ and TP53BP1-/PAR- predicted worst PFS (HR 6.89, $P = 0.001$ and HR 4.76, $P = 0.005$, respectively), while TP53BP1-/RAD51+ predicted worst PFS and OS (HR 2.97, $P = 0.01$ and HR 3.28, $P = 0.007$, respectively). Post-NACT, ATM-/PAR-, and FANCD2+/RAD51+ predicted worst PFS and OS (PFS HR 1.9, $P = 0.022$ and HR 2.38, $P = 0.008$; OS HR 2.94, $P = 0.002$, and HR 3.11, $P = 0.003$, respectively).

Conclusions This is one of the first studies addressing the dynamics of DDR markers under NACT. At baseline, advanced OC is associated with a loss of DDR effectors in a significant subset, and during treatment major changes are observed. An evaluation of DDR marker expression at diagnosis and after NACT offers prognostic information. Whether the pattern of DDR markers post-NACT may also predict sensitivity to subsequent PARP inhibitors merits investigation.

369 - Poster Session

Diagnostic value of bioactive factors from blood sample for the early detection of uterine sarcoma

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Objective: The reliable biomarker of uterine sarcoma for early diagnosis can enable early and complete resection, leading to improving the prognosis. The comprehensive study of bioactive factors from body fluids based on genome data has been reported to be a novel diagnostic approach for the early diagnosis of cancer. The aim of our study is to clarify the role and application of the bioactive factor as an early diagnostic biomarker in uterine sarcoma.

Method: To identify the candidate factors for the early detection of uterine sarcoma, the genome-wide expression data from 57 uterine sarcoma, 23 leiomyoma, and 23 myometrium were used. Four candidate genes were identified as the uterine sarcoma specific-bioactive factors, and these concentrations were measured by enzyme-linked immunosorbent assay from

blood samples of patients with gynecologic tumors (12 leiomyoma, 8 ovarian, 10 cervical, 6 endometrial cancer, and 5 uterine sarcoma).

Results: A comprehensive analysis of genome data identified four candidate gene, Midkine, Osteopontin, GDF-15, and Granulin. Uterine sarcoma revealed higher concentrations of Midkine (6732 ± 4500 pg/ml) compared with leiomyoma (2634 ± 1585 pg/ml) ($P > 0.05$). Uterine sarcoma showed significantly higher concentrations of Osteopontin, GDF-15, and Granulin (5058 ± 1173 , 1152 ± 610.7 , and 16508 ± 2890 pg/ml) than leiomyoma (2226 ± 200.6 , 165.3 ± 16.56 , and 9065 ± 608.3 pg/ml, respectively) ($P < 0.01$). GDF-15 was only bioactive factor that revealed significantly higher concentration in uterine sarcoma than in all other gynecologic tumors ($P < 0.01$).

Conclusion: We demonstrated that the measurement of bioactive factors based on related gene analysis can offer high diagnostic performance for early diagnosis of uterine sarcoma. The combined analysis of these bioactive factors might improve the sensitivity in diagnosing uterine sarcoma.

370 - Poster Session

Neoadjuvant chemotherapy for gynecologic high-grade serous carcinoma: Correlation of tumor response with tumor morphology and immunophenotype

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Objective: Increasingly, select patients with advanced-stage gynecologic high-grade serous carcinoma (HGSC) are treated with neoadjuvant chemotherapy (NACT) prior to debulking surgery. Comparing patients with <1 cm and ≥ 1 cm residual histopathologic disease post-NACT, we sought to characterize NACT-induced tumor morphology and immunophenotype alterations.

Method: Patients with gynecologic HGSC treated with NACT followed by debulking surgery and having pre- and post-NACT tumor specimens available at a single academic institution from 2009 to 2017 were included. Amount of residual disease post-NACT was measured histopathologically on gross specimens. A single gynecologic pathologist blinded to clinical information assessed tumor morphology (multinucleation, chromatin smudging, cytoplasmic eosinophilia, fibrosis, inflammation, foamy histiocytes) in patient-matched pre- and post-NACT samples. P53, PAX8, and WT1 protein expression were determined by immunohistochemistry (IHC). Both morphologic and IHC findings were described according to standardized protocols. Clinical data were abstracted from medical charts.

Results: A total of 29 patients met study criteria with a median age of 62 years (range 45–81). Of these, 89% had stage III disease. Patients received an average of 5 cycles (range 3–9) of platinum-based combination NACT. Post-NACT, all patients showed improvement in bulk of disease on imaging, and 88% of patients showed a $>90\%$ decrease in serum CA-125 values. Debulking specimens revealed histopathologic <1 cm residual disease in 45% ($n = 13$), whereas ≥ 1 cm residual disease was seen in 55% ($n = 16$). There was no difference in residual disease based on number of NACT cycles given. NACT tumors with ≥ 1 cm residual disease showed higher mitotic activity (5–20/HPF) and less cytological and stromal alteration. P53 and PAX8 showed similar positivity pre- and post-NACT in all patients. WT1 showed complete absence or decreased expression in 71% of patients with ≥ 1 cm residual disease post-NACT, but retained expression in those with <1 cm residual disease.

Conclusion: HGSC exhibits significant cytological and stromal alterations in response to NACT. While P53 and PAX8 protein expression remains constant pre- and post-NACT, a key IHC alteration is in WT1 expression. A less favorable response to NACT seems to correlate with complete loss or decreased expression of WT1.

371 - Poster Session

The predictive value of CA-125 during neoadjuvant chemotherapy

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Objective: To assess the prognostic value of the decline in serum CA-125 levels in patients who undergo neoadjuvant chemotherapy (NACT) for ovarian cancer.

Method: All consecutive patients with advanced ovarian cancer ($n = 109$) who were selected to undergo NACT because complete primary cytoreduction was not expected to be possible because of diffuse carcinomatosis or severe comorbid conditions.

Results: A reduction rate of more than 80% in marker levels by the second cycle of chemotherapy was significantly associated with complete cytoreduction (82.8% vs 59.4%, $P = 0.021$) and improved outcome (median OS 44.5 vs 34.2 months, $P = 0.016$) (Figure 1). A reduction of less than 50% after three cycles of NACT was associated with poor outcome (median OS 29.5 vs 42.2 months, $P = 0.012$, and median progression-free survival 1.8 vs 12.0 months, $P = 0.001$). CA-125 levels prior to NACT were not correlated with outcome of patients.

Conclusion: Decreases in serum CA-125 levels during NACT are strongly correlated with cytoreduction and outcome in patients with advanced ovarian cancer.

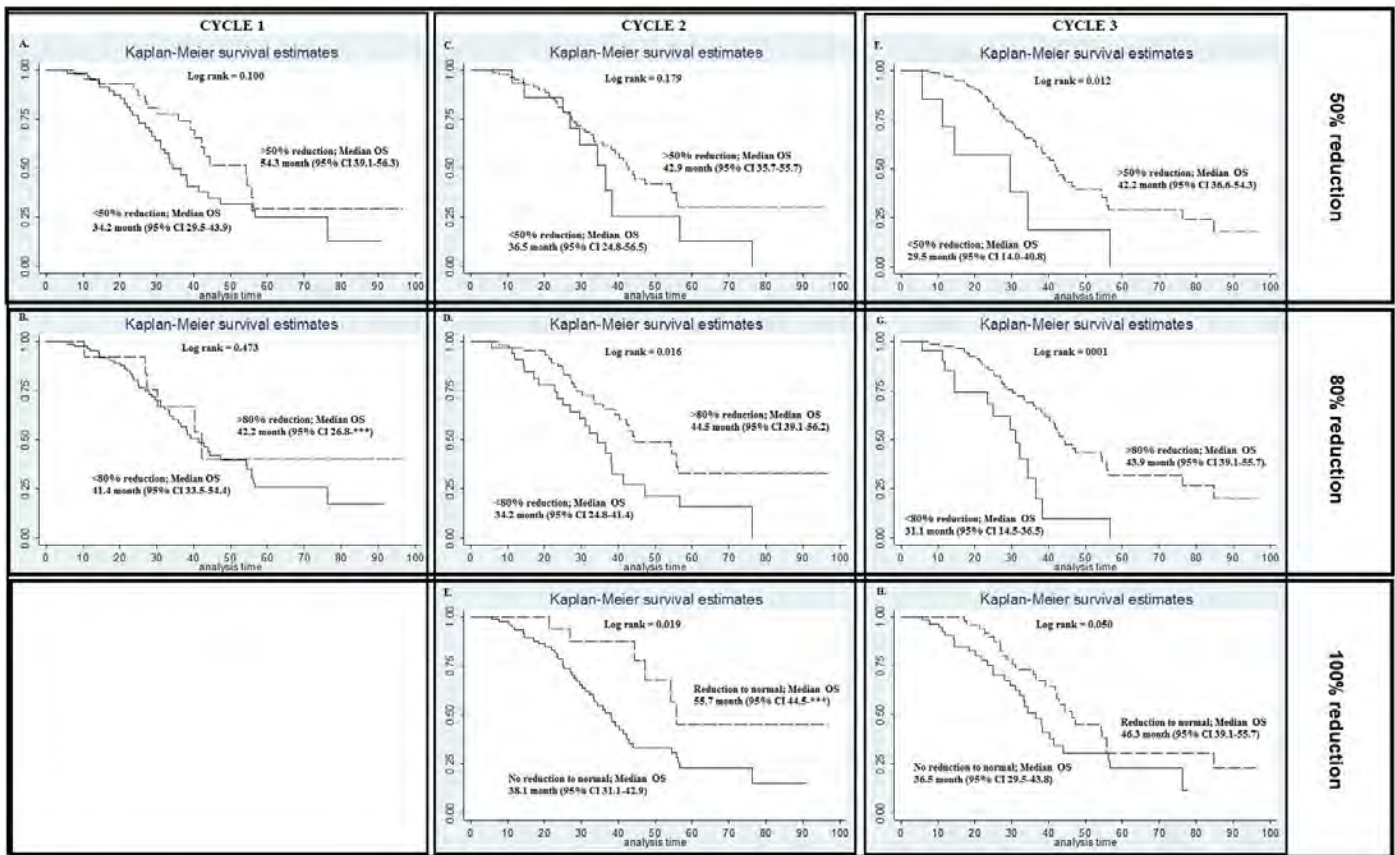


Fig. 1.

372 - Poster Session

Tumor genetic sequencings as predictor for surgical outcomes in epithelial ovarian cancer

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Objective: Molecular characterization of epithelial ovarian cancer (OvCa) has been well described and has been mostly used to identify potential therapeutic targets. However, associations of genetic alterations to prognostic markers and clinical outcomes have not been well described. We aim to examine the genomic analysis and its correlation with clinical outcomes in OvCa patients who had tumor genetic sequencing.

Method: We retrospectively analyzed patients with a diagnosis of OvCa and CLIA certified comprehensive next-generation sequencing (NGS) of 315 or 467 cancer genes between January 1, 2014, and June 1, 2017. All patients were treated in a single institution, underwent surgical staging, and received platinum-based neoadjuvant or adjuvant chemotherapy. Molecular, demographic, and clinical data were analyzed using descriptive statistics and the Fischer exact test. Multivariate analysis was performed using logistics and Cox regression analysis.

Results: Among the 93 patients included in this analysis, there were a total of 317 genetic alterations (GA), with an average 3.4 alterations per tumor. Figure 1 and Table 1 summarizes the mutational landscape of our OvCa cohort (Figure 1) as well as the patients' clinical characteristics (Table 1). On multivariate analysis controlling for age, histology and stage, we found that PTEN mutations were significantly more common in patients who had suboptimal debulking ($P = 0.006$, OR 32.088, 95% CI 2.685–383.48). TP53 mutation was significantly associated with high-grade ($P = 0.0133$) and stage III/IV disease ($P < 0.01$). Serous histology is strongly associated with TP53 mutation ($P = 0.0012$) and negatively associated with PIK3CA, KRAS, and ARID1A mutations ($P = 0.0026$, $P = 0.0482$, and $P = 0.0461$, respectively). Patients with ERBB2 GA had shorter OS (153.4 vs 60.3 months, $P = 0.001$). Of interest, there were no significant genomic differences between Hispanic and non-Hispanic patients except in pathways involving genes related to homologous recombination, in which there was a nonsignificant trend towards significance ($P = 0.065$).

Conclusion: In a racially diverse cohort of OvCa patients, the prognostic significance of PTEN, ERBB2, and HR pathway mutations should be confirmed in prospective studies. There does not appear to be a significant difference in molecular pathways altered in Hispanic patients with OvCa compared to non-Hispanic patients.

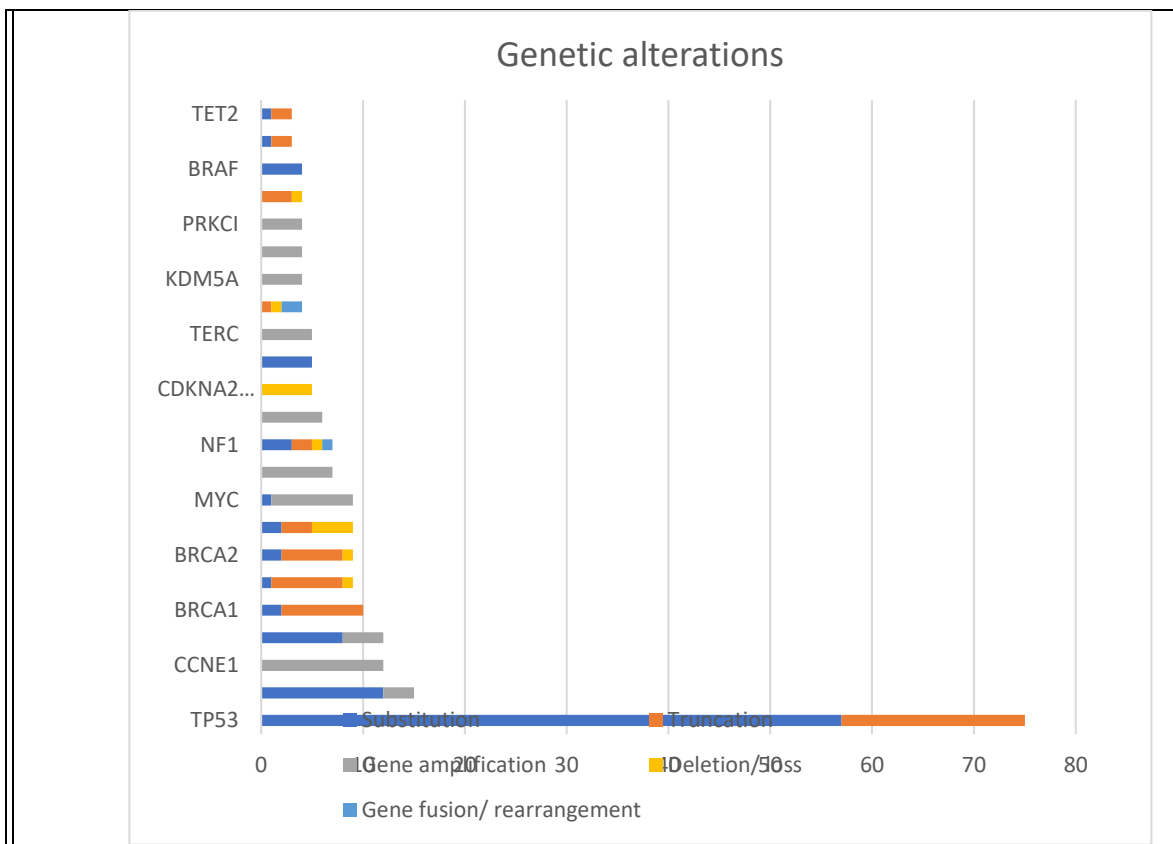


Fig. 1. Frequency and type of genetic alterations from distinct patients with epithelial ovarian, fallopian tube or peritoneal carcinoma.

Table 1. Demographic and clinical characteristics in patients with epithelial ovarian cancer ($n = 93$, mean age = 63 years).

Characteristic	Percentage (number/total patients)
Ethnicity	
White	64% (60/93)
Hispanic	20% (19/93)
Asian	4.3% (4/93)
Black	3.2% (3/93)
Others	7.6% (7/93)
Family history of cancer	
Breast	21% (20/93)
Ovary	7% (7/93)
Colon	7% (7/93)
Uterus	4% (4/93)
Surgical variables	
Primary cytoreductive surgery	76% (68/89)
No residual tumor	85% (73/86)
Presence of ascites	46% (35/76)
Preoperative CA125, mean (SD)	1,012 U/ml (269)
Tumor characteristics	
Stage III-IV	81% (73/90)
Histology	
Serous	71% (64/90)
Clear cell	13% (12/90)
Endometrioid	7.8% (7/90)
Poorly differentiated	4.4% (4/90)
Mucinous	2.2% (2/90)
Grade 3	89% (67/75)
Treatment	
Neoadjuvant chemotherapy	26% (23/86)
Platinum sensitive	69% (51/74)
Prior lines of regimen (median, range)	2 (1-15)

373 - Poster Session

Intraluminal tumor cells are associated with adverse prognostic factors and survival among women with endometrial cancer

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Objective: Stage is a critical determinant of treatment and prognosis for endometrial cancer (EC) patients. We have reported that EC patients who are status post-tubal ligation for sterilization have improved survival, secondary to lower stage at presentation, suggesting that transtubal spread may represent an important route of metastasis. To assess the importance of transtubal spread in EC patients, we evaluated the presence of intraluminal tumor cells (ILTCs) in relation to tumor characteristics and clinical outcomes.

Method: One pathologist evaluated fallopian tube hematoxylin and eosin slides of 295 EC patients treated at our institution for presence of ILTCs. We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between age, stage, lymphovascular space invasion (LVSI), and histology with ILTCs. Cox regression was used to estimate hazard ratios (HRs) and 95% CIs for ILTCs with EC-specific mortality and recurrence risk, overall and among women with stage I disease.

Results: ILTCs were present in 16.1% of nonendometrioid (22/137), 9.8% of high-grade endometrioid (6/61), and 7.2% (7/97) of low-grade endometrioid tumors. In univariate models, advanced-stage (stage IV vs stage I, OR 11.94, 95% CI 4.50–31.64), LVSI (OR 2.9, 95% CI 1.4–6.0), serous histology (vs low-grade endometrioid, OR 3.2, 95% CI 1.1–9.6), and age (≥ 65 vs 55–64 years, OR 0.3, 95% CI 0.1–0.7) were associated with ILTCs. In unadjusted Cox models, ILTCs were associated with higher EC-specific mortality and recurrence risk; however, adjustment for age, stage, and histology attenuated these associations. Among 139 women with stage I disease, ILTCs were associated with increased EC-specific mortality (HR 3.9, 95% CI 3.5–55.1) and recurrence risk (HR 7.6, 95% CI 2.1–24.5).

Conclusion: Our findings suggest that the ILTCs are associated with adverse tumor characteristics, and among women with uterine confined disease, ILTCs were related to clinical outcomes.

374 - Poster Session

Homologous recombination pathway mutations in freshly isolated tumor cells from patients with ovarian cancer correlate with outcome

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Objective: To evaluate DNA alterations in homologous recombination pathway genes and correlation with outcome in patients who underwent neo-adjuvant chemotherapy (NACT) or primary debulking surgery (PDS).

Method: A total of 97 patients with high-grade serous ovarian cancer (HGSC) underwent either PDS or NACT. Tumor tissue was obtained at the time of surgery. After quality control, DNA analysis was performed using 90 samples of patients with HGSC (51 PDS and 39 NACT). Massive-parallel DNA sequencing was used to sequence 400 carcinogenesis-associated loci. The variants were annotated and filtered to enrich for pathogenic variants.

Results: In the PDS group, patients with homologous recombination mutations had significantly improved OS and PFS. This effect remained significant for OS (HR 0.52, 95% CI 0.14–0.75, $P < 0.01$) and PFS (HR 0.35, 95% CI 0.17–0.71, $P < 0.005$) after controlling for age, BMI, stage, and surgical outcomes. The frequency of tumor homologous recombination mutations was lower in the NACT group than in the PDS group, and no association with outcome was observed in the NACT group. (See Figures 1-4.)

Conclusion: The presence of tumor homologous recombination mutations in untreated ovarian cancer cells is associated with improved patient outcome, but this association disappeared in the cells that were still present at the time of surgery after NACT.

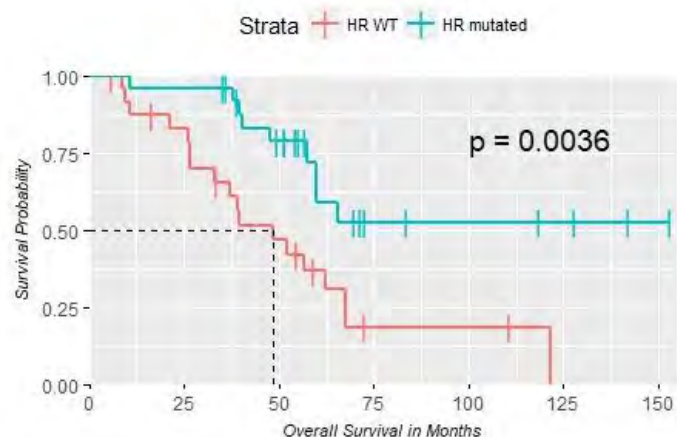
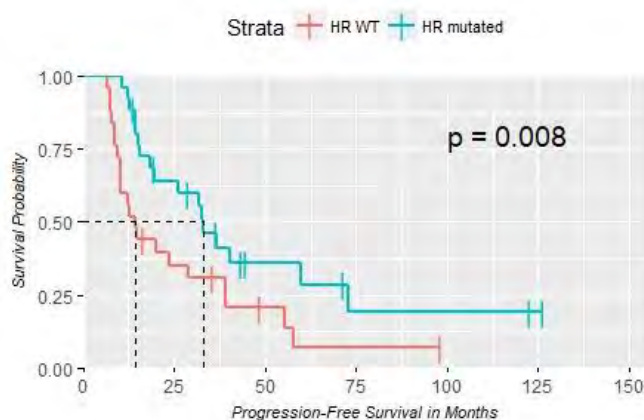


Fig. 1. Effect of HR mutations on PFS in the PDS Group.

Fig. 2. Effect of HR mutations on OS in the PDS Group.

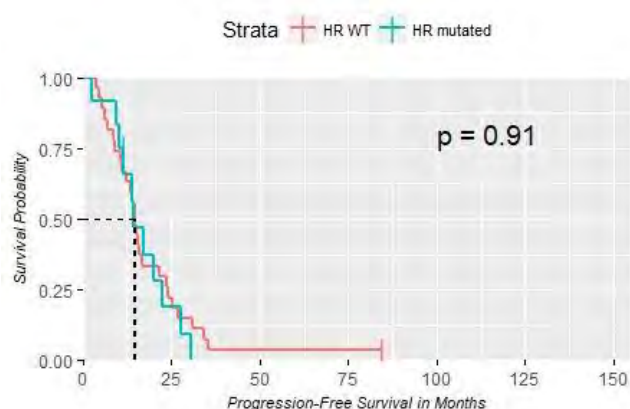


Fig. 3. Effect of HR mutations on PFS in the NACT Group.

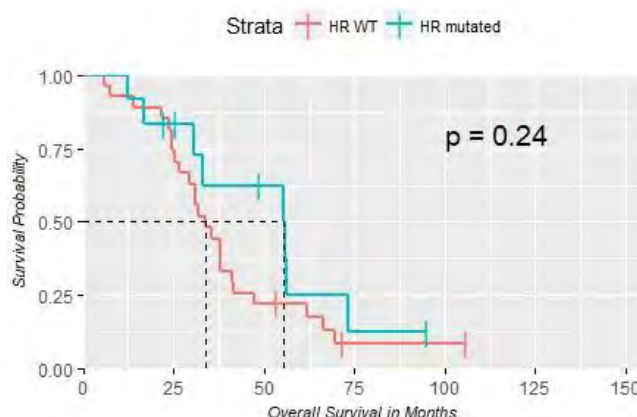


Fig. 4. Effect of HR mutations on OS in the NACT Group.

375 - Poster Session

The utility of pretreatment imaging assessment to predict treatment response in locoregionally advanced cervix cancer

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Objective: To compare pretreatment and post-treatment computerized tomography (CT) imaging characteristics from a computer-aided detection (CAD) scheme to identify the most highly performing radiographic tumor features that may accurately predict response to treatment with chemoradiation for locoregionally advanced cervical cancer (LACC).

Method: A single institution dataset of 36 patients with LACC (stage IB2 to IVA) was retrospectively assembled. Using RECIST 1.1 criteria, each patient was classified by pre- and post-therapy imaging as either a “responder” with complete response or “nonresponder” by stable or progressive disease. A CAD program was applied to segmented tumors previously tracked by radiologists on CT. Each segmented tumor feature can be divided into four groups, namely, (1) shape-based features, (2) density-based features, (3) texture-based features, and (4) wavelet transform-based features. The performance of each feature was assessed by computing the area under the receiver operating characteristic (ROC) curve method (AUC) and was then used to determine whether differences in pretreatment imaging features accurately predict response after treatment with chemoradiation for LACC.

Results: Descriptive analysis of baseline demographics and treatment was performed between the responders ($n = 21$) and nonresponders ($n = 15$), and no significant differences between the groups were found. The CAD scheme initially computed 119 features, applying the particle swarm optimization algorithm and support vector machine classifier on the initial features; 14 features were selected as the optimal feature cluster, which achieves an AUC of 0.85 and prediction accuracy of 0.778 (threshold 0.602).

Conclusion: Use of CAD schemes to identify specific radiographic tumor features can be utilized to identify poor responders in LACC prior to chemoradiation. Future uses for CAD include integration in determination of pelvic and aortacaval nodal status based on pretreatment positron emission tomography (PET)/CT, which highly affects radiation treatment planning, prognosis, and survival.

376 - Poster Session

Promise versus practicality: Integration of molecular tumor profiling for gynecologic malignancies

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Objective: To describe experience with genomic tumor profiling (GTP) in women with primary gynecologic malignancies at an NCI-designated comprehensive cancer center.

Method: We reviewed all patients at our center with gynecologic malignancies who had GTP between March 2013 and July 2017. Descriptive statistics were calculated for patient, tumor characteristics, and GTP findings.

Results: A total of 100 samples were sent for GTP between March 25, 2013, and July 24, 2017. GTP was completed in 95 samples from 89 unique patients; DNA extraction failed in 5. Average age at initial diagnosis was 55 years (range 16–81). Primary sites were 55 (58%) ovary/tube/peritoneum, 15 (16%) endometrium, 8 (8%) cervix, 7 (7%) uterine leiomyosarcoma, and 10 (11%) other. Patients received a mean of 3 (range 0–8) cytotoxic chemotherapy drugs or biologic agents prior to GTP. Of the 95 completed assays, 89 (94%) identified 1 or more mutations targeted by a drug, either commercially available (67) or in an open clinical trial (22). Five assays (5%) had mutations that had neither an associated FDA-approved drug nor a clinical trial option; 1 assay found no mutations. Among the 67 patients with a mutation targeted by an FDA-approved agent, 5 expired and 2 entered hospice shortly after GTP was completed; four, all with commercial insurance, were denied coverage for recommended treatment. Only 12 (18%) began treatment based on GTP. Of those 12, 4 discontinued treatment because of side effects; 2 entered hospice; 2 discontinued due to tumor progression; and 1 was lost to follow-up. Three remain on GTP recommended treatment. The other 44 patients did not start GTP recommended treatment for a variety of reasons including proceeding with other chemotherapy or continuing current chemotherapy. A vast majority of patients were candidates for assay-directed molecularly targeted therapy; however, only a relatively small minority received a targeted agent.

Conclusion: Most gynecologic oncology patients are candidates for assay-directed targeted therapy, but molecular profiling is done late in the disease course and few patients get targeted agents. Expanded access to clinical trials, liberalized prescription drug coverage, updated FDA drug labels, tumor profiling well before end of life, early recognition of resistance to conventional drugs, and earlier consideration of targeted agents should encourage integration of these promising agents into routine practice.

377 - Poster Session

Lower uterine segment involvement in non-endometrioid endometrial cancer is correlated with a lack of driver mutations and unfavorable outcome

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Objective: This study aimed to determine the impact of lower uterine segment involvement (LUSI) on patient outcomes in nonendometrioid endometrial cancer, and to evaluate its associated mutational profiles.

Method: Clinicopathological parameters were correlated with survival in a cohort of 83 patients. Using next-generation sequencing, 400 genomic hotspots commonly implicated in carcinogenesis were analyzed in 42 patients with pathologically confirmed uterine papillary serous carcinomas.

Results: LUSI was diagnosed in 31.3% of patients. During a median follow-up of 45.5 months (range 1.7–103.7 months), patients with LUSI developed more local and distant recurrences (local, 19.2% vs 3.5%, $P = 0.03$; distant, 50% vs 17.5%, $P = 0.004$) and progression events (73.1% vs 26.3%, $P < 0.001$), with shorter mean progression-free survival (16 months compared to 26.5 months, $P < 0.01$). In a multivariate analysis adjusted for tumor size, lymphovascular space involvement, age, and FIGO stage, LUSI was associated with a 2.9-fold increase in the risk of progression ($P = 0.007$) and a 2.6-fold increase in the risk of death ($P = 0.02$). Mutations were identified in 60 genes, including *TP53* (61.9%), *PIK3CA* (14.3%), and *BRCA1/2* (28.6%). Serous tumors located in the lower uterine segment had less DNA repair pathway mutations (20% vs 62.5%, $P = 0.03$) and PI3K/mTOR pathway mutations (20% vs 75%, $P = 0.003$). See Figure 1.

Conclusion: LUSI is a significant adverse prognostic factor for tumor recurrence and survival that is associated with a unique mutational profile. Molecular profiling of nonendometrioid carcinomas can be used as a reference for targeted therapies in future clinical trials.

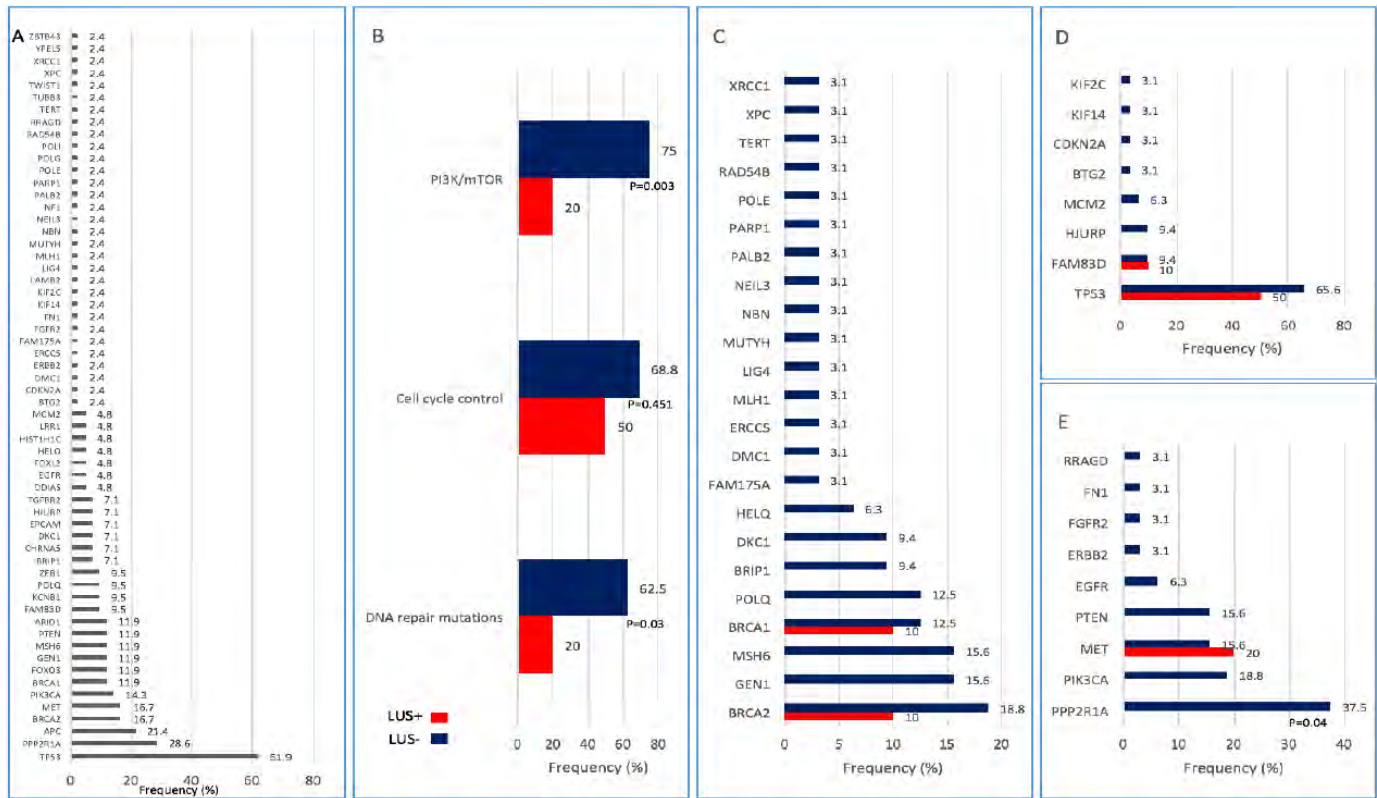


Fig. 1. Somatic mutations profiles of lower uterine segment UPSC versus upper uterine tumors: (A) The frequency of 60 gene mutations in 42 samples of UPSC (LUS+ in 10 samples). (B) Mutational distribution by their molecular pathway. (C) DNA repair pathway mutations. (D) Cell-cycle pathway mutations. (E) PI3K/mTOR pathway mutations.

378 - Poster Session

Long non-coding RNA *Tsix* is associated with human cervical cancer progression

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Objective: The functions of many long noncoding RNAs (lncRNAs) in human cancers remain to be clarified. Molecularly, random X inactivation is posited to be controlled in cis by a pair of oppositely transcribed X-linked long noncoding (lnc) RNAs, *Xist* and *Tsix*. The lncRNA *Tsix* is the master regulator of X inactivation in mammals. Despite the proposed models of *Tsix* function, the significance of *Tsix* RNA remains unclear in cancer. In this study, we examined the expression and the functional role of *Tsix* in cervical carcinoma.

Method: *Tsix* expression was determined in cervical cancer tissues ($n = 101$) and corresponding normal tissues ($n = 33$) by using real-time polymerase chain reaction, and its correlation with clinical parameters and prognosis was analyzed. To determine the role of *Tsix* in cell proliferation, migration, and invasion, RNA interference was used to knockdown *Tsix* expression in SiHa and Me-180 cervical cancer cells.

Results: The expression level of *Tsix* in cervical cancer tissues was higher than that in corresponding noncancerous tissues. High *Tsix* expression correlated with lymph node metastasis, and it was a significant prognostic factor for predicting cervical cancer recurrence. Knockdown of *Tsix* reduced cell proliferation, migration, and invasion.

Conclusion: *Tsix* is highly expressed in cervical cancer tissues and is associated with cervical cancer progression and prognosis. *Tsix* may represent a novel biomarker for predicting recurrence and prognosis and serve as a promising therapeutic target in cervical cancer.

379 - Poster Session
Withdrawn at author's request

380 - Poster Session

A clinical prediction model for recurrence in endometrial cancer

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Objective: Endometrial cancer is the most common gynecologic malignancy. Recurrence rates for early-stage endometrial cancer are low. However, when it recurs, treatment is not always curative. At present, there is no accepted model for predicting which patients are at risk to recur. The objective of this study is to use available clinical data at completion of treatment to predict recurrence of disease in endometrioid endometrial cancer (EEC) patients.

Method: After approval by the institutional review board, patient charts were reviewed, and clinical variables of interest were extracted of 82 patients diagnosed with EEC at our institution. Univariate and multivariate Cox regression hazard models to identify clinical variables associated with recurrence of disease were performed. Significance level was considered a P value < 0.05 for both. Prediction models were constructed using only significant variables available at baseline (right after surgery), analyzed with the lasso regression method and measured with area under the curve (AUC).

Results: Five-year survival in patients without recurrence was 100%, compared to 52% in patients with recurrence ($P = 0.99$). Univariate analysis revealed that white blood cell count (WBC, OR = 1.31), positive pelvic (OR = 1.56), and paraaortic (OR = 12.6) lymph nodes, myometrial invasion (OR = 1.03), lymphovascular space invasion (OR = 11.68), positive peritoneal cytology (OR = 3.33), stage (OR = 1.74), risk level (OR = 9.30), and adjuvant treatment (OR = 4.31) were significantly associated recurrence of disease. On multivariate analysis, only positive lymph nodes (OR = 35.06) and WBC (OR = 1.47) were associated with recurrence. Finally, a prediction model using WBC, lymph node status, and risk level was created with an AUC of 86% (95% CI 81%–91%) for predicting recurrence after treatment in patients with EEC; see Figure 1.

Conclusion: The clinical prediction model predicts EEC recurrence with an AUC of 86%. Predicting patients who are likely to recur may guide adjuvant treatment. Furthermore, we anticipate that the addition of molecular data to the current model will improve its performance. Prediction models that integrate clinical and molecular data could help us understand the characteristics of patients who experience recurrence and may inform alternative targeted therapy for these patients.

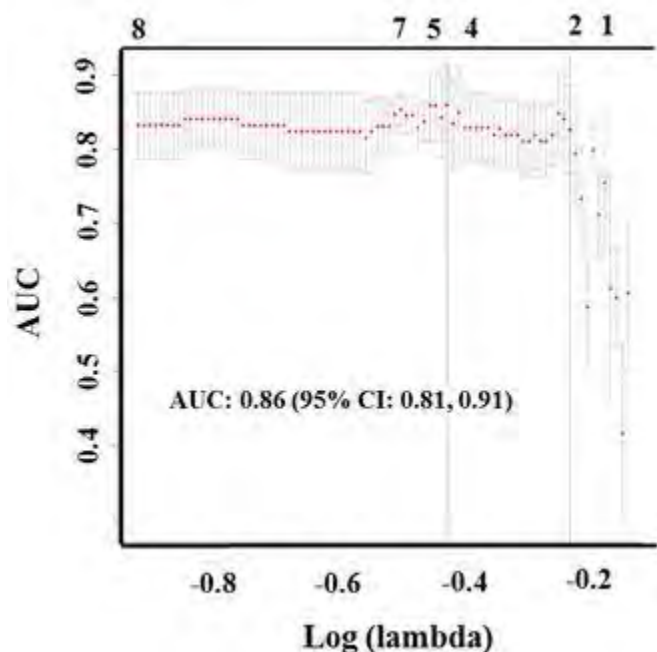


Fig. 1.

381 - Poster Session

SPR965, a PI3K/mTORC1/2 inhibitor, as a targeted therapy in endometrial cancer

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Objective: Alterations in the PI3K/mTOR pathway are prevalent in endometrial cancer (EC). First-generation mTORC1 inhibitors, however, have had only modest effects in EC clinical trials. SPR965 (Sphaera), a dual PI3K/mTOR inhibitor, targets PI3K as well as both mTORC1/2, potentially improving on the efficacy of first-generation mTOR inhibitors. Thus, we assessed SPR965's potential as an antitumorigenic agent in EC using cell lines and a genetically engineered mouse model (LKB1^{fl/fl}p53^{fl/fl}) of endometrioid EC.

Method: Cell proliferation was assessed by MTT assay after exposure to SPR965 for 72 hours in the HEC-1A, KLE, Ishikawa, and ECC-1 EC cell lines. Two representative cell lines, ECC-1 and KLE, were used for further studies. Cell cycle progression and apoptosis were assessed by Celigo Image Cytometry. Cellular stress was evaluated by DCFH-DA assay. ATP and lactate were determined by Lumimetric ATP assay and colorimetric D-lactate assay, respectively. Western immunoblotting was performed to assess downstream targets of the PI3K/mTOR pathway. LKB1^{fl/fl}p53^{fl/fl} mice were fed a control low-fat diet (10% calories from fat, lean) versus a high-fat diet (60% calories derived from fat, obese) to mimic diet-induced obesity, starting at 3 weeks of age. AdCre was injected at 6 weeks of age to induce invasive EC. Mice were treated with placebo or SPR965 (3 mg/kg/day, IM) following tumor onset for 4 weeks ($n = 10$ mice/group).

Results: SPR965 inhibited cell proliferation in a dose-dependent manner in all 4 EC cell lines (IC50 range 0.5–8 nM). SPR965 treatment resulted in G1 arrest and induction of cellular stress in both the ECC-1 and KLE cell lines ($P < 0.05$); however, apoptosis was not induced. SPR965 treatment decreased ATP levels and increased lactate levels in a dose-dependent manner in both cell lines ($P < 0.01$ – 0.05). Western immunoblotting demonstrated reduced phosphorylation of AKT and S6 within 24 hours of exposure. Expression of cell-cycle proteins was also decreased in a dose-dependent fashion in both EC cell lines after 18 hours. Last, SPR965 reduced tumor weight in obese mice and lean mice compared to control groups (63%–65%, $P < 0.05$).

Conclusion: SPR965 potently inhibited cell proliferation and tumor growth in EC cell lines and an EC mouse model. SPR965 should be considered for ongoing investigation in clinical trials for EC.

382 - Poster Session

Genomic alterations in extramammary Paget's disease of the vulva

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Objective: Extramammary Paget's disease of the vulva is an exceedingly rare malignancy with a chronic and relapsing course. We sought to identify genomic alterations that can be potential therapeutic targets.

Method: Patients with extramammary Paget's disease of the vulva treated at a tertiary cancer center were consented to an institutional review board-approved protocol for tumor-normal sequencing using a unique next-generation sequencing assay (Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets [MSK-IMPACT]). Primary tumor samples were sequenced and compared to matched germline DNA, and tumor somatic mutations were identified. Patient clinical data were abstracted from electronic medical records. Appropriate statistical analyses were used.

Results: We identified 7 patients with extramammary Paget's disease of the vulva who were consented for tumor sequencing. Median age at diagnosis was 66 years (range 51–77 years). No patient had invasive disease. Five patients were treated with primary surgery (wide local excision or partial vulvectomy), and 2 patients were started on imiquimod at diagnosis. After a median follow-up of 70 months (range 4–207 months), all patients were alive with disease and no documented evidence of invasion. Mutation burden varied from 4 to 31 mutations per tumor (Figure 1). The most common altered genes were *TP53*, *PIK3CA*, and *ERBB2*; each was identified in 4 tumor samples (57% of the cohort). Of note, the *PIK3CA*^{E545} codon alteration was present in 2 tumor samples (29% of the cohort), and 1 of these patients was successfully treated with a *PIK3CA*-targeted therapy. Copy number alterations (amplifications) were noted in *ERBB2* and *CDK12*, each present in 1 patient (14% of the cohort). All tumors were noted to be microsatellite stable.

Conclusion: This is the first study to evaluate somatic genomic alterations in extramammary Paget's disease of the vulva. We identified 3 unique gene alterations that were present in more than 50% of the cohort, and 2 of these (*PIK3CA* and *ERBB2*)

have targeted therapies available or in development. Our future work will focus on expanding this cohort to validate our early findings.

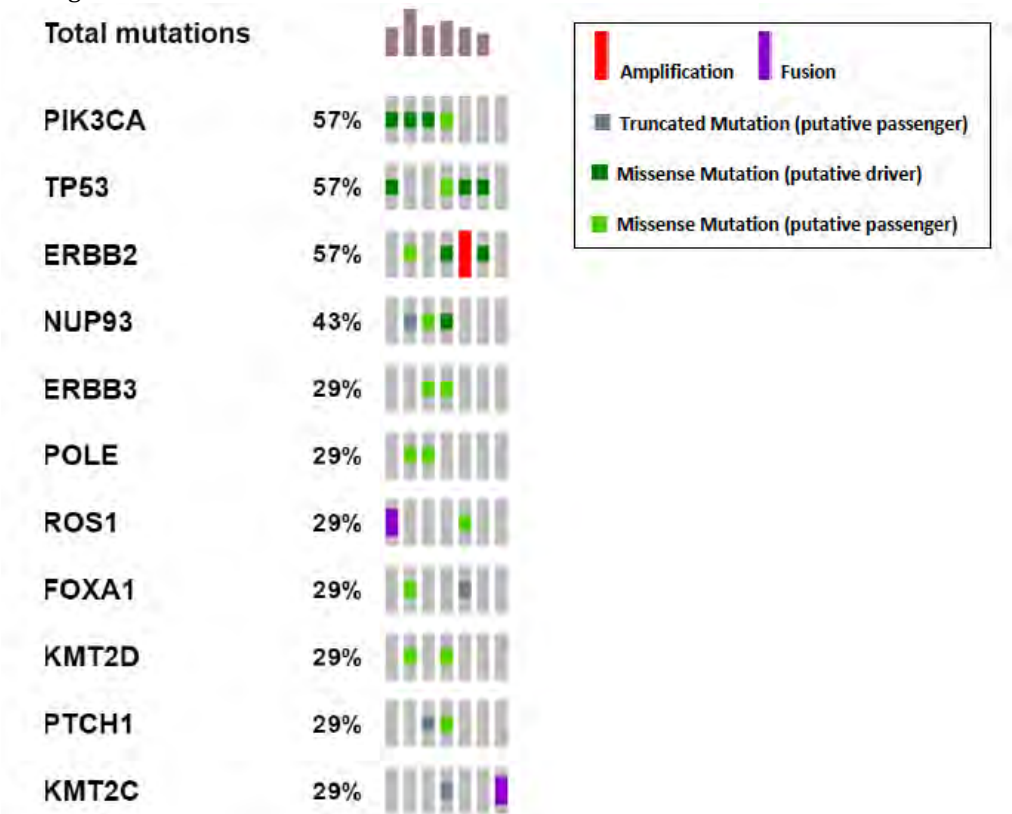


Fig. 1. Seven samples of extramammary Paget’s disease of vulva were sequenced by MSK-IMPACT. Gene alterations that were seen in at least 2 samples are noted here. Each gray vertical bar represents an individual patient sample. Percentages represent percentage of all samples that have the specific mutation.

383 - Poster Session

Classification of prospectively collected endometrial cancers into prognostically relevant subgroups using massively parallel sequencing and immunohistochemistry

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Objective: Endometrial cancer (EC) is a heterogeneous group of tumors with distinct molecular, clinical, and biologic features. Using massively parallel sequencing, The Cancer Genome Atlas (TCGA) identified 4 molecular subgroups in endometrioid and serous ECs that are associated with progression-free survival: (1) POLE-exonuclease domain mutated (EDM, ultramutated), (2) microsatellite unstable (MSI-H, hypermutated), (3) copy number-low/endometrioid-like (CNL-EL), and (4) copy number-high/serous-like (CNH-SL). The aim of this study was to prospectively classify ECs in the clinical setting, including histologic subtypes not studied by TCGA, into the 4 TCGA molecular subgroups using targeted sequencing and immunohistochemistry (IHC).

Method: Between May 2016 and July 2017, all primary ECs and corresponding normal tissue from patients who consented to the study were subjected to MSK-IMPACT, a massively parallel sequencing assay targeting all exons and select introns of 468 cancer genes. All tumors underwent IHC for DNA mismatch repair (MMR) proteins and p53. Tumors were classified into 1 of the 4 TCGA subgroups: (1) POLE EDM-mutant tumors were classified as POLE; (2) ECs with abnormal DNA MMR IHC and/or hypermutated phenotype and/or high MSI score by sequencing (MSI sensor) as MSI-H; and (3) ECs displaying abnormal p53 IHC and/or TP53 mutations and/or abundant gene copy number changes as CNH-SL. All remaining cases (e.g., TP53/p53, POLE, and MMR wild-type) were classified as CNL-EL. The concordance between IHC and sequencing results was also defined.

Results: Among the 179 ECs of various histologic types included in the study (Table 1), the distribution of molecular subgroups was POLE 7.8%, MSI-H 28.4%, CNL-EL 38.5%, and CNH-SL 25.1%. Distinct histologic subtypes displayed different

distributions of molecular subgroups (Table 1). IHC and MSK-IMPACT sequencing yielded concordant results with regard to p53/TP53 assessment in 87.7% of cases and in 93.3% of MSI-H ECs.

Conclusion: A subset of ECs are distinctly classified based on the addition of genomics to IHC and POLE mutation status, suggesting that a combined approach may be most robust in defining prognostically relevant molecular subgroups of ECs.

Table 1. Histologic and TCGA subtypes of 179 primary endometrial cancers.

Histologic type	POLE	MSI-H	CNL-EL	CNH-SL
Endometrioid (n=118)	12 (10.2%)	40 (33.9)	61 (51.7%)	5 (4.2%)
FIGO 1 (n=71)	6 (8.5%)	16 (22.5%)	46 (64.8%)	2 (2.8%)
FIGO 2 (n=35)	3 (8.6%)	17 (48.6%)	14 (40%)	1 (2.9%)
FIGO 3 (n=12)	3 (25%)	7 (58.3%)	1 (8.3%)	1 (8.3%)
Serous (n=17)	0	0	0	17 (100%)
Carcinosarcoma (n=11)	0	2 (18.2%)	0	9 (81.8%)
Clear cell (n=7)	1 (14.3%)	1 (14.3%)	1 (14.3%)	4 (57.1%)
De/Undifferentiated (n=7)	0	5 (71.4%)	2 (28.6%)	0
Mixed endometrioid/clear cell (n=7)	0	3 (42.9%)	4 (57.1%)	0
Mixed serous/endometrioid (n=4)	0	0	0	4 (100%)
Mixed serous/clear cell (n=3)	0	0	0	3 (100%)
High grade endometrial cancer, not otherwise specified (n=3)	1 (33.3%)	0	0	2 (66.7%)
Other (n=2)	0	0	1 (50%)	1 (50%)

384 - Poster Session

Circulating tumor DNA is an independent prognostic factor in patients with early-stage epithelial ovarian cancer

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Objective: Circulating tumor DNA (ctDNA) is an attractive source for liquid biopsy to understand the molecular phenotype of a tumor noninvasively; it is also expected to be a diagnostic and prognostic marker in cancer patients. Since most of the research for ctDNA analysis has been focused on advanced-stage disease, our aim is to clarify the clinical significance of ctDNA in patients with localized ovarian cancer.

Method: *PIK3CA* and *KRAS* are among the most frequently mutated genes in early-stage epithelial ovarian cancer (EOC). In addition, their hotspot mutations have been already identified and used for ctDNA analysis in this study. Tumor specimens and plasma samples (before surgery) of patients with ovarian tumors were investigated for *PIK3CA* or *KRAS* mutations using droplet digital (ddPCR). We defined ctDNA detection as positive when the corresponding mutations were detected in the plasma cell-free DNA.

Results: We screened 327 patients with ovarian tumors for somatic *PIK3CA* or *KRAS* mutations by ddPCR. A total of 124 patients with ovarian tumors were found to have somatic *PIK3CA* and/or *KRAS* mutations. A total of 85 patients had EOC among the patients with those mutations. The detection rates for ctDNA were 20% (13/66) and 53% (10/19) in patients with stage I-II disease and stage III-IV disease ($P = 0.0077$), respectively. No correlation was found between the detection frequency of ctDNA and other clinicopathological features. We examined the association of ctDNA with patient survival in early-stage EOC. ctDNA detection was associated with shorter recurrence-free survival in early-stage EOC patients ($P = 0.0095$,

log rank test). Multivariate analysis revealed only ctDNA remained an independent risk factor for recurrence when age, stage, peritoneal cytology, and histotype were included in the model ($P = 0.027$).

Conclusion: ctDNA was detected in approximately 20% of early-stage EOC patients in this study. The presence of ctDNA in the blood was an indicator for recurrence, which suggests potential tumor spread even when tumors were localized.

385 - Poster Session

From fat to fit: Diet switch reverses obesity-driven upregulation of lipid biosynthesis in endometrial cancer

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Objective: Obesity is associated with increased risk and worse outcomes in endometrial cancer (EC). Improvements in diet and weight loss are logical strategies for risk reduction, but little is known about the effect of these interventions on endometrial tumor metabolism. Thus, we sought to investigate the impact of dietary changes in a genetically engineered mouse model of endometrioid EC (LKB1^{fl/fl}p53^{fl/fl} mouse model).

Method: LKB1^{fl/fl}p53^{fl/fl} mice were fed a low-fat diet (LFD, 10% calories derived from fat) versus a high-fat diet (HFD, 60% calories from fat) starting at 3 weeks of age. At 18 weeks of age, the diet was switched in half of the mice, resulting in 4 dietary groups: (1) LFD ($n = 15$), (2) HFD ($n = 15$), (3) LFD switched to HFD (L-HFD, $n = 7$), and (4) HFD switched to LFD (H-LFD, $n = 20$). AdCre was injected into the left uterine horn in all mice at 28 weeks of age to induce EC, and the right uterine horn was used as the uninjected normal uteri. Mouse and tumor weight were measured after sacrifice at 40 weeks. Global, untargeted metabolomics, and lipidomics were performed to identify differences between normal and malignant uteri in each dietary group (LFD, HFD, L-HFD, and H-LFD).

Results: Mouse and tumor weight were increased in the HFD (50 g, 0.82 g) versus LFD (30 g, 0.27 g) mice ($P < 0.05$). Diet switch resulted in significant changes in body and tumor weight with L-HFD mice increasing in body and tumor weight (43 g, 0.48 g) and H-LFD mice decreasing in body and tumor weight (30 g, 0.32 g) ($P < 0.05$). Metabolomics revealed few differences between HFD and LFD normal uteri except for heightened lipid biosynthesis ($P < 0.05$). Comparing normal versus malignant uteri, many metabolic pathways were upregulated; however, further upregulation of lipid biosynthesis was unique to the HFD versus LFD mice. Lipids, amino acids, and nucleic acids were increased in ECs from HFD compared to LFD mice. L-HFD and H-LFD resulted in increased and decreased lipid content and biosynthesis in the endometrial tumors, respectively.

Conclusion: Exposure to a HFD was associated with increased mouse and tumor weight, as well as upregulation of lipid metabolism in both the normal and malignant uteri. A diet switch from HFD to LFD reversed these detrimental effects. These findings highlight the importance of improvements in diet as a means to affect EC outcomes and even overcome prior diet transgressions.

386 - Poster Session

Alterations in the uterine microbiome in women and mice with endometrial cancer: Variations by race and obesity

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Objective: Obesity and race are known to have a negative impact on clinical outcomes in endometrial cancer (EC). We sought to evaluate the microbiota of murine and human ECs and to assess for variations by obesity and race status.

Method: Banked tumor specimens of patients undergoing hysterectomy for endometrioid EC were identified. Tumors were analyzed from African-American and Caucasian women and stratified as obese (BMI ≥ 30 kg/m²) or nonobese (BMI < 30 kg/m²). Endometrioid ECs from obese and nonobese LKB1^{fl/fl}p53^{fl/fl} mice were also compared. The microbiota of the murine and human ECs were characterized by bacterial 16S rRNA high-throughput sequencing, and data were analyzed using Qiime. Global, untargeted metabolomics of murine ECs was performed.

Results: Twenty-one human EC specimens were evaluated. Of these, 11 were from African-American (52%) and 10 from Caucasian (48%) women. Median age was 69 years. The majority of women were postmenopausal ($n = 17$, 81%) and obese ($n = 14$, 66.7%). Tumor grade was evenly distributed with 7 grade 1 (33%), 6 grade 2 (29%), and 8 grade 3 (38%). EC microbiota richness was higher in African-American than in Caucasian women ($P = 0.02$). Analysis by race and obesity status showed

significant differences in EC microbiota composition. The microbiota composition differed between obese Africa-American and obese Caucasian women ($P = 0.04$). In obese woman, the distribution of Proteobacteria was 55% African-American versus 31% Caucasian women ($P = 0.02$), while Actinobacteria abundance was 18% versus 34%, respectively ($P = 0.05$). Among Caucasian women, the EC microbiota profile differed between obese and nonobese ($P = 0.07$). At the genus level, the relative abundances of *Delftia*, *Finelgoldia*, *Geobacillus*, *Propionibacterium*, and *Pseudomonas* varied by obesity and race. Comparing obese and nonobese murine ECs, variations in microbiome associated metabolites were seen ($P < 0.05$), including benzoate compounds and aromatic amino acids derivatives. Overlap was seen in obesity-associated microbiota between mice and women that included *Delftia*, *Bacteroides*, and *Pseudomonas*.

Conclusion: Distinct microbiota profiles were found between ECs of obese and nonobese women and mice. Furthermore, EC microbiota diversity was greater in the tumors of African-American versus Caucasian women. Better understanding of the interrelationship of obesity and race on the EC microbiota may provide critical insight into the disparate clinical outcomes between African-American and Caucasian women with EC.

387 - Poster Session

Can an *a priori* decision be made based solely on endometrial epithelial characteristics as to when to stage lymph nodes in biopsy proven grade I, type I uterine adenocarcinomas?

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Objective: Endometrial epithelium obtained from diagnostic endometrial sampling can provide *a priori* clues as to which patients with grade 1 endometrial cancer benefit from lymph node staging.

Method: Pathological and clinical data of 252 consecutive hysterectomy-confirmed grade 1 endometrial uterine cancers and 43 hysterectomy-confirmed grade 3 nonserous, non-clear-cell endometrial cancers were reviewed and compared to risk factors predictive of extra-uterine disease encompassing Variant IHC-staining (ER negative, PR negative, p53-mutated, or wildtype PTEN); MSI-high status; >25% villoglandular tumor epithelium; and microcystic, elongated, and fragmented (MELF) gland invasion in the hysterectomy specimen. Five groups were created: G1, nonserous, non-clear-cell grade 3 tumors; G2, grade 1 tumors with variant IHC-staining; G3, grade 1 tumors with MELF invasion; G4, grade 1 tumors with variant IHC-staining and MELF invasion; and G5, grade 1 tumors negative variant IHC-staining and MELF-invasion.

Results: Based on data separation at the level of $P < 0.05$, 76 G2 tumors resembled 43 G1 tumors with exception of less vascular invasion. Fifty-six G3 tumors resembled G1 tumors with exception of less spread beyond the uterine corpus. One hundred twelve G4 tumors resembled G1 tumors with exception of less vascular invasion. G2 tumors differed from 140 G5 tumors with regard to vascular invasion, stage IA confinement, and stage >II spread. G3 tumors differed from G5 tumors with regard to vascular invasion, stage IA and IB confinement, stage >II spread, and MSI-high status. Of G3 tumors, 80.4% showed >25% villoglandular growth pattern. G4 tumors differed from G5 tumors with respect to vascular invasion, stage IA confinement, and stage >II spread. A total of 140 G5 tumors showed no significant villoglandular growth.

Conclusion: Grade 1 endometrial cancers with variant IHC-staining or >25% villoglandular growth resemble grade 3 endometrial cancers and differ from grade 1 tumors without variant IHC staining. We identified 106 (94.6%) of 112 variant or MELF-invasive grade 1 endometrial cancers that would have benefited from lymph node dissection, with 18 cases (17.0%) showing more than FIGO IIIA spread. By categorizing the tumors in this manner, we would reduce the need for frozen section to less than 60% of all grade 1 cases.

388 - Poster Session

Development and implementation of a targeted next generation sequencing methylation panel for the assessment of methylation in ovarian and endometrial cancers

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Objective: To develop a tool for assessing the contributions of DNA repair gene methylation in ovarian and endometrial carcinoma.

Method: A methylation sequencing panel targeting the CpG islands and adjacent shores of 57 genes associated with DNA repair was designed based on Agilent's Sureselect MethylSeq technology and was implemented to study methylation in carcinomas. For initial analysis we included 13 ovarian carcinoma cases from a university-based gynecologic oncology tissue bank. Four endometrial cancer cases with normal germline and somatic sequencing at all the Lynch syndrome DNA mismatch repair genes and unexplained IHC loss of MSH2 and MSH6 were referred for methylation analysis from a university clinical laboratory. DNA from frozen and formalin-fixed paraffin-embedded cancer was prepared for target enrichment, hybridized, and captured to regions of interest. After hybridization, the captured DNA libraries were bisulfite treated to differentiate methylated and unmethylated DNA segments. Bisulfite-modified and -captured DNA libraries were then amplified, indexed, and pooled for multiplex deep sequence analysis using an Illumina HiSeq. The bioinformatics pipeline included alignment to a theoretical bisulfite-modified genome to obtain annotated, interpretable output. The Integrative Genomics Viewer (IGV) was used to visualize output in each region and assess depth of coverage.

Results: Six ovarian carcinomas were identified as methylated at 3 genes by methylation sensitive PCR including 2 each at the *BRCA1*, *RAD51C*, and *MLH1* promoters. All were found to be methylated with MethylSeq generating 100% concordance. Methylation sequencing of 7 additional ovarian carcinoma tumors, whose methylation status was unknown showed 1 case, LS519, with methylation of *MLH1*. One of 4 unsolved endometrial cancers with unexplained MSH2/MSH6 deficiency in the tumor was found to be positive for methylation at the *MSH2* promoter in the region previously linked to down-regulation of MSH2. See Figure 1.

Conclusion: The methylation panel for genes associated with DNA repair is a useful tool for assessing promoter methylation at many DNA repair genes simultaneously. We are now using this panel to assess methylation in DNA repair genes in ovarian carcinomas and relating to response to treatment and development of resistance.

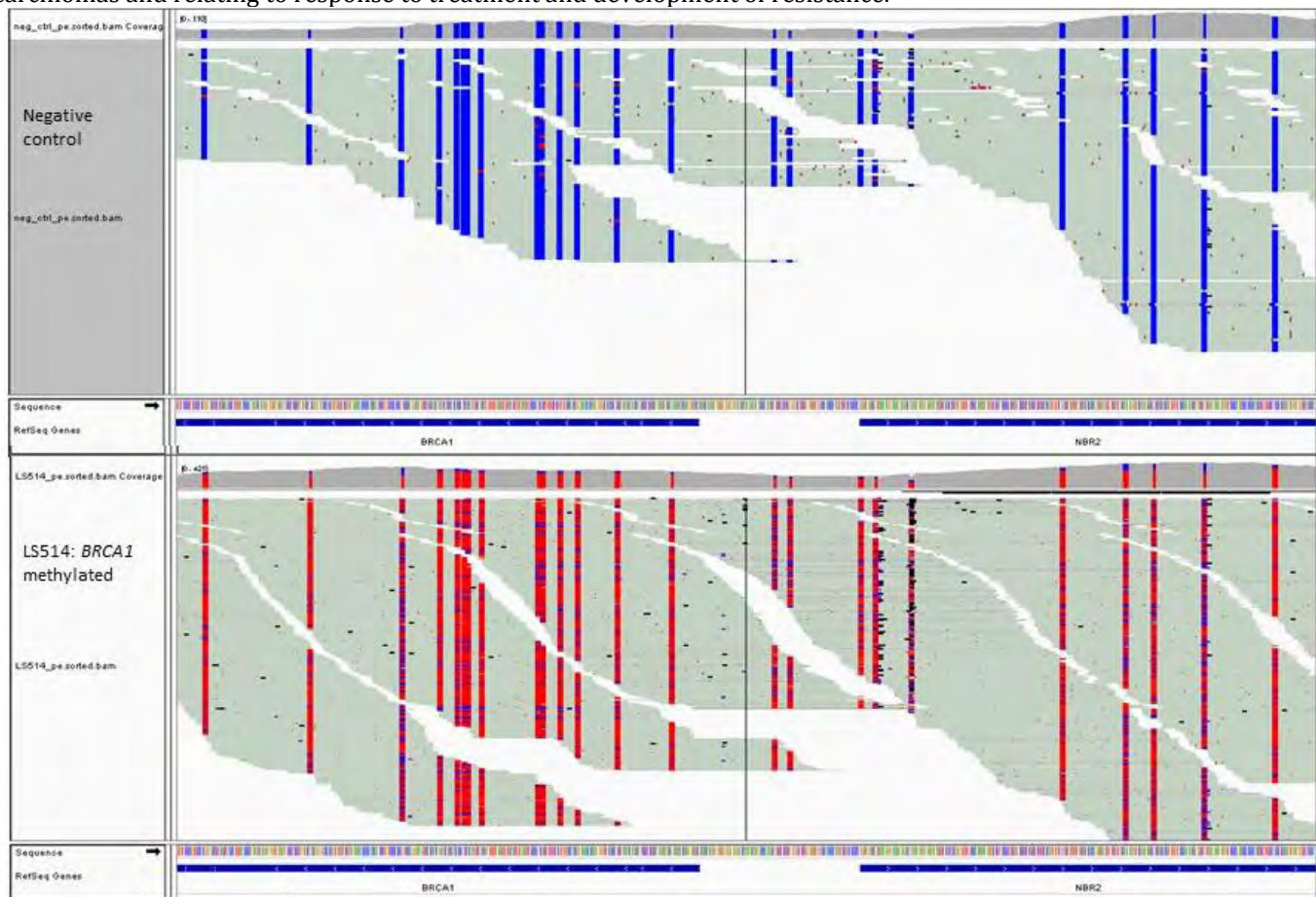


Fig. 1. IGV visualization of DNA libraries that have undergone bisulfite conversion and sequencing. The bisulfite mode on IGV is highlighted in reads with a red or blue nucleotide corresponding to the position of the cytosine in the reference genome. For forward reads, a red C denotes a non-converted cytosine, implying methyl or other protection, while a blue T denotes a bisulfite converted cytosine. The figure shows the promoter region of *BRCA1*, with the top panel showing the reads for an unmethylated control; bottom panel shows reads for a methylated ovarian carcinoma sample.

389 - Poster Session

Toxicity associated with long-term bevacizumab use in patients with recurrent ovarian cancer: A multi-institutional study

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Objective: Bevacizumab is commonly used in the treatment of ovarian cancer (OC). While acute side effects of bevacizumab are well known, there is limited information on the toxicities associated with its prolonged use. We aimed to characterize toxicities associated with long-term bevacizumab use in women with recurrent OC and compare these with short-term side effects.

Method: We conducted a multiinstitutional, retrospective review of patients with recurrent OC who were treated with bevacizumab for at least 18 cycles between 2006 and 2016. Demographic, clinical, and pathological data were analyzed with descriptive statistics. Toxicities were defined and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Toxicities during cycles 1–17 were compared with toxicities during cycles ≥ 18 using exact McNemar tests. The Kaplan-Meier method was used to determine overall survival (OS).

Results: Study criteria were met by 82 patients. Mean age at diagnosis was 59.9 years (range 28.9–81.8 years). The majority of patients (61%) had stage IIIC OC, and the most common histology was serous (69.5%). The median number of total bevacizumab cycles was 26 (range 18–114). The median OS was 140.8 months. Adverse effects more common during cycles 1–17 than cycles ≥ 18 included anorexia (48.8% vs 28.0%, $P < 0.05$), fatigue (75.3% vs 62.2%, $P < 0.05$), and headaches (42.7% vs 25.6%, $P = 0.01$). Prolonged bevacizumab treatment was associated with a grade 1–2 increase in creatinine (30.0% vs 36.6%, $P = 0.01$). There was no difference in any other toxicities between the two time points, including fistula, proteinuria, epistaxis, hypertension, and thromboembolic events (all $P > 0.05$).

Conclusion: In the present study, prolonged bevacizumab treatment was associated only with a grade 1–2 increase in creatinine. Although this study is limited by its retrospective nature and small sample size, there appear to be few toxicities associated with long-term use of bevacizumab. Larger studies are warranted to validate these findings.

390 - Poster Session

Proteomic profiling of chemotherapy naïve versus neoadjuvant treated ovarian tumors

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Objective: Epithelial ovarian cancer is the most lethal gynecologic malignancy with nearly 75% of women diagnosed with advanced-stage disease. The objective of this study was to determine the proteomic profiles of matched chemotherapy naïve and neoadjuvant-treated (NACT) serous ovarian tumors.

Method: Twenty-six patients with chemotherapy naïve and post-NACT ovarian tissue were identified. Formalin-fixed, paraffin-embedded tissues were hematoxylin and eosin stained to enable selective harvest of tumor cells by laser microdissection. Proteins were extracted and digested with trypsin. Samples were labeled with tandem-mass tag (TMT) isobaric labeling reagents and analyzed using a multiplexed, quantitative proteomics strategy. Data were searched against a Swiss-Prot human protein database, and significant protein alterations were analyzed by Ingenuity Pathway Analysis.

Results: Differential analyses of 3,459 proteins quantified by at least 2 peptide spectral matches across pre- and post-NACT treated tissues revealed 151 proteins significantly altered between these groups (LIMMA, adjusted $P \leq 0.05$). A heat map demonstrated enrichment (red) and decreased (green) proteins involved in pathways that were further analyzed via pathway analysis tools (Figure 1). These 151 protein alterations accurately classified most pre- and posttreatment samples. Functional inference revealed activation of pathways regulating cell survival, fatty-acid metabolism, and leukocyte movement and

inhibition of pathways regulating migration and metastasis in post- versus pre-NACT tissues. Network alterations supporting impaired hormone signaling and cell survival and activation of protein kinase C signaling were noted in post- versus pre-NACT tumor cells. Further evaluation by high versus moderate disease distribution in post-NACT tumors revealed 109 proteins significantly altered between these groups, with network analysis supporting modulation of cell adhesion signaling, integrins, and Mitogen Activated Protein Kinase signaling.

Conclusion: Significant proteomic alterations in ovarian tumors treated with NACT reveal evidence of increased cell survival and altered metabolism in post-NACT tumor cells, suggesting areas to further investigate toward improving treatment of NACT-treated ovarian cancer patients.

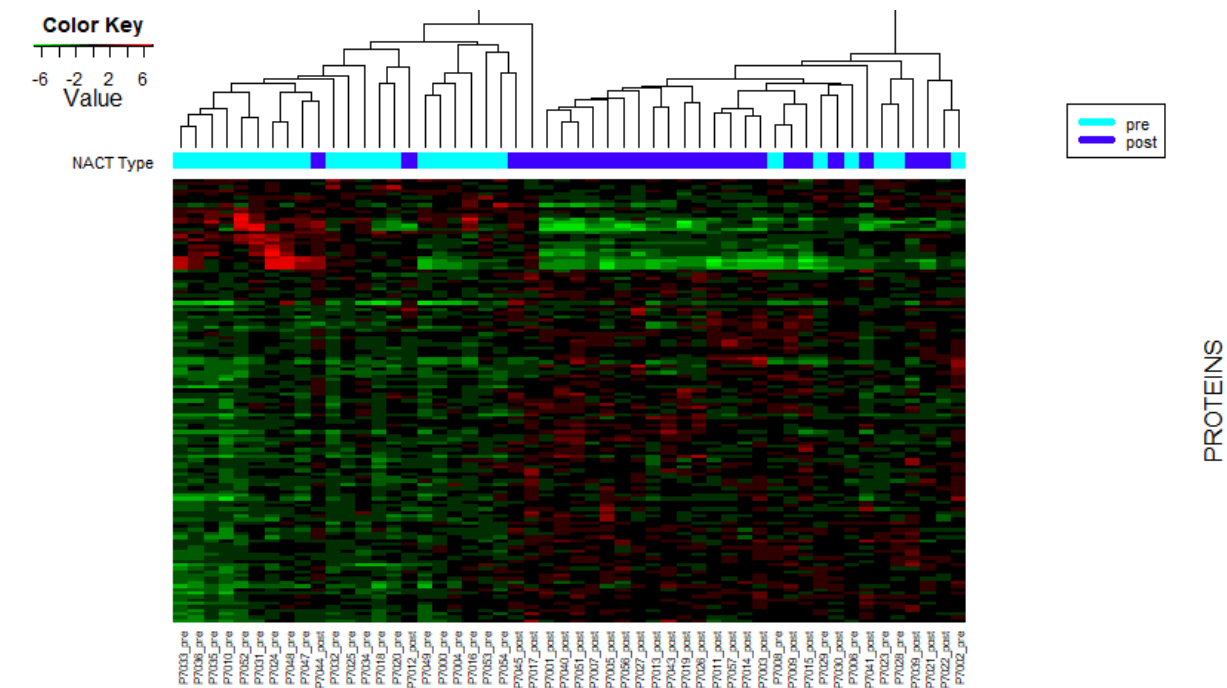


Fig. 1. Supervised analysis of quantitative proteomic data collected from matched formalin fixed paraffin embedded tissue biopsies harvested from high-grade serous ovarian cancer patients ($n = 26$), pre- versus post-neoadjuvant chemotherapy (NACT) treatment (“pre”: pre-NACT, “post”: post-NACT).

391 - Poster Session

Molecular variations in uterine carcinosarcomas: Are there therapeutic opportunities?

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Objective: Uterine carcinosarcomas (MMMTs) account for only 5% of uterine cancers, yet they account for disproportionately more uterine cancer-related deaths owing to their aggressive behavior. Even in patients with early-stage disease, recurrence rates approach 50%. Molecular profiling may explain the aggressive nature of these cancers and lead to the discovery of potential therapeutic targets.

Method: CGP results (including gene mutation, gene fusion, copy number amplification [CNA], CISH, and immunohistochemistry [IHC]) for patients with uterine MMMT were retrieved from the CARIS Life Sciences database. Proportion of patients with positive test results was calculated.

Results: We identified 168 patients with primary MMMT. Median age was 67 years; 124 (74%) of specimens were obtained from the uterus, the remaining 44 (26%) from metastatic sites. In a 592-gene panel, tumor mutation load (TML) was low in most cases (77%), 18% were moderate, and 5% were high; two tumors harbored POLE mutations. Most tumors were microsatellite (MS) stable (94%). In a subset analysis, a significant association was seen between TML and MS instability ($P = 0.000$). The following aberrations were observed in mutational analyses: *TP53* (86%), *PIK3CA* (34%), *FBXW7* (23%), *PTEN* (18%), *KRAS* (16%), and *PPP2R1A* (10%). Other genes (e.g., *ATM*, *RB1*, *KMT2D*, *NF1*, *KMT2C*, *BRCA2*, *DICER1*, and *FGFR2*) were

mutated at $\leq 6\%$ frequency. CNA was observed for *CCNE1* in 16% of specimens and *AKT2* in 8%. *HER2* was amplified in 3/33 (9%) of patients by CISH. A majority (95%) of patients were *TOP2A* positive by IHC, while *TS* (80%), *PTEN* (76%), *TUBB3* (66%), and *PD1* (54%) also had high expression. ER and PR staining was generally low (26% and 14%, respectively). *SPARC* staining was 100%, which has been associated with *VEGF* overexpression.

Conclusion: To our knowledge, this is the largest cohort of MMTs that has been molecularly described. Our data suggest CGP may inform treatment, for example, targeting the PI3K/AKT pathway with mTOR inhibition, chromatin remodeling therapies including EZH2 or PARP inhibition, or VEGF inhibition. PD-1/PD-L1 inhibition may be useful in a subset of patients with high TML/MS instability. Clinical trials are needed to validate these observations.

392 - Poster Session

Targeting BMI1 for the treatment of endometrial cancer

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Objective: Advanced or recurrent endometrial cancer carries a dismal prognosis with a high rate of chemoresistance. Strategies to improve response rates are greatly needed. BMI1, a member of the polycomb repressor complex-1, regulates chromatin structure and is indispensable for self-renewal of both normal and cancer stem cells. BMI1 is upregulated in many malignancies including endometrial cancer. Targeting BMI1 inhibits cell viability and leads to caspase-dependent apoptosis in endometrial cancer cell lines. Here we examine BMI1 levels in patient tissue samples and demonstrate in vivo efficacy of anti-BMI1 therapy.

Method: A tissue microarray consisting of 203 patient samples was utilized for IHC of BMI1. A standardized H-score was used to quantify BMI1 expression. Standard statistical methods were used to examine relationships between BMI1 expression and various clinicopathologic variables. An in vivo mouse xenograft model was developed using female athymic nude mice and an endometrial carcinosarcoma cell line. Mice were randomized into 3 treatment groups: placebo, carboplatin/paclitaxel (C/T), and PTC-028 (a small molecule from PTC Therapeutics, South Plainfield, NJ, that decreases the level of BMI1). Mice were treated for 2 cycles and followed for survival. Survival analysis was performed using Kaplan-Meier curves and log rank analysis.

Results: On IHC of the tissue microarray, BMI1 expression correlated with nonendometrioid histology ($P = 0.007$). Patients with high BMI1 expression had worse overall survival on multivariate analysis ($HR = 2.4$, $P = 0.02$). The in vivo mouse xenograft model demonstrated a significant increase in tumor doubling time in mice treated with PTC-028 compared to vehicle (4.9 vs 1.9 days). Overall survival (Figure 1) was also significantly improved compared to the vehicle group ($P = 0.03$) and C/T group ($P = 0.43$).

Conclusions: An in vivo mouse xenograft model supports the use of anti-BMI1 strategies in endometrial cancer patients. In addition, improvement of overall survival in an aggressive carcinosarcoma model as well as its association with type 2 endometrial cancer histologies suggest that this strategy may provide the most benefit in those at highest risk of presenting with advanced or recurrent disease.

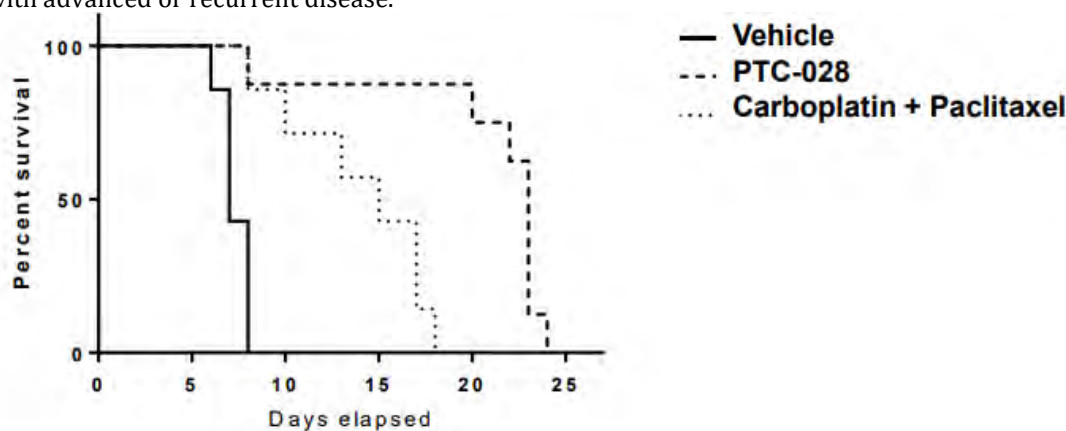


Fig. 1. Overall survival of a carcinosarcoma mouse xenograft model.

393 - Poster Session

PARPi after PARPi in epithelial ovarian cancer

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Objective: To describe the treatment experience of patients who are receiving an inhibitor of poly(ADP-ribose) polymerase (PARPi) for treatment or maintenance of recurrent epithelial ovarian cancer (EOC) and have a history of prior PARPi exposure.

Method: We conducted a multiinstitutional, retrospective review of patients with epithelial ovarian cancer who received at least 2 lines of therapy containing a PARPi. Demographic, clinical, and pathological data were analyzed with descriptive statistics. The Kaplan-Meier method was used to determine progression free survival (PFS) and overall survival (OS).

Results: Of the 11 identified patients, 9 (81.8%) were stage III, and 2 (18.2%) were stage IV. Four patients (36.4%) were *BRCA* negative; 4 (36.4%) were *gBRCA1+*; 2 (18.2%) were *gBRCA2+*; and 1 (9.1%) was *tBRCA1+*. Initial PARPi was given as treatment in combination with other chemotherapeutic agents; 10 patients (90.9%) received veliparib, and 1 (9.1%) received olaparib resulting in 8 complete responses (CR), 2 partial responses (PR), and 1 progressive disease (PD). First PARPi was discontinued because the planned number of cycles was reached ($n = 7$) and because of progression ($n = 2$) and adverse effects to other chemotherapy agents in the regimen ($n = 1$). Second PARPi was given for treatment ($n = 9$) and for maintenance ($n = 1$). Seven patients (63.6%) received niraparib; 2 (18.2%) received olaparib; and 2 (18.2%) received rucaparib resulting in 3 PR, 4 stable disease (SD), and 2 PD. Second PARPi was discontinued due to progression ($n = 6$), toxicity ($n = 3$), and financial reasons ($n = 1$). In this small cohort of patients, response to initial PARPi, *BRCA* status, and gross residual disease at completion of cytoreductive surgery were not significant predictors of response to PARP inhibitors ($P > 0.05$). Two patients (18.2%) experienced grade 3 or 4 thrombocytopenia, and 1 (9.1%) experienced grade 3 or 4 neutropenia. Following second PARPi, median PFS was 7.4 months; median OS was 20.8 months.

Conclusion: In this multiinstitutional study, a second PARPi demonstrated activity in patients with recurrent EOC. Now that there are 3 FDA-approved PARPi for different indications, repeat use of PARPi may become more common. More data are needed regarding the efficacy and safety of this approach.

394 - Poster Session

Understanding resistance to PARPi using a novel radiotracer based methodology

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Objective: [¹²⁵I]KX1 is a radiolabeled poly (ADP-ribose) polymerase inhibitor (PARPi) that allows for the in vitro quantification of the affinity of PARPi to the PARP-1 enzyme. The objectives of this study were to engineer cells resistant to PARPi and to employ [¹²⁵I]KX1 to assess whether PARPi resistance in *BRCA1*-mutant ovarian cancer cells could emerge owing to reduced binding affinity of the clinical inhibitors to the PARP-1 enzyme.

Method: *BRCA1*-mutated UWB1.289 ovarian cancer cell lines resistant to PARPi were generated either by deletion of 53BP1, REV7, or PTIP gene or by isolation of spontaneous clones after prolonged culture with increasing concentrations of olaparib, a PARPi. Cell viability assays were used to determine the relative levels of PARPi resistance in these lines compared to parent control. Western blot analysis was performed in the resistant cell lines to assess whether the presence of *BRCA* reversion mutation and loss of PARP1 expression is a mechanism of resistance. Last, [¹²⁵I]KX1 competitive inhibition experiments were performed for olaparib, rucaparib, and niraparib in vitro using a whole cell assay with the resistant cell lines to determine the PARPi affinity to the PARP-1 enzyme.

Results: Both the engineered and spontaneously resistant cells showed reduced sensitivity to PARPi. In the spontaneous clones, we observed a *BRCA1*-delta 11q alternative splice isoform intragenic mutation that promotes therapeutic resistance to PARPi. PARP expression was variable in the resistant clones. These resistant clones revealed no pharmacologic differences in their binding affinity to all three PARPi.

Conclusion: In our study, resistance to PARPi was not due to secondary mutations within the catalytic domain of the PARP enzyme, which would reduce the affinity of PARPi. This suggests that PARPi resistance can emerge even when PARPi can effectively interact with PARP-1 enzyme. Clinically, radiotracer tools like KX1 would be more relevant to assess for resistance only in patients who lack PARP-1 expression on imaging, and these patients may not be candidates for therapy with PARPi. Future studies are needed to examine the causes of PARP-1 expression variability in models of resistance and determine whether this is relevant to the overall resistance.

395 - Poster Session

Distinct molecular profiles and potential therapeutic targets in androgen receptor stratified ovarian cancer patients

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Objectives: Growing literature in breast cancer suggests that androgen receptor (AR) should be used to stratify patients with triple negative breast cancer (TNBC). Compared with AR+ TNBC, “quad negative” patients differ in their prognosis, response to therapy, and molecular profiles. It is unknown whether AR status confers similar prognostic and treatment benefit in other tumor types. We aim to explore molecular and genomic features of AR+ and AR- ovarian cancer.

Method: A total of 8,321 epithelial ovarian tumors were evaluated by Caris Life Sciences from 2009 to 2016 by multiplatform profiling, which included protein expression (IHC), NextGen sequencing (SEQ), and/or in situ hybridization. AR expression higher than (1+, 10%) was determined positive. Two-tailed χ^2 test was used for comparison; significance was defined as $P < 0.05$.

Results: Overall, positive AR expression was seen in 39% of EOC tumors: 35% in serous, 32% in endometrioid, 21% in carcinosarcoma, 4.3% in mucinous, and 3.9% in clear cell histologies. Compared to AR- tumors, AR+ tumors had significantly less frequent mutations on KRAS (4.6% vs 10%, $P = 4.2E-11$), PIK3CA (4.5% vs 8%, $P = 1.85E-06$), SMAD4 (0.1% vs 0.5%, $P = 0.03$), and GNAS (0 vs 0.3%, $P = 0.03$), and more frequent AKT1 (0.7% vs 0.3%, $P = 0.03$) mutations. In addition, the AR+ cohort showed significantly higher expression of ER (73% vs 36%, $P = 3.1E-206$), PR (41% vs 17%, $P = 2.3E-116$), lower frequency of PTEN loss by IHC (21% vs 33%, $P = 4E-27$), and lower frequency of TOP2A (IHC, 67% vs 75%, $P = 6E-10$; ISH, 0.9% vs 6.7%, $P = 0.02$), Her2 (1% vs 2%, $P = 0.002$; 2.1% vs 3.9%, $P = 0.0003$), and cMET (10% vs 14.7%, $P = 1.8E-6$; 0.w% vs 0.9%, $P = 0.01$) protein expression and gene amplification. In the ER-/PR- cohort ($n = 3,717$), AR+ was seen in 9.9% of tumors. When AR+/ER-/PR- tumors were compared to AR-/ER-/PR- tumors, KRAS (1.5% vs 10.8%, $P = 1.5E-6$) and PIK3CA (3.4% vs 9.3%, $P = 0.001$) differences and cMET expression (11.3% vs 19%, $P = 0.001$) remain significant. Also, the TP53 mutation rate was higher in the AR+ cohort compared to the AR- cohort (76% vs 62%, $P = 7.7E-6$).

Conclusion: Our findings suggest distinct molecular profiles in AR-stratified ovarian cancer, providing potential targets for therapeutic exploitation. Drugs targeting the PI3KCA/Akt/mTOR, MAPK, cMET, and cell cycle control pathways, as well as hormonal agents, may benefit selected subsets of patients stratified by AR expression.

396 - Poster Session

Obesity is associated with altered angiogenic gene expression in endometrioid endometrial cancer

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Objective: Obesity has been associated with worse outcomes in endometrioid endometrial cancer (EEC) and increased tumor aggressiveness in a genetically engineered mouse model. We sought to evaluate the association between obesity and angiogenic genes and determine whether metformin mitigates these effects.

Method: We evaluated the association between 168 angiogenic candidate genes and body mass index (BMI) in the TCGA endometrial cancer database (including all patients with endometrioid histology, available BMI, and available RNA-seq data, $n = 290$), and evaluated this association in a unique EEC LKB1^{fl/fl}p53^{fl/fl} mouse model ($n = 20$). Mice received 60% calories from fat in a high-fat diet (HFD), mimicking diet-induced obesity, versus 10% calories from fat in a low-fat diet (LFD). After confirming tumor growth, HFD ($n = 5$) and LFD mice ($n = 5$) were treated with metformin (200 mg/kg/day) or control. Tumors were analyzed using RNA-seq for differential expression of angiogenic genes.

Results: Twenty-one candidate angiogenic genes (based on a false-discovery rate threshold $P < 0.1$) were differentially associated with BMI in the TCGA database. None of these genes validated in the mouse data based on a Bonferroni adjusted type I error rate of 0.05. In the TCGA cohort, higher BMI values were associated with higher levels of *Edil3* ($P = 0.01$, q value = 0.092). Evaluation of these genes in the mouse model revealed association between increased *Edil3* expression in HFD versus LFD mice (2.44-fold change, unadjusted $P = 0.03$). HFD mice receiving metformin demonstrated an interaction effect with reduction of *Edil3* expression ($P = 0.009$). Exploratory analysis in the mice revealed differential expression of 21 angiogenic genes including increased expression of the following potent pro-angiogenic genes (*Lep*, 4.0-fold; *Vegfa*, 2.8-fold).

Conclusion: Obesity may alter the tumor microenvironment and promote tumor progression via differential modulation of angiogenic pathways in EEC. Specifically, *Edil3* may play an important role in this microenvironment and serve as a novel target. Metformin was associated with reduction of pro-angiogenic genes.

397 - Poster Session

Clinical genomic profiling identifies potential prognostic markers in patients with gynecologic carcinosarcoma

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Objective: Carcinosarcomas comprise de-differentiated carcinomatous and sarcomatous components. Limited data are available on this rare tumor, and our goal was to correlate clinicopathologic and tumor sequencing characteristics of exceptional and poor responders in patients with carcinosarcoma of gynecologic origin.

Method: We retrospectively analyzed patients with a diagnosis of uterine or ovarian carcinosarcoma who had CLIA certified comprehensive next-generation sequencing (NGS) of 315 or 467 cancer genes between January 1, 2014, and May 1, 2017. All patients were treated in a single institution, underwent surgical staging, and received platinum-based chemotherapy as their adjuvant treatment. Molecular, demographic, and clinical data were analyzed using descriptive statistics and Fischer exact test. Multivariate analysis was performed using logistics and Cox regression analysis.

Results: From 20 patients, 22 tumors were available for sequencing. Patient and molecular characteristics are summarized in Table 1. Overall, 96 mutations were detected in 54 genes. The most common mutations were TP53 (68%), CCNE1 (32%), PTEN (27%), PIK3CA (23%), and FBXW7 (18%). Two patients received targeted therapy as result of NGS (10%). A shorter progression-free survival (PFS) was significantly associated with FBXW7 mutation on multivariate analysis ($P = 0.0173$, HR = 7.626, 95% CI 1.453–45.236). TP53 mutation had a trend towards decreased overall survival (OS) ($P = 0.06$). Mutations associated with the chromatin remodeling pathway (ARID1A/B, BCOR, DNMT3A, EZH2, MLL2, MLL3, MYST3, SPOP) accounted for 17% of detected genes alterations and were significantly associated with platinum sensitivity ($P = 0.04$). On multivariate analysis, there was a nonsignificant trend towards improved PFS ($P = 0.08$). Of the tumors tested, none of cases were mismatch repair deficient. There was no significant difference between gene alterations in CS of uterine or ovarian origin. Improved OS was associated with receipt of radiation therapy and negative surgical margins ($P < 0.01$).

Conclusion: FBXW7 and genes within chromatin remodeling pathways may be clinically relevant as prognostic markers for patients with carcinosarcoma of gynecologic origin and should be studied in prospective clinical trials.

Table 1. Clinical and tumor characteristics in patients with uterine or ovarian carcinosarcoma.

Patient Characteristic		% (number/total patients), <i>n</i> = 20
Age, median years (range)		65 (49-78)
BMI, median (range)		29 (19-46)
Ethnicity		
	White	35% (7/20)
	Hispanic	40% (8/20)
	Black	15% (3/20)
	Others/Unknown	10% (2/20)
Tumor characteristics		
	Uterine origin	80% (16/20)
	Ovarian origin	20% (4/20)
	Stage I	15% (3/20)

Stage II	15% (3/20)
Stage III/IV	70% (14/20)
Pelvic washings positive	61% (8/13)
ER+ staining	56% (9/16)
PR+ staining	38% (6/16)
Microsatellite stable	100% (12/12)
Elevated CA-125	68% (13/19)
Platinum sensitive	43% (7/19)
Treatment^a	
Neoadjuvant chemotherapy	20% (4/20)
mTOR inhibitor therapy	10% (2/20)
Whole pelvic radiation therapy (WPRT)	50% (10/20)
Vaginal brachytherapy and WPRT	20% (4/20)
Tumor characteristic	% (number/total), n = 22
Tumor site	
Primary tumor	82% (18/22)
Metastasis	18% (4/22)
Genetic alterations	
TP53	68% (15/22)
CCNE1	32% (7/22)
PTEN	27% (6/22)
PIK3CA	23% (5/22)
FBXW7	18% (4/22)
Tumor Mutation Burden	
Low	56% (5/9)
Intermediate	33% (3/9)
High	11% (1/9)
Pathways affected (N = 54 genes)^b	
PI3K/AKT	33% (18/54)
MAPK	22% (12/54)
Chromatin remodeling	17% (9/54)
Cell cycle	15% (8/54)
^a All patients with neoadjuvant received carboplatin/paclitaxel. 19/20 patients who received adjuvant chemotherapy: 18 received carboplatin/paclitaxel and 1 received ifosfamide.	
^b 54 genes found to be altered were segregated in pathways as listed below. Ref: Fabregat A, Sidiropoulos K, Garapati P, et al. The Reactome pathway Knowledgebase. Nucleic Acids Research. 2016;44(Database issue):D481-D487. doi:10.1093/nar/gkv1351.	

398 - Poster Session

Ember trial: Evaluation of multiple protein and molecular biomarkers to estimate risk of cancer in gynecology patients presenting with a pelvic mass

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Objective: Emerging technologies for the isolation and interrogation of rare circulating cells present an opportunity for detection of cancer with a simple blood test (liquid biopsy). Approximately 5%–10% of women will be diagnosed with a pelvic mass, with 13%–21% being malignant. The present study was designed to evaluate a liquid biopsy assay combining serum biomarkers with rare cell gene expression analyses for detection of cancer in women with a pelvic mass.

Method: This was an institutional review board-approved prospective clinical trial conducted through the Wilmot Cancer Institute Gynecologic Oncology Division. Women with a pelvic mass scheduled for surgery or biopsy were eligible. Blood was obtained preoperatively and processed for capture of rare cells using the Parsortix™ system. mRNA was isolated from captured cells and analyzed for expression of 60 ovarian cancer-associated and housekeeping genes. Serum levels for several commonly assayed ovarian cancer protein biomarkers were measured. Univariate and multivariate logistic regression

analyses of the gene expressions and serum protein biomarker levels were performed, and ROC curves were constructed and compared.

Results: A total of 183 evaluable patients were enrolled (average age 56 years, range 19–91 years). There were 104 benigns, 17 LMP tumors, and 62 cancers (21 stage I–II EOC, 21 stage III–IV EOC, and 20 metastatic). Comparison of ROC-AUCs for single and all combinations of genes and/or serum biomarkers to detect benign versus cancer showed that a multivariate model combining the expression levels of as few as 8 genes and 4 serum protein biomarkers achieved the highest AUC (95.1%). This combined rare cell gene expression and serum biomarker model significantly outperformed: HE4 and CA-125 (AUC = 86.9%, $P < 0.001$); CA-125, prealbumin, apo-A1, transferrin, and β -2-microglobulin (AUC = 87.4%, $P < 0.001$) and CA-125, transferrin, apo-A1, FSH, and HE4 (AUC = 89.9%, $P = 0.017$). Further, the combined gene expression and serum protein biomarker model achieved an AUC of 89.6% for patients with stage I–II EOC and 98.3% for patients with stage III–IV EOC.

Conclusion: The combination of rare cell gene expression with serum biomarker levels significantly improves the detection of cancer in women with a pelvic mass compared to current serum biomarker approaches. Further optimization of this approach is in progress.

399 - Poster Session

Classification of serous ovarian cancer patients with suboptimal surgical outcomes by clinical molecular features

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Objective: If surgical maximal cytoreductive effort cannot achieve <1 cm of residual disease in serous ovarian cancer (HGS), the surgery is considered suboptimal. However, the surgery should also be considered “suboptimal” if patients experienced delays of more than 8 weeks on chemotherapy initiation or died within 90 days due to surgery—a “suboptimal surgical outcome.” The aim of this study is to stratify patients with suboptimal surgical outcome based on their genomic and clinical features.

Method: The Cancer Genome Atlas HGS database was extracted. We included patients with “suboptimal surgical outcome”: (1) patients who had residual disease after surgery >1 cm, (2) patients who died within 90 days postoperatively, or (3) patients who started chemotherapy more than 8 weeks after surgery. First, we performed a genome-wide unsupervised “cluster of clusters” integrating gene copy number variation, gene and miRNA expression, and DNA promoter methylation to determine different patterns in these patients with suboptimal outcome. Then we added clinical variables (including surgical treatment) and somatic mutations to the resulting clusters or groups of patients. Finally, we performed a pathway analysis for each of the resulting clusters to identify targetable processes.

Results: Three genomic profiles emerged among suboptimal patients. Cluster 1 had older patients, often on stage 4, with macroscopic residual disease. Also, they had more somatic TP53 mutations and promoter gene methylation was decreased. Cluster 3 patients were more often stage 3, with more microscopic residual disease. Also, they had the most copy gain of genes, relatively higher gene expression, and better median survival than the rest ($P = 0.03$). Cluster 2 patients were the youngest and had the most copy gene loss. Pathway enrichment analysis revealed that cluster 1 had aberrations in cell adhesion, phagocytosis, and complement; cluster 2 had anomalies in protein digestion, angiogenesis (i.e., VEGF) and cell cycling; and cluster 3 had alterations in intracellular signaling, including MAPK, Jak-STAT, and TGF-beta pathways.

Conclusion: There were 3 distinct profiles of patients with suboptimal surgical outcome. The resulting classification may characterize different groups of patients at risk of failing initial surgical treatment and may help inform alternative or additional treatments to improve outcomes.

400 - Poster Session

Prognostic model for disease-free survival, lymphatic and/or hematogenous recurrence, in patients with early stage cervical cancer treated with radical hysterectomy: A Korean Gynecologic Oncology Group study

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Objective: Models predicting disease-free survival (DFS), lymphatic and/or hematogenous recurrence, and overall survival in patients with early-stage cervical cancer are important in patient management. We developed and validated a prognostic

model with a simple method of scoring those predictive factors to quantify outcome in patients with cervical cancer treated primarily with radical hysterectomy.

Method: We retrospectively analyzed 1,441 patients of a Korean Gynecologic Oncology Group (KGOG) multiinstitutional cohort with early-stage cervical cancer patients treated between 2000 and 2008. Patients were assigned to a model development cohort ($n = 788$), and the others to a validation cohort ($n = 653$). After developing a model that can predict the risk for recurrence (DFS or hematogenous and/or lymphatic) and survival in patients with early-stage cervical cancer after surgery using Cox proportional hazards regression analysis, stepwise and best-model options were used to identify the best combinations as predictors and to calculate adjusted risk ratios. The prognostic performance of the model was assessed in an independent patient cohort.

Results: A total of 1,441 patients were included in the study, and 134 recurrence and 72 cancer-related deaths were observed during the follow-up period. Cox regression analysis identified histology, FIGO stage, depth of invasion, lymphovascular invasion, paraaortic node status, parametrial involvement, and hemoglobin level as independent risk factors for survival ($P < 0.05$), and histology, pelvis, and paraaortic node status, lymphovascular invasion, depth of invasion, and hemoglobin level as risk factors for DFS. The model incorporating these factors appeared to be accurate and predicted the outcomes better than current guidelines (intermediate or high-risk factors). When applied to a separate validation set, the model also showed similar predictive accuracy. Overall survival and hematogenous recurrence models performed reasonably better in our study cohort.

Conclusion: We have developed a robust model to predict 5-year survival, DFS, lymphatic, and/or hematogenous recurrence in patients with early-stage cervical cancer. This model may improve decision making in clinical practice.

401 - Poster Session

MMR deficiency identifies patients with high intermediate risk (HIR) endometrial cancer at highest risk of recurrence: A prognostic and possible predictive biomarker for HIR endometrial cancer

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Objective: The prognostic significance of mismatch repair deficiency (dMMR) in high intermediate-risk (HIR) endometrial cancer (EC) is unknown. The objective of this study was to assess recurrence patterns and progression-free survival (PFS) of patients with HIR EC and dMMR.

Method: A review of consecutive patients diagnosed with EC between 2007 and 2016 was undertaken. dMMR was assessed by IHC for MLH1, PMS2, MSH2, and MSH6 and defined by lack of expression of at least 1 protein. Patients with endometrioid histology and classified as HIR by GOG 249 criteria (risk factors, RF: grade 2 or 3 tumor, (+) lymphovascular space invasion, $\geq 50\%$ myometrial invasion; and age 70 years or older with 1 RF, age 50 or older with 2 RF, age 18 years or older with 3 RF) were included. Factors associated with recurrence were assessed by logistic regression. PFS and associated factors were assessed by Kaplan-Meier survival analysis and Cox proportional hazards model.

Results: A total of 198 patients (65 dMMR and 133 MMR proficient) were included, of which 32 (16.2%) experienced recurrence. Median follow-up time was 60 months; 54.5% received no adjuvant therapy, 27% vaginal brachytherapy, 7.5% pelvic radiation, and 11% chemotherapy. There were no significant differences between women with and without dMMR with in age, BMI, presence of LVSI, or adjuvant therapy. Women without dMMR were more likely to have deep myometrial invasion ($P = 0.05$) and stage II tumors ($P = 0.003$). Women with dMMR were more likely to have grade 2 or 3 tumors ($P < 0.0005$). After controlling for stage, both presence of dMMR (OR = 5.18, $P < 0.0005$, 95% CI 2.13–12.55) and receiving any form of adjuvant radiation therapy (OR 0.34, $P = 0.02$, 95% CI 0.14–0.85) were found to be significantly associated with recurrence. Presence of dMMR was also associated with distant recurrence (OR = 5.18, $P = 0.01$, 95% CI 1.53–17.54), but not with local recurrence. PFS was shorter in those with dMMR (5-year PFS, 66% vs 89%, $P = 0.001$). After controlling for stage, both presence of dMMR (HR = 4.0, $P < 0.0005$, 95% CI 1.92–8.33) and lack of adjuvant radiation (HR = 0.37, $P = 0.01$, 95% CI 0.17–0.81) significantly reduced PFS.

Conclusion: The presence of dMMR in patients with HIR EC cancer is highly associated with increased odds of recurrence, higher rate of distant recurrence, and decreased PFS, despite similar adjuvant treatment across groups. Novel treatment options are needed, and dMMR can serve as an integral biomarker for patients with HIR endometrial cancer.

402 - Poster Session

Somatic reversion mutations in hereditary ovarian carcinomas predict platinum sensitivity

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Objective: Secondary somatic reversion mutations restoring *BRCA1*, *BRCA2*, *RAD51C*, and *RAD51D* function in hereditary ovarian carcinomas can be a mechanism of chemotherapy resistance. We analyzed somatic reversion mutations in *BRCA1* and *BRCA2* as well as other homologous recombination repair (HRR) genes in a large series of primary and recurrent ovarian, fallopian tube, or primary peritoneal cancer (collectively termed OC), assessing their relationship with chemotherapy resistance.

Method: OC from patients with known damaging germline mutations in key HRR genes were tested. In OC with low neoplastic cellularity, malignant cells were purified with laser-capture microdissection, and haplotyping was performed by Sanger sequencing the germline mutation and 2–3 nearby intragenic heterozygous single-nucleotide polymorphisms (SNPs). OC had a reversion event if a novel frameshift mutation was identified that restored the open reading frame or if wildtype sequence was identified in association with the mutant haplotype.

Results: A total of 76 paired primary and recurrent OC from 35 patients as well as 71 unpaired primaries and 10 recurrences were analyzed. Patients had deleterious germline mutations in *BRCA1* (74, 63.2%), *BRCA2* (30, 25.6%), *RAD51C* (3, 2.6%), *RAD51D* (3), *BRIP1* (3), and *PALB2* (2, 1.7%). Three (2.8%) reversion mutations were identified in 106 primary OC, 2 from patients with previous chemotherapy exposure for breast cancer. In 51 recurrent OC, 14 (27.5%) had reversion mutations. Of 27 patients with platinum-resistant or refractory recurrences, 10 (37%) had reversions, compared with 1 (5.3%) in 19 patients with platinum-sensitive recurrences ($P = 0.016$). Three secondary somatic mutations (17.6%) were novel frameshift mutations that restored the open reading frame, while 14 (82.4%) were reversion-to-wildtype sequence. All reversion mutations were identified in *BRCA1* or *BRCA2*.

Conclusion: Reversion mutations were, with 1 exception, seen only in women previously treated with chemotherapy and were associated with resistance to platinum chemotherapy. Of the reversion mutations, 80% were reversion-to-wildtype sequence, suggesting that current next-generation sequencing methods and cell free DNA tests will fail to identify the vast majority of reversion events.

403 - Poster Session

Mechanisms to increase cascade testing in hereditary breast and ovarian cancer: Impact of introducing standardized communication aids into genetic counseling

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Objective: Increasing the precancer identification of women with hereditary breast and ovarian cancer (HBOC) could prevent up to 20% of these related ovarian cancers. The study objective is to determine whether standardized Facing Our Risk of Cancer Empowered (FORCE) materials are acceptable to patients, improve knowledge of HBOC, and increase disclosure to family members.

Method: A prospective cohort is being identified prior to genetic testing. Subjects complete a baseline validated 11-question knowledge survey and are provided 3 communication aids: an informational brochure, a worksheet identifying at-risk family members, and a template letter to share results. Knowledge and acceptability are reassessed at a follow-up visit. At 6 months, disclosure and testing of family members are collected. The retrospective cohort was identified through chart review of women who had already undergone genetic testing prior to the intervention. Enrolled by telephone, subjects completed the knowledge survey and were asked about disclosure of results and uptake of testing in family members. Demographic and clinical characteristics were abstracted from the medical record. The primary outcome was increase in HBOC knowledge, requiring 20 pre- and postknowledge scores to detect a 10% difference. Disclosure and cascade testing rates will be compared between the retrospective and prospective cohorts.

Results: There are 19 subjects in the retrospective and 11 subjects in the prospective cohort (Table 1). The median age at cancer diagnosis was 58 years; the majority were white (90%), had ovarian cancer (87%), and were stage III–IV (56%). Sixty percent had a family history of breast or ovarian cancer. Baseline knowledge of HBOC was moderate, with a median score of

6.5/11 and 7/11 for the prospective and retrospective cohorts, respectively. In the retrospective cohort, 1 patient had not disclosed testing to any relatives, while the remainder had disclosed to between 17% and 100% of first-degree relatives. All subjects found the resources easy to use, understandable, and helpful in communicating with family.

Conclusion: Inclusion of standardized communication tools is acceptable to patients. Knowledge of HBOC was moderate without these resources. Impact of the aids on knowledge and disclosure of testing results will be updated in the coming months.

Table 1: Demographics of study population by intervention cohort.

Characteristic	Retrospective <i>n</i> = 19 (%)	Prospective <i>n</i> = 11 (%)
Median age at diagnosis (years)	58 [46,70]	50 [47,64]
Race		
Non-Hispanic White	17 (89)	10 (91)
Non-Hispanic Black	2 (11)	1 (9)
Marital status		
Single	5 (26)	2 (18)
Married	13 (68)	7 (64)
Divorced/Separated	1 (6)	2 (18)
Insurance		
Medicare/Medicaid	8 (42)	6 (55)
Private	10 (52)	3 (27)
Uninsured	1 (6)	2 (18)
Parity		
Nulliparous	0 (0)	3 (27)
Parous	19 (100)	8 (43)
Cancer		
Ovarian	19 (100)	7 (64)
Breast	0 (0)	4 (36)
Stage*		
I	1 (6)	4 (37)
II	0 (0)	3 (27)
III	8 (42)	3 (27)
IV	10 (52)	1 (9)
Family history ovarian cancer	2 (11)	2 (18)
Family history breast cancer	11 (58)	5 (45)
Median Baseline Knowledge Score (out of 11)	7 [5,9]	6.5 [6,7]
Health literacy		
Inadequate/marginal	1 (6)	2 (18)
Adequate	18 (94)	9 (82)

Median age presented as median [25th quartile, 75th quartile]

*Information on stage unknown for 1 subject

404 - Poster Session

Treatment with SQ1274, a novel tubulin polymerization inhibitor, results in improved therapeutic efficacy compared to paclitaxel in serous gynecologic cancers

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Objective: To determine whether SQ1274, a novel tubulin polymerization inhibitor, is a more effective chemotherapeutic agent than paclitaxel; examine whether this inhibitor downregulates the receptor tyrosine kinase, AXL (an active pathway in ovarian and uterine cancer metastasis); and evaluate the therapeutic potential of SQ1274 in a xenograft mouse model.

Method: Ovarian chemosensitive and chemoresistant (OVCAR3, OVCAR8, OVCAR3TP) and uterine serous cancer (ARK1) cell lines were treated with SQ1274 (Sequoia Sciences, St. Louis, MO), a synthetic analogue of the plant compound bifidenone. Viability assays were performed after 72 hours of treatment with either SQ1274 or paclitaxel, and IC50s were calculated using GraphPad Prism. Western blots of treated cells were also performed to identify markers of chemotherapy resistance, cellular apoptosis, and potential pathways that may be affected by SQ1274. In vivo studies were performed using nude or nod-SCID mice injected with 10 million OVCAR8 or ARK1 cells subcutaneously followed by 3 cycles of therapy or vehicle control.

Results: In the chemoresistant ovarian cancer cells, the IC50 of SQ1274 was 6-fold less than paclitaxel (0.94 nM vs 6.16 nM) in OVCAR8, and 3-fold less (0.57 nM vs 1.7 nM) in the OVCAR3TP when compared to the sensitive line, OVCAR3, which showed a less impressive, though significant decrease (0.97 nM vs 1.22 nM). In uterine serous chemoresistant cells, there was a 3-fold less IC50 for SQ1274 than paclitaxel (0.5 nM vs 1.5 nM) in ARK1 tumor cells. Furthermore, SQ1274 substantially inhibited p-AXL and AXL pathway expression by 90% by Western blotting in both uterine (ARK1) and ovarian (OVCAR8) cancer cell lines. Expression of other known factors in metastasis, Gas6 and pSRC, was substantially decreased by SQ1274, and cPARP expression was increased in cells exposed to SQ1274. Furthermore, xenograft models for ovarian and uterine serous cancer in mice treated with SQ1274 had significantly less tumor volume than those treated with control ($P = 0.015$ OVCAR8 and $P = 0.003$ ARK1).

Conclusion: SQ1274 has improved killing efficacy compared to paclitaxel at equivalent doses in vitro with decreased expression of chemoresistance markers and increased expression of pro-apoptotic pathway proteins, as well as demonstrates activity *in vivo*. SQ1274 shows promise as a novel therapeutic agent.

405 - Poster Session

Targeting inflammation and polyamine synthesis in epithelial ovarian cancer: PDE10 and ODC1 inhibition in c-Myc amplified disease

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Objective: The rate-limiting step for polyamine synthesis involves the enzyme ornithine decarboxylase (ODC), a known downstream target of c-Myc. The inflammatory/procarcinogenic enzyme, phosphodiesterase PDE10A (PDE10A), also alters transcription of c-Myc, which is associated with poor disease prognosis. We therefore hypothesize that the combination of ODC and PDE10A inhibition is a rational therapeutic approach that can disrupt oncogenic c-Myc in epithelial ovarian cancer (EOC).

Method: Survival analysis of the TCGA EOC patients with high expression of PDE10A and ODC1 was conducted using the cBioPortal (RNA Seq V2 RSEM). ODC1, PDE10A and c-myc expression were measured in various ovarian cancer cells via Western blotting. In vitro growth inhibition was measured in TOV112D cells after exposure to the ODC inhibitor, difluoromethylornithine (DFMO), with and without MCI-030, a novel PDE10A inhibitor. The treatment effect of combining DFMO and MCI-030 was quantified by a clonogenic assay and Western blotting for cleaved PARP and caspase-3 to measure apoptosis.

Results: ODC1 and PDE10A were both over-expressed in TOV112D cells. TCGA survival analysis revealed that EOC patients with dual upregulation of PDE10A and ODC1 had significantly shorter overall survival than patients with only high ODC1 expression (10 vs 45 months, respectively, $P = 0.0001$). The combination of DFMO and MCI-030 resulted in more significant in-vitro growth inhibition than either agent alone and with increased potency. Caspase-3 and cleaved PARP were both significantly increased after TOV112D cells were treated with DFMO and MCI-030. See Figure 1.

Conclusion: Survival analysis suggests that PDE10A and ODC1 may act synergistically to enhance ovarian tumorigenicity. Targeting these processes both upstream and downstream of amplified c-Myc with combination therapy in tumor cells appears to result in a potent, synergistic growth inhibition. As c-Myc amplification has a suggested impact on clinical prognosis, DFMO + MCI-030 thus represents a novel molecularly targeted, rational combination for EOC patients, hence warranting further study.

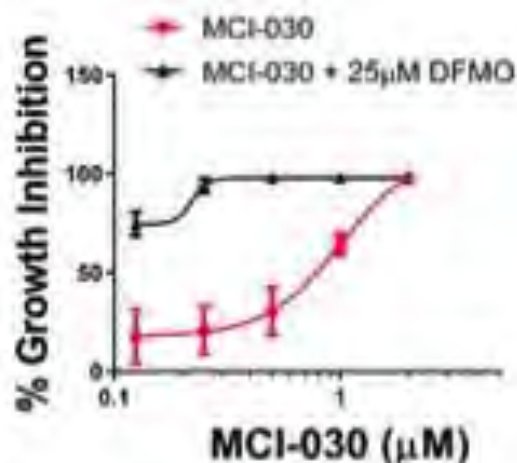


Fig. 1.

406 - Poster Session

TLE3 expression is associated with favorable outcomes in taxane-treated patients with non-serous ovarian carcinoma: A multi-institution study

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Objective: Transducin-like enhancer of split 3 (TLE3) is a homolog of the drosophila Groucho protein and a transcriptional corepressor of beta-catenin in the Wnt pathway. TLE3 is expressed in approximately 30% of ovarian cancers. In a previous smaller study, we found that TLE3 expression was associated with improved progression-free survival in patients who had received a taxane as part of their treatment regimen. Here, in an independent, large, multiinstitution cohort, we sought to validate TLE3 expression as a potential predictive marker for taxane-based chemotherapy in women with ovarian cancer.

Method: We performed immunohistochemical staining for TLE3 on tissue microarrays prepared from formalin-fixed paraffin-embedded ovarian cancer tissue specimens from 3 institutions in 2 continents. Progression-free survival (PFS) and overall survival (OS) were assessed to explore associations between TLE3 expression and response to taxane therapy.

Results: Of a total of 1,055 patients, 620 (59%) had serous tumors and 435 (41%) had nonserous tumors. Treatment data were available in 980 (93%) patients, of whom 632 (64%) underwent taxane treatment. TLE3 expression was seen in 465 (52%) tumors, without statistically significant differences in expression frequencies between serous (50%) and nonserous (56%) tumors ($P = 0.11$). TLE3 expression was associated with favorable outcome only in patients with nonserous tumors who had received paclitaxel as part of their treatment regimen ($n = 158$): 3-year PFS (HR = 0.57, 95% CI 0.34–0.96, $P = 0.03$) and 5-year OS (HR = 0.53, 95% CI 0.28–0.97, $P = 0.04$). The predictive association between TLE3 expression and outcome was strongest in taxane-treated tumors with clear cell histology ($P = 0.02$): 3-year PFS (HR = 0.44, 95% CI 0.19–1.00, $P = 0.04$) and 5-year OS (HR = 0.26, 95% CI 0.10–0.73, $P = 0.01$).

Conclusion: This multiinstitution study validates the association between TLE3 expression and a favorable response to taxane-containing chemotherapy regimens in patients with nonserous ovarian cancer, particularly in tumors with clear cell histology.

407 - Poster Session

P53 and p16 immunostaining patterns in squamous cell carcinoma of the vulva predicts disease recurrence and prognosis

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Objective: Vulvar squamous cell carcinoma (SCC) and its precursor vulvar intraepithelial neoplasia (VIN) occur via 2 pathways: HPV-related (usual type VIN) and non-HPV-related (differentiated type VIN). Over-expression of p16 is a hallmark

of HPV-related VIN and SCC, whereas aberrant p53 expression is often seen in differentiated VIN and SCC. This study aims to correlate p16 and p53 immunostaining patterns in vulvar SCC with disease recurrence and patient survival.

Method: A total of 76 women with vulvar SCC were included in the study. All patients had at least 5 years of clinical follow-up. Immunohistochemical stains of p16 and p53 were performed on selected formalin-fixed tissue blocks. Immunostaining results were categorized as negative (-), focally positive (+), and diffusely positive (++) for both p16 and p53 antibodies. Total loss of p53 immunostaining, representing p53 allelic deletion, was also included in p53 (++) for its aberrant expression. The combination of immunostaining patterns of p16 and p53 was correlated with recurrence and disease-related death (DOD).

Results: Strong p16 (++) staining pattern was seen in 32 cases and strong p53 (++) in 36 cases of vulvar SCC. Forty-four cases of mutually exclusive staining pattern, including 13 cases of p16++/p53- and 31 cases of p16-/p53++. Overall disease recurrence was seen in 36.8% (28/76), and DOD was documented in 25% (19/76) of women in our cohort. Tables 1 and 2 correlate p16 and p53 staining pattern with recurrence and DOD, respectively. Recurrence and DOD occurred in 66.7% (24/36) and 44.5% (16/36) of patients, respectively, with strong p53++ staining pattern. In contrast, recurrence and DOD were seen only in 6.3% (2/32) of patients with strong p16++ staining pattern. Disease recurrence and DOD significantly correlate with p53++ and p16++ staining pattern ($P < 0.001$).

Conclusion: Women with vulvar SCC showing an aberrant p53(++) staining pattern confers a worse prognosis in terms of recurrence and DOD compared to a strong p16(++) with wildtype p53 staining pattern. Our data indicate that p53 status dictates survival and prognosis even in those patients with HPV-infection and that application of p53 and p16 immunostaining may provide prognostic value in the clinical management of patients with vulvar SCC.

Table 1. Correlation of Recurrence with p16/p53 Immunostaining Patterns in Vulvar SCC.

	p16 neg	p16 (+)	p16 (++)	Total Cases	Recurrence	Recurrent %
p53 neg	1 (0)	1 (1)	13 (0)	15	1	6.7%
p53 (+)	3 (0)	4 (1)	18 (2)	25	3	12.0%
p53 (++)	31 (20)	4 (4)	1 (0)	36	24	66.7%
Total cases	35 (20)	9 (6)	32 (2)	76	28	36.8%

Table 2. Correlation of DOD with p16/p53 Immunostaining Patterns in Vulvar SCC.

	p16 neg	p16 (+)	p16 (++)	Total	Total DOD	DOD %
p53 neg	1 (0)	1 (1)	13 (0)	15	1	6.7%
p53 (+)	3 (0)	4 (0)	18 (2)	25	2	8.3%
p53 (++)	31 (15)	4 (1)	1 (0)	36	16	44.5%
Total cases	35 (15)	9 (2)	32 (2)	76	19	25.0%

408 - Poster Session

The utility of comprehensive genomic profiling in selection of actionable targeted therapy in recurrent or refractory epithelial ovarian, fallopian tube and peritoneal carcinoma

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Objective: Precision medicine has prompted significant changes in clinical cancer research, giving rise to numbers of new therapeutic agents that hold promise in the treatment of recurrent or refractory epithelial ovarian cancer (EOC) when no standards of care exist. Yet in clinical practice, the utility of comprehensive genomic profiling (CGP) for treatment planning remains unknown. Our objective is to identify the use of CGP in adopting precision-based target therapy.

Method: We conducted a retrospective analysis of patients with a diagnosis of EOC and CGP via next-generation sequencing of 315 or 467 cancer genes between January 1, 2014, and May 1, 2017. All EOC patients were consecutively diagnosed and treated in a single institution and, by institution-based protocol, had CGP if adjuvant chemotherapy was warranted. Molecular, demographic, and clinical data were analyzed by using descriptive statistics and the Fischer exact test. Multivariate analysis was performed by using Cox regression analysis.

Results: Out of the 93 patients included in the study, a total of 317 genetic alterations (GA) were identified, with an average 3.4 alterations per tumor. Sixty-one patients (65%) had 1 or more actionable mutations compatible with either FDA-approved or nonapproved therapy. Table 1 summarizes the clinical and demographic characteristics of the 10 out of 61 patients (16%) who received the recommended target therapies: 7 received PARP inhibitor, 2 received Her2 inhibitor, and 1 received mTOR inhibitor. All patients who received PARP inhibitors had defect(s) in genes relating to the homologous recombination repair pathway ($n = 20$). All patients received their treatments during progressive or recurrent disease. Out of the 10 patients, 5 had received therapies according to FDA approval in the patients' tumor type and 3 in FDA approval in another tumor type, and 2 received drugs with off label. There was no significant survival difference in patients who received targeted therapy and those who did not.

Conclusion: While the majority of our EOC cohort had an actionable mutation compatible with a targeted therapy by CGP, these results had a direct impact on clinical care in only a minority of patients during recurrent or progressive disease. Prospective studies examining the reasoning behind limited adoption of targeted therapy in practice is warranted.

Table 1. Clinical and demographic characteristics of patients with EOC who received targeted therapies based on actionable mutations from comprehensive genomic profiling of their tumor.

Patient	Actionable Genomic Alteration	Recommended Target therapy	Age	Ethnicity	Stage	Histology	Number of regimens prior targeted treatment	Interval between first diagnosis to targeted treatment (months)	PFS (months)	OS (months)
1	ERBB2 amplification	Lapatinib	39	white	3	clear	5	17.9	6.23	19.27
2	ERBB2 amplification	Trastuzumab	58	white	1	clear, endometrioid	2	7.8	5.40	11.67
3	Germline BRCA2 mutation	Olaparib	61	white	4	serous	6	83.3	22.97	119.33
4	Germline BRCA1 mutation	Olaparib	59	black	4	serous	4	37.8	20.50	38.33
5	Germline BRCA2 mutation	Olaparib	77	hispanic	3	endometrioid	4	68.1	31.37	81.27
6	PIK3R2 truncation	Everolimus	80	white	3	serous	10	89.6	34.20	102.97
7	Germline BRCA1 mutation	Olaparib	67	white	3	serous	10	130.4	33.33	153.37
8	Germline BRCA2 mutation	Olaparib	71	white				0.8		4.67
9	Somatic BRCA1 mutation	Olaparib	68	white	4	serous	3	46.38	19.67	54.07
10	Germline BRCA2 mutation	Olaparib	60	black	3	serous	4	43.33	20.50	46.80

409 - Poster Session

Molecular profiling of endometriosis and endometriosis-associated ovarian cancer

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Objective: Endometriosis appears to be associated with some specific histologic subtypes of epithelial ovarian cancer, especially clear cell and endometrioid adenocarcinoma. However, the pathogenesis of ovarian cancer development from endometriosis is not well understood. The purpose of this study is to investigate the molecular association of endometriosis and endometriosis-associated ovarian cancer (EAOC).

Method: RNA was extracted from 66 paraffin tissue blocks comprising endometriosis ($n = 9$), atypical endometriosis ($n = 18$), endometriosis adjacent to cancer ($n = 10$), and endometriosis-associated ovarian cancer ($n = 29$). Lesions of endometriosis or cancer from whole paraffin-embedded tissue sections were obtained by laser capture microdissection, and differentially expressed genes were analyzed using RNA sequencing technology. Expressions of selected candidate genes involving cellular process were validated by real-time PCR and immunohistochemistry.

Results: Differential expression analysis revealed upregulation of 2,530 genes in EAOC, 403 genes in atypical endometriosis, and 369 genes in adjacent endometriosis compared to endometriosis, respectively (>2 fold, $P < 0.05$, FDR < 0.05). Thirty genes among commonly upregulated genes reveal upward increase by comparison merge analysis (>2 fold, $P < 0.05$, FDR < 0.05) and 10 candidate genes involving cellular process were selected from gene ontology. Levels of KRT7, TSPAN13, and MAPK15 expression were elevated among atypical endometriosis ($P = 0.57$, $P = 0.97$, $P = 0.55$), adjacent endometriosis ($P = 0.03$, $P = 0.51$, $P = 0.13$), and EAOC ($P < 0.01$, $P = 0.03$, $P < 0.01$) compared with endometriosis, respectively.

Conclusion: This study revealed gene alteration involving endometriosis and EAOC. These findings may be an important resource for studying the pathogenesis of ovarian cancer developing from endometriosis.

410 - Poster Session

Loss of USP10 expression is associated with tumor progression and poor prognosis in epithelial ovarian cancer

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Objective: Ubiquitin-specific protease 10 (USP10), a deubiquitinating enzyme, has been pronounced in malignancies. However, the role of USP10 in epithelial ovarian cancer has not yet been elucidated. Here, we investigated USP10 expression, its clinical significance, and its relationship with p14ARF in epithelial ovarian cancers (EOCs).

Method: The effects of USP10 on cell growth were assessed in EOC cell lines. Immunohistochemical analyses of USP10 and p14ARF were performed using tissue microarray analysis of 336 ovarian tumors and the data compared with clinicopathologic variables, including the survival of ovarian cancer patients. We also examined USP10 and p14ARF methylation near the putative transcriptional start site (TSS) in the 5' CpG islands of the genes in ovarian cancer cells and fresh frozen tissues.

Results: USP10 knockdown promoted cell proliferation and colony formation, whereas USP10 over-expression occurred in both properties in OVCA cells. USP10 and p14ARF expression was significantly decreased in ovarian cancer compared to normal ovarian epithelium (both, $P < 0.001$). Immunoreactivity significantly correlated with tumor stage (USP10, $P < 0.001$) and tumor grade (p14ARF, $P = 0.007$). USP10 expression showed strong positive correlation with that of p14ARF (Spearman $\rho = 0.430$, $P < 0.001$) in cancer patients. Using the Cox proportional hazards model, low USP10 expression (HR = 3.77, 95% CI, 1.65–8.60, $P = 0.002$) and a combined USP10-/p14ARF- expression (HR = 4.35, 95% CI 1.58–11.90, $P = 0.005$) were the independent prognostic factors. Methylation-specific PCR analysis showed that the USP10 and p14ARF CpG island was highly methylated in cancer tissues (62% and 87%, respectively) and cells (both 95%) and at lower percentages in normal tissues (3% and 13%, respectively).

Conclusion: Low expression of USP10 or combined USP10/p14ARF is an indicator of bad prognosis in ovarian cancer, suggesting their potential utility as prognostic tests in clinical assessment.

411 - Poster Session

Identification of clinical-molecular characteristics associated with recurrent endometrial cancer

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Objective: Endometrial cancer is the most common gynecologic malignancy in the United States. Most women present at early stage, and their disease will not recur after initial treatment. There is no method that accurately predicts who will recur. Our goal was to create a model that would predict which patients with endometrioid endometrial cancer (EEC) will recur. The model was constructed by integrating clinical and molecular data from the Cancer Genome Atlas (TCGA). Based on these clinical-molecular (CM) features, we stratified patients into subgroups.

Method: We included 271 TCGA patients with EEC, of which 50 experienced recurrence. To identify elements associated with recurrence, a univariate analysis of clinical data—gene and miRNA expressions, DNA methylation, gene copy number, and mutation analysis—was performed. A multivariate analysis was done to identify variables independently associated with recurrence. Recurrent patients were classified into subgroups based on CM features using a genome-wide unsupervised "cluster of clusters," and pathway analysis was performed to identify targetable processes.

Results: Elements of clinical data, gene expression, miRNA expression, DNA methylation, somatic mutations, and copy number variations were independently associated with disease recurrence. Three main CM clusters were identified. Cluster 1 included 71% of patients; cluster 2 included 25%; and cluster 3 included 4% of patients with recurrent EEC. Pathway analysis revealed that the molecular features of cluster 1 were mostly associated with host-immune interactions, including both cellular and humoral immunity, as well as cytokine signaling ($P < 0.001$ – 0.048). The molecular features of cluster 2 were mostly associated with cell cycle regulation, including glycan degradation and DNA replication ($P = 0.002$ – 0.035). The wnt signaling pathway was included in both clusters with $P = 0.038$ for cluster 1 and 0.022 for cluster 2.

Conclusion: Integrating clinical and molecular data helps to predict patients at risk for EEC recurrence and improves knowledge of the biological processes involved in treatment failure. Cluster analysis stratified patients at risk for recurrence based on CM features and gave an insight into processes involved in treatment failure for each subgroup, informing potential targeted therapies.

412 - Poster Session

Treatment of elderly women with epithelial ovarian cancer: Is chemotherapy alone appropriate?

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Objective: To compare the outcomes of elderly women (75 years and older) with epithelial ovarian cancer who received chemotherapy alone versus neoadjuvant chemotherapy followed by surgery.

Method: Data were obtained from the National Cancer Data Base from 2004 to 2013. Kaplan-Meier methods and Cox proportional hazards model adjusted for covariates were used for analyses.

Results: Of 1,530 patients, the median age was 79 years (range 75–89). Whites, blacks, Hispanic, Asians, and others accounted for 88.2%, 7.3%, 0.9%, 3.1%, and 0.5% of the group, respectively. Serous, clear cell, endometrioid, and mucinous histology was present in 86.5%, 1.0%, 1.4%, and 1.2%, respectively, with 77 (5.0%) stage I–II and 1,453 (95%) stage III–IV disease. A total of 877 (53.7%) had chemotherapy alone versus 653 (42.7%) who had neoadjuvant chemotherapy followed by cytoreductive surgery. We then divided the study group into 3 time periods (2004–2006, 2007–2009, and 2010–2013). The proportion of those who underwent neoadjuvant chemotherapy followed by surgery increased from 22.7% to 43.2% to 50.4% with a corresponding decrease in the use of chemotherapy alone from 77.4% to 56.8% to 49.7%, respectively. Those who had chemotherapy alone were older (80 vs 78 years, $P < 0.001$) and more likely to have advanced-stage disease (98.1% vs 90.8%, $P < 0.001$) and serous histology (97.2% vs 95.6%, $P = 0.004$). There was no difference in treatment based on race/ethnicity, income, and education. The 5-year survival of the study group was 13.9%. Those who had chemotherapy alone had a survival of 5.9% compared to 25.1% in the neoadjuvant with surgery group ($P < 0.001$). In multivariate analysis, older age (HR = 1.03, $P < 0.001$), black race (HR = 1.29, $P = 0.03$), advanced stage (HR = 2.00, $P < 0.001$), and clear cell and mucinous histologies (HR

= 2.09, $P = 0.02$, and $HR = 2.22$, $P = 0.001$) were associated with poorer survival. Neoadjuvant chemotherapy was associated with improved survival ($HR = 0.43$, $P < 0.001$).

Conclusion: In elderly ovarian cancer patients, the use of neoadjuvant chemotherapy has increased over time and demonstrated an overall survival of 25%. Chemotherapy alone was associated with a survival of only 5.9%. Older age, black race, advanced stage, clear cell, and mucinous histology were poor prognostic factors.

413 - Poster Session

Timing of initiation of chemotherapy after primary surgery for women with epithelial ovarian cancer: Does it matter?

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Objective: To assess the differences in survival among ovarian cancer patients according to the time interval between primary surgery and initiation of chemotherapy for epithelial ovarian cancer patients.

Method: Data were obtained from patients who underwent primary surgery followed by adjuvant chemotherapy from the National Cancer Data Base during 2006–2013. The Kaplan-Meier method and the Cox proportional hazards model adjusted for covariates were used for analyses.

Results: Of 36,593 patients (median age 60, range 18–89 years), the median time for the initiation of adjuvant chemotherapy was 40 days. Whites, blacks, Hispanics, Asians, and others accounted for 85.2%, 6.2%, 4.8%, 2.8%, and 1.0%, respectively, of the study group. Serous, clear cell, endometrioid, and mucinous histology was present in 73.5%, 9.3%, 13.7%, and 3.5%, respectively, of patients. Most women presented with stage III–IV (67.7%) than with stage I–II (32.3%) disease. The timing of initiation of chemotherapy was divided into 20-day intervals (range 0–80 days). The 5-year survival of those who started chemotherapy at 0–19, 20–39, 40–59, and 60–79 days was 47.7%, 56.7%, 53.8%, and 50.8%, respectively. More specifically, in those with early-stage disease, survival was 82.3%, 85.2%, 83.8%, and 80.7%, respectively. Similarly, survival of those with advanced-stage disease was 36.1%, 42.9%, 40.1%, and 38.2%, respectively. From multivariate analysis, older age ($HR = 1.02$, $P < 0.001$), advanced stage ($HR = 4.82$, $P < 0.001$), clear ($HR = 1.42$, $P < 0.001$) and mucinous cell types ($HR = 2.02$, $P < 0.001$), and initiation of chemotherapy before and after 20–39 days (0–19 days, $HR = 1.23$, $P < 0.001$, and 60–79 days, $HR = 1.12$, $P < 0.001$) were independent predictors for poorer survival.

Conclusion: Our data suggest that starting chemotherapy 20–39 days after surgery was associated with the most optimal survival in ovarian cancer patients.

414 - Poster Session

Adherence to NCCN guidelines for the treatment of endometrial cancer: Will mismatch repair status matter?

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Objective: Currently, the National Comprehensive Cancer Network (NCCN) guidelines contain no information about treatment of endometrial cancers based on DNA mismatch repair class (MMR). It has been shown that women with epigenetic MMR defects have worse prognostic factors and higher recurrence risk compared to those with intact MMR or probable MMR mutations. In this study, we sought to explore clinical outcomes by MMR class in a large cohort of endometrioid endometrial cancer (EEC) patients.

Method: Retrospective chart review was completed for patients with confirmed EEC treated at a single institution from January 1, 2014, to June 30, 2016. Clinical MMR immunohistochemistry (IHC) with reflex *MLH1* methylation testing was performed on all specimens. Tumors were classified as MMR proficient, epigenetic MMR defective, or probable MMR mutation. Data were analyzed using χ^2 , independent t , and log rank tests.

Results: A total of 498 EEC patients had complete MMR data: 75.3% as MMR proficient, 19.4% epigenetic MMR defects, and 4.8% as probable MMR mutations. MMR class was associated with advanced stage, higher grade, and presence of

lymphovascular space invasion. Both risk of recurrence and death (HR = 11.14, 95% CI 3.957–31.35, $P < 0.0001$, and HR = 17.11, 95% CI = 2.854–102.6, $P = 0.0019$) were significantly lower for patients with epigenetic defects. Overall, 5.2% of patients recurred (12 MMR proficient, 13 epigenetic defect, and 1 probable MMR mutation). Twenty women (10 MMR proficient and 10 epigenetic) were treated with standard therapy for relapse with 13 successfully salvaged. Of the 7 patients who were not salvaged, 5 were in the epigenetic MMR defect group, while 2 were in the MMR intact cohort. Five patients declined standard therapy for recurrence, and all 5 died of disease.

Conclusion: EEC patients with epigenetic MMR defects have worse survival outcomes than patients with intact MMR or probable MMR mutations. Standard-of-care chemotherapy and radiation for recurrent ECC as described in the NCCN guidelines are highly effective overall; however, patients with epigenetic MMR defects appear to have worse salvage rates. Given these data, the NCCN guidelines should consider the inclusion of alternative therapies including immunotherapy as an option for relapsed MMR defective endometrial cancer.

415 - Poster Session

Using gene expression and DNA mutations to predict recurrence in high-intermediate risk endometrial cancer

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Objective: To identify a gene signature that could help determine which early-stage H-IR EMCA patients are at the highest risk for recurrence.

Method: Clinical data were collected on all patients who underwent surgery at the University of Alabama and met H-IR EMCA criteria based on GOG 99 between 2000 and 2010 ($n = 292$). Patients who did not receive adjuvant treatment and recurred were matched on a case-by-case basis with patients who did not recur. NextSeq, a custom-designed SureSelect XT assay (592 whole-gene targets), was performed on 30 archival FFPE primary tumors (15 that recurred, 15 controls). All variants were detected with >99% confidence based on allele frequency and average coverage of >500 and an analytic sensitivity of 5%. Gene expression data were collected for 770 genes using the NanoString nCounter® PanCancer Pathways Panel on 26 primary tumors (13 that recurred, 13 control) and on recurrent tumors from 5 of the patients that recurred. Molecular profiles and pathway analysis of the cohorts (recurred vs did not; primary vs recurrent) were compared using nSolver Advanced Analysis Software. Genes were evaluated using a ± 2 -fold change and a $P > 0.05$.

Results: Similar numbers of DNA mutations were found in patients who recurred compared to patients who did not. Patients who recurred were more likely to be MSI-high and have mutations in *JAK1*, *DICER1*, *BRD3*, *PMS2*, *PDE4DIP*, and *BCOR* genes. RNA expression pathway analysis showed significant upregulation in cell cycle-apoptosis ($P = 0.02$) and DNA damage pathways ($P = 0.05$) in patients who recurred. In recurrent tumor samples, 9 of 13 anonical pathways were significantly altered compared to primary tumors, the most significantly altered being driver genes ($P = 0.003$), DNA damage repair ($P = 0.004$), and MAPK ($P = 0.019$).

Conclusion: Although our numbers are low, the preliminary data suggest that gene signature differences could help stratify H-IR EMCA patients based on a high versus low risk of recurrence. Defining this DNA mutation and RNA expression signature from FFPE archival tissue could help identify patients who could avoid the toxicity of adjuvant treatment and those who may warrant adjuvant systemic chemotherapy and/or radiation. Additional studies are ongoing to validate these findings in a larger cohort of patients.

416 - Poster Session

Risk of new breast and ovarian cancers and utility of incremental genetic testing in a high-risk BRCA negative cohort

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Objective: To determine the incidence of new breast cancer (BC) and epithelial ovarian cancer (EOC), and the role of incremental genetic testing, in a cohort of BRCA-negative (BRCA-) women selected from high-risk families.

Method: Women enrolled in a prospective cohort study who underwent genetic testing from January 2002 to February 2011 were identified. *BRCA*– women with a personal history of EOC at any age or invasive BC at age 60 were included if they also had at least 1 close female relative with EOC or BC at age 60. Kindred were classified as site-specific breast (SSB) or familial breast and ovary (FBO). Follow-up data were collected via questionnaire and medical record review. Ratios of observed/expected cancers were analyzed using age caps and assuming a Poisson distribution. In kindreds with a new report of BC or EOC, germline panel testing was performed anonymously using a 76-gene institutional assay.

Results: A total of 765 probands with 2,594 living female relatives were followed for a median 4.3 years. New cancers compared with expected are outlined in Table 1. Of the 26 SSB kindreds with new BC, 22 samples were available for testing and 2 mutations (9%) were identified (*PALB2*, *TP53*), as well as incidental findings of 2 monoallelic *MUTYH* mutations and 1 *RB1* mutation. Of the 3 FBO kindred with a new BC, 1 mutation (33%) was identified (*RAD51D*). Of the 4 kindreds with a new EOC, 1 mutation (25%) was identified in an FBO kindred (*RAD51D*).

Conclusion: In keeping with our understanding of cancer risk associated with moderate-penetrance genes, women and their close relatives from *BRCA*– SSB kindred were confirmed to have an increased rate of new BC, but not EOC. Similarly, *BRCA*– women from FBO kindred have an increased risk of EOC, but may not be at increased risk of BC. Incremental testing of high-risk kindreds identified expected high- and moderate-penetrance risk genes. However, in this cohort selected for increased risk, a majority remains without identifiable germline mutation, and risk assessment remains driven by family history.

Table 1. New cancers.

		All	Site-specific breast kindred	Hereditary breast-ovary kindred
New Breast Cancers				
Probands	Number with tissue at risk	<i>N</i> = 320	<i>N</i> = 228	<i>N</i> = 92
	Observed cancers	15	13	2
	Expected cancers	4.63	3.24	1.29
	Hazard ratio	3.24	4.01	1.55
	95% Confidence Interval	1.81-5.34	2.14-6.86	0.19-5.60
	<i>P</i> value	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> = .37
1 st degree relatives	Number	<i>N</i> = 907	<i>N</i> = 688	<i>N</i> = 219
	Observed cancers	14	13	1
	Expected cancers	7.94	6.11	1.83
	Hazard ratio	1.76	2.13	0.55
	95% Confidence Interval	0.96-2.96	1.13-3.64	0.01-3.04
	<i>P</i> value	<i>P</i> = .03	<i>P</i> = .01	<i>P</i> = .84
New Ovarian Cancers				
Probands	Number with tissue at risk	<i>N</i> = 353	<i>N</i> = 288	<i>N</i> = 65
	Observed cancers	2	0	2
	Expected cancers	0.49	0.39	0.09
	Hazard ratio	4.08	0	22.22
	95% Confidence Interval	0.49-14.74	0-9.46	2.69-80.27
	<i>P</i> value	<i>P</i> = .09	1	<i>P</i> < .01
1 st degree relatives only	Number	<i>N</i> = 907	<i>N</i> = 688	<i>N</i> = 219
	Observed cancers	2	2	0
	Expected cancers	0.78	0.60	0.18
	Hazard ratio	2.56	3.33	0
	95% Confidence Interval	0.31-9.26	0.40-12.04	0-20.49
	<i>P</i> value	<i>P</i> = .18	<i>P</i> = .12	<i>P</i> = 1

1-sided *P* values were utilized

417 - Poster Session

Multigene panel testing increases the detection of clinically actionable mutations in ovarian cancer patients

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Objective: Beyond *BRCA1/2*, a number of genes are associated with an increased risk for ovarian and/or other cancers. The majority of these genes have associated National Comprehensive Cancer Network (NCCN) guidelines for cancer risk management. We aimed to determine the frequency of pathogenic germline mutations in genes, other than *BRCA1/2*, among women with ovarian cancer undergoing multigene panel testing (MGPT).

Method: All cases of ovarian, fallopian tube, or primary peritoneal cancer submitted to a clinical diagnostic laboratory for MGPT targeting breast and/or ovarian cancer genes between 2012 and 2016 were included ($n = 12,806$). Genetic test results and clinical histories (as provided on test requisition forms or via clinical documentation) were retrospectively reviewed. Frequencies of pathogenic mutations/likely pathogenic variants (herein referred to as pathogenic mutations) were calculated for each gene (*ATM*, *BARD1*, *BRIP1*, *CDH1*, *CHEK2*, *EPCAM*, *MLH1*, *MRE11A*, *MSH2*, *MSH6*, *MUTYH*, *NBN*, *NF1*, *PALB2*, *PMS2*, *PTEN*, *RAD50*, *RAD51C*, *RAD51D*, *SMARCA4*, *STK11*, and *TP53*) and then summed to determine the combined mutation frequency.

Results: Most patients self-identified as Caucasian (71.3%, $n = 9,136$). The average age at ovarian cancer diagnosis was 49 years, and 26.2% ($n = 3,351$) had a history of 1 or more additional primary cancers. The combined frequency of pathogenic mutations in breast and/or ovarian cancer risk genes beyond *BRCA1/BRCA2* was 8.3%. Pathogenic mutations were most commonly detected in Lynch syndrome genes (1.7%), *CHEK2* (1.6%), *ATM* (0.9%), *BRIP1* (0.9%), and *RAD51C* (0.8%); 92.9% (762/820) of pathogenic mutations were identified in genes for which there are NCCN cancer risk management guidelines; 47.3% (388/820) of mutations occurred in genes where prophylactic oophorectomy should be considered (Lynch syndrome genes, *BRIP1*, *RAD51C*, and *RAD51D*); and 68.4% (561/820) of mutations occurred in genes where increased screening (and prophylactic surgery in some cases) is recommended for other cancers such as breast, colorectal, or endometrial cancer.

Conclusion: Testing beyond *BRCA1/2* with MGPT can significantly increase detection of clinically actionable mutations in ovarian cancer patients, allowing for more personalized management recommendations of patients and their at-risk relatives.

418 - Poster Session

Comprehensive genomic characterization of small cell neuro-endocrine carcinoma of the cervix

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Objective: Small cell neuroendocrine carcinoma of the cervix (SCNEC) is a rare clinical entity, associated with poor oncologic outcome. Following dramatic response to single-agent checkpoint inhibition in 2 patients with high-grade neuroendocrine carcinoma, we looked to explore the molecular signatures of a cohort of SCNEC cases (1, 2).

Method: Comprehensive genomic profiling of 80 SCNEC clinical formalin-fixed paraffin embedded (FFPE) specimens by hybridization-capture of up to 315 cancer-related genes (FoundationOne) provided targetable genomic alterations (GA) (short variants, indels, copy number aberrations, rearrangements). For 78 cases, tumor mutational burden (TMB) was calculated by counting mutations across a 0.8–1.1 Mb region (TMB-low, <6 muts/Mb; TMB-intermediate, 6–19.9 muts/Mb; TMB-high, ≥20 muts/Mb). Microsatellite status (MSI-high, MSI-intermediate, or MSI-stable) was assigned by a computational algorithm examining 114 intronic homopolymer loci for 57 cases.

Results: A total of 80 specimens with histologically confirmed SCNEC were identified. Two patients (2.5%) were found to be TMB-high, with ≥20 muts/Mb. One patient was MSI-H (49.5 muts/Mb), and the other was MSI-intermediate. An additional 16 specimens (20%) were TMB-intermediate (6–19.9 muts/Mb), 3 of which had >10 muts/Mb, and all were MSI-stable. Among the two patients who were TMB-high, one was found to be HPV-positive (HPV-16). The most frequently identified GA in the TMB-intermediate and TMB-high patient populations included *PIK3CA* (28%), *RB1* (22%), *PTEN* (22%), and *TP53* (22%). Six percent of patients were found to have *BRCA2* and *MLH1* alterations. The most frequent GA in the TMB-low group included *MYC* (19%), *TP53* (17%), *PTEN* (12%), and *PIK3CA* (10%).

Conclusion: In a modest subset of patients with SCNEC, molecular characterization allowed for the identification of an actionable mutation, notably high- to intermediate-TMB, suggesting potential benefit with the use of immune checkpoint inhibition. In 2 separate case reports, prolonged durable responses (>18 months) were described in heavily pretreated patients with large-volume disease recurrence. Molecular characterization of these uncommon tumors may be critical in identifying effective therapies, addressing an area of unmet clinical need.

419 - Poster Session

Risk stratification in serous ovarian cancer using a classifier based on 30 transcripts

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Objective: A transcript-based classifier for serous ovarian cancer (SOC) was developed to improve risk stratification. Performance of the classifier was evaluated using Affymetrix, RNA sequencing, and Agilent platforms.

Methods: Transcriptomic data were acquired from the cBioPortal for Cancer Genomics, the Harvard Medical School curated Ovarian Data, and the National Center for Biotechnology Information, U.S. National Library of Medicine GEO Profiles, and an unpublished cohort. Eligible patients had serous adenocarcinoma of the ovary with frozen tumor for evaluation, clinicopathologic details, vital status, and survival time. The relationship with overall survival was evaluated using univariate Cox modeling. Survival distributions were compared using log rank testing.

Results: A 4-step selection process based on Affymetrix transcriptomic data using univariate Cox modeling was implemented in 2 discovery cohorts (D1 and D2) and validated in an Affymetrix validation (V1) cohort, a RNA-sequencing validation (V2) cohort, and an Agilent validation (V3) cohort. The initial pool of 22,227 transcripts was successively narrowed to 30 based on strength of univariate and lasso combined associations with SOC survival in the D1 followed by the D2 cohorts. Sixteen transcripts were positive prognosticators (Figure 1A), while 14 were negative prognosticators (Figure 1B). An integrated classifier was generated using coefficients for the 30 transcripts from a multivariate Cox model in the D1 cohort (Figure 1C). The RS30 risk score was then calculated for each patient and categorized into tertiles as low, middle, or high. The categorized RS30 risk score effectively stratified survival for SOC based on expression data from V1 (Figure 1D), V2 (Figure 1E), and V3 (Figure 1F). Patients with RS30 scores in the lowest tertile had significantly improved survival compared to the middle and high tertiles (Figure 1G). The RS30 risk score was also associated with older age at diagnosis (≥ 65 years), advanced stage, suboptimal debulking, and the aggressive molecular subtypes.

Conclusion: The RS30 risk score effectively stratified risk in SOC and may inform more tailored management in this disease setting.

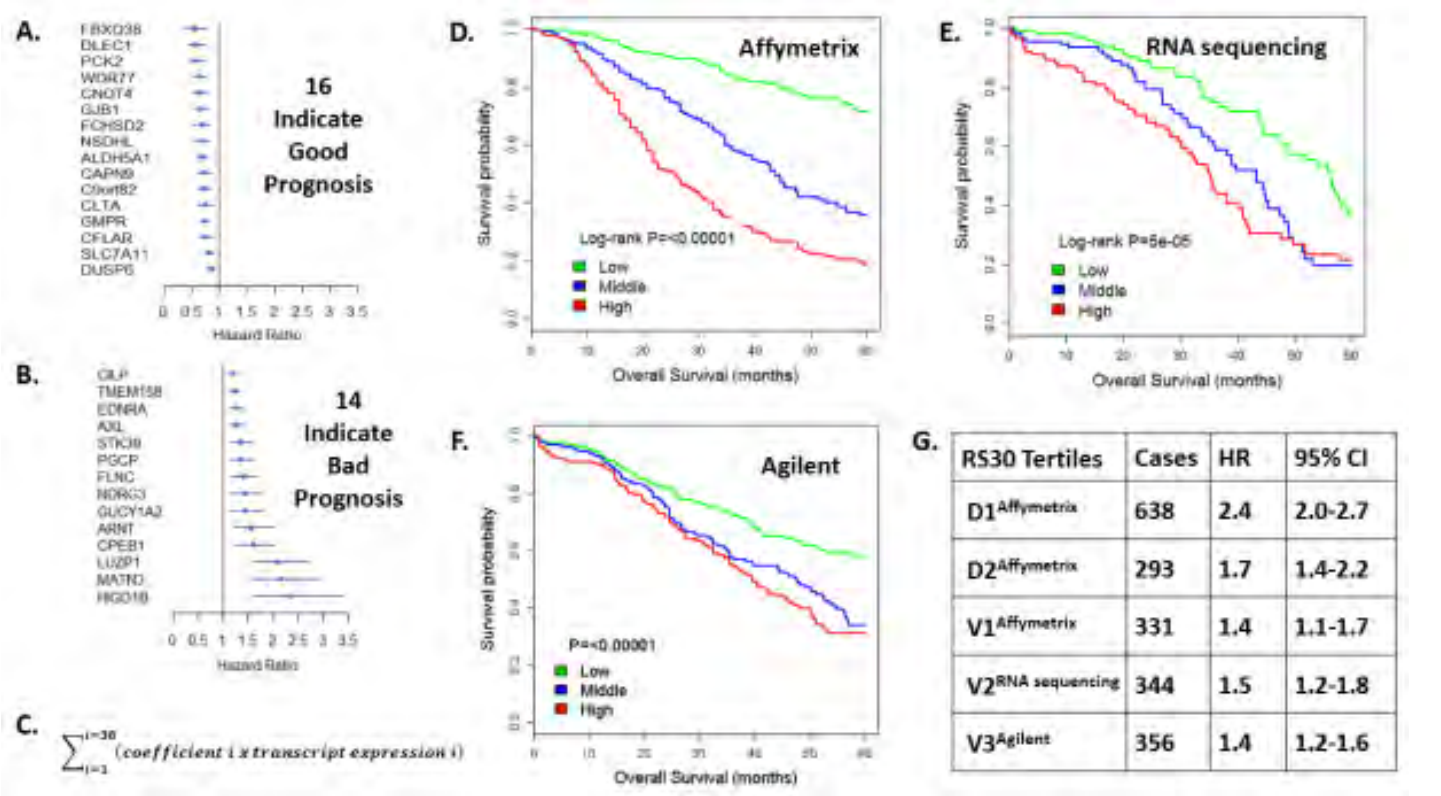


Fig. 1. Forest plot with hazard ratio (HR) and 95% confidence interval (CI) for the 16 transcripts in the RS30 classifier associated with a good prognosis (A) and the Forest plot for the 14 transcripts associated with a poor prognosis (B). The formula for the RS30 classifier (C). Kaplan-Meier plots for the RS30 classifier by tertile score (low, middle, high) in the D1 Affymetrix Cohort (D), the V2 RNA sequencing cohort (E) or the V3 Agilent Cohort (F) with survival distributions compared using log-rank testing. The relationship between the RS30 classifier categorized into tertiles and overall survival from univariate Cox modeling in the two discovery and three validation cohorts (G). There were 252 patients with Affymetrix data in the V1 cohort and with RNA sequencing data in the V2 cohort.

420 - Poster Session

Role of adjuvant chemotherapy in the management of ovarian non-granulosa sex cord-stromal tumors

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Objective: To investigate the role of adjuvant chemotherapy (CT) in the management of ovarian nongranulosa cell (GC) sex cord-stromal tumors (SCSTs).

Method: The National Cancer Data Base was accessed, and a cohort of women diagnosed between 2004 and 2013 with a malignant non-GC SCST was evaluated. Those who did not undergo cancer-directed surgery and those with less than 1 month of follow-up and unknown CT status were excluded from further analysis. Median and 5-year overall survival (OS) were estimated following generation of Kaplan-Meier curves and compared with the log-rank test. Multivariate survival analysis was performed with the construction of a Cox regression model. Factors associated with the administration of CT were evaluated with the χ^2 test and multivariable binary logistic regression.

Results: A total of 391 women with a median age of 39 years were identified. The most common histotype was Sertoli-Leydig cell tumor (SLCT) (73.2%), followed by steroid cell (12%) and Sertoli carcinoma (6.1%). Based on available information, 84.8% of women had early-stage disease (stage I-II). However, in this cohort, only 49.7% of patients had lymph node sampling/dissection. A total of 203 (51.9%) patients received CT. Higher administration rates were observed among women with advanced stage ($P < 0.001$), bilateral ($P = 0.04$) and >10 cm ($P = 0.001$) tumors of SLCT histology ($P < 0.001$), Caucasian race ($P = 0.003$), and premenopausal age ($P = 0.007$). By multivariate analysis, advanced-stage, Caucasian race, tumor size, and SLCT histology were associated with the administration of CT. For patients with early-stage disease, there was no difference in OS between those who did ($n = 134$) and did not receive CT ($n = 157$; $P = 0.4$); 5-year OS rates were 81.7% and 84.6%, respectively. No mortality benefit was observed (HR 0.73, 95% CI 0.38, 1.4) after controlling for tumor histology. Median OS of women with advanced-stage disease who received CT ($n = 41$) was 34.96 months compared to 15.51 months for those who did not ($n = 11$; $P = 0.013$).

Conclusion: Adjuvant CT was associated with improved survival for women with advanced stage non-GC SCSTs. No clear benefit was found for those with early-stage disease.

421 - Poster Session

Non-small cell neuroendocrine tumors of the ovary: An analysis of the National Cancer Data Base

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Objective: To investigate the clinicopathological characteristics and survival of women diagnosed with malignant non-small-cell neuroendocrine ovarian tumors.

Method: The National Cancer Data Base was accessed, and a cohort of women diagnosed between 2004 and 2014 with a malignant ovarian carcinoid (OC) or large-cell neuroendocrine carcinoma (LNEC) was drawn. Demographic and clinicopathological characteristics of patients with each histologic subtype were compared using the Mann-Whitney and χ^2 tests. Overall survival (OS) was assessed for women who had cancer-directed surgery (CDS) with 1 month or more of follow-up and was compared with the log-rank test after generation of Kaplan-Meier curves.

Results: A total of 794 women were identified; 689 (86.8%) and 105 (13.2%) were diagnosed with OC and LCNEC, respectively. Women with OC were younger (median age 54 vs 66 years, $P < 0.001$) and less likely to be of Caucasian race (75.9% vs 86.7%, $P = 0.014$). They more commonly presented with unilateral tumors (95% vs 68.4%, $P < 0.001$) of smaller

size (median 3.5 vs 11 cm, $P < 0.001$) that were confined to the ovary (86.9% vs 10.9%, $P < 0.001$). Lymph node metastasis was more frequent for patients with LCEC (50% vs 7.8%, $P < 0.001$) who were less likely to undergo CDS (65.7% vs 99.4%, $P < 0.001$). Women with OC confined to the ovary ($n = 231$) had an excellent OS (5-year, 90.5%), while those with advanced-stage disease ($n = 34$) had a median OS of 47.6 months. Patients with LCNEC had a poor prognosis regardless of disease stage; median OS for early ($n = 10$) and advanced-stage ($n = 39$) disease was 19.1 and 25.9 months, respectively ($P = 0.53$), and administration of chemotherapy (CT) was not associated with improved OS (median 20.34 vs 15.61 months, $P = 0.32$). Similarly, for women with OC that had spread beyond the ovary, CT was not associated with improved OS (median 41.95 vs 47.61 months, $P = 0.6$). CT was rarely administered for patients with early-stage OC (2.8%), with no survival benefit ($P = 0.49$).

Conclusion: Non-small-cell neuroendocrine ovarian tumors consist of two distinct entities with unique clinicopathological characteristics and prognosis. OCs are typically unilateral, large tumors confined to the ovary, arising in perimenopausal women. LCNEC primarily affects postmenopausal patients and is associated with a poor prognosis. Adjuvant CT was not associated with improved OS in any histotype.

422 - Poster Session

A new era: Changing patterns of high-grade serous fallopian tube cancer diagnosis

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Objective: Accumulating evidence suggests that the majority of nonuterine high-grade serous carcinomas (HGSC) of gynecologic origin are of fallopian tube rather than ovarian origin. We sought to explore the patterns of classification of diagnosis of HGSC relative to the establishment of the World Health Organization (WHO) guidelines for histopathologic classification of gynecologic malignancies (Kurman et al. 2014).

Method: All patients newly diagnosed with nonuterine HGSC of gynecologic origin who underwent debulking surgery at a single academic institution from January 1, 2006, to May 31, 2017 were reviewed. Original histopathologic cancer diagnosis and clinical data were abstracted from medical charts. Reassignment of primary site (fallopian tube, ovary, primary peritoneal, tubo-ovarian) using 2014 WHO criteria was made based on review of surgical pathology reports. Descriptive statistics were employed, and the χ^2 test was used to assess whether there was an association between timeframe and cancer site classification.

Results: A total of 276 patients with a median age of 63 years (range 33–88) were identified and analyzed. The majority of patients were non-Hispanic white (70%, $n = 189$) and had stage III (78%, $n = 216$) disease. Of the cohort, 22% ($n = 62$) were initially diagnosed with fallopian tube cancer, whereas 62% ($n = 171$) were diagnosed with HGSC of ovarian, 9% ($n = 25$) primary peritoneal, and 3% ($n = 18$) tubo-ovarian origin. Based on 2014 WHO criteria, 72% ($n = 198$) were reclassified as having disease of fallopian tube, 25% ($n = 68$) ovarian, 3% ($n = 8$) primary peritoneal, and <1% ($n = 2$) tubo-ovarian origin (Figure 1). There was a statistically significant ($P < 0.001$) difference in the rate of pathologist-determined fallopian tube cancer diagnosis before and after 2014. However, when the association of timeframe and fallopian tube cancer diagnosis based on WHO criteria reclassification was assessed, there was no difference ($P = 0.18$) before and after 2014.

Conclusion: Although the rate of diagnosis of HGSC of tubal origin at our institution has increased dramatically since the advent of the 2014 WHO guidelines, this development represents the changed criteria for diagnosis of tubal HGSC and not a true change in anatomic disease site. These findings add credence to the use of salpingectomy as a truly risk-reducing strategy.

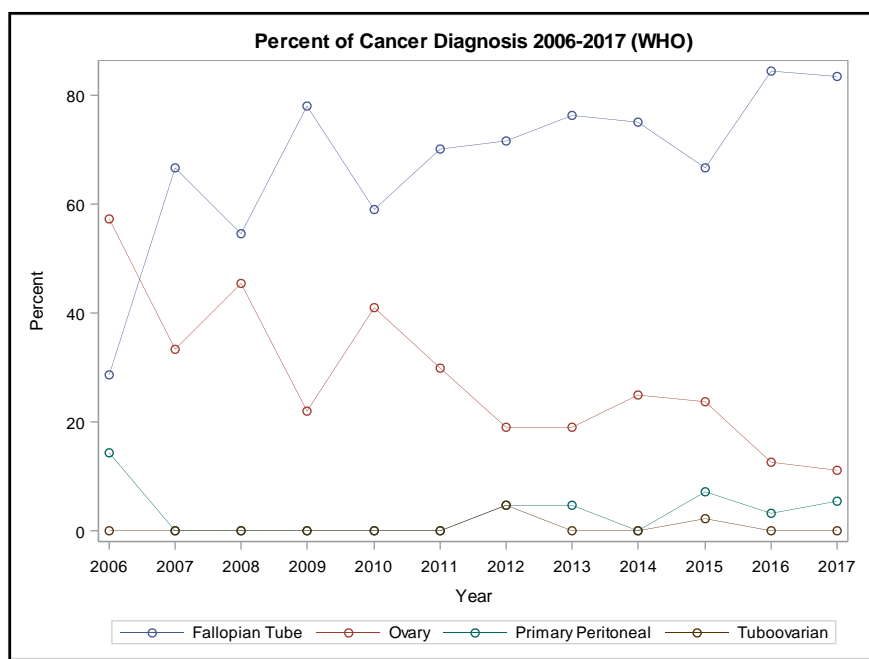


Fig. 1. Non-uterine HGSC breakdown of site of origin using 2014 WHO criteria by year.

423 - Poster Session

A comparison between vulvar melanoma and vulvar squamous cell carcinoma, and other mucocutaneous melanomas with a focus on racial disparities

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Objective: To compare the demographic and clinicopathologic features of patients with vulvar melanoma (VM) and vulvar squamous cell carcinoma (SCC), as well as other mucocutaneous melanomas (MCM).

Method: The Surveillance, Epidemiology and End Results (SEER) cancer registry was queried for women diagnosed with VM, SCC, and MCM from 2004 to 2012. the χ^2 and Student t tests and Kaplan-Meier curves were used for statistical analysis using SPSS.

Results: There were 530 VM, 6,323 SCC, and 2,797 MCM patients. The majority of patients in all three groups were white (93.5%, 88.2%, and 94.7%, respectively). A higher percentage of black patients were diagnosed with SCC than with VM (9.1% vs 2.9%, respectively, $P < 0.01$). There was no statistical difference in race between VM and MCM patients ($P = 0.06$). The mean age of diagnosis was 66 years for VM and SCC patients ($P = 0.99$) and 64 years for MCM patients ($P = 0.01$) compared to VM patients. Of SCC patients, 58.7% presented with local disease compared to 66.0% of VM patients ($P < 0.01$), and 5.2% and 8.7% presented with advanced disease, respectively ($P < 0.01$). Of MCM patients, 74.3% presented with local disease ($P < 0.01$) and 9.7% with advanced disease ($P < 0.01$) compared to VM patients. Race did not seem to affect stage at presentation for SSC and VM patients ($P = 0.87$ and 0.30 , respectively). Black patients were more likely to be diagnosed with advanced-stage MCM than their white counterparts (16.2% vs 8.2%, respectively; $P = 0.04$). Overall survival was 56 months for VM, compared to 67 months for SCC patients ($P < 0.01$) and 69 months for MCM patients ($P < 0.01$). In SCC patients, black patients had an overall survival of 72 months compared to 66 months for the white cohort ($P = 0.01$). In VM atients, black patients had a overall survival of 27 months compared to 58 months for their white counterparts ($P = 0.01$). There was no statistical difference in the overall survival in black and white patients with MCM (64 and 69 months, respectively; $P = 0.46$). Most patients diagnosed with VM underwent surgery (92.6%) compared to 82.4% of SCC patients ($P < 0.01$) and 45.8% of MCM patients ($P < 0.01$). Only 6.8% of VM patients received radiation. A total of 17.5% of SCC patients ($P < 0.01$) and 12.1% of MCM patients ($P < 0.01$) received radiation.

Conclusion: While VM patients share similarities to SCC and MCM patients, black patients are more likely to be diagnosed with advanced MCM disease, and those with VM had shorter survival rates. This warrants further investigation into the tumor biology of melanomas.

424 - Poster Session

Prognostic significance of residual disease in advanced stage malignant ovarian germ cell tumors

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Objective: Given the chemosensitivity of malignant ovarian germ cell tumors (MOGCTs), the necessity of extensive debulking surgery has been recently reevaluated. We aimed to investigate the prognostic significance of complete gross resection for patients with advanced-stage MOGCTs.

Method: The National Cancer Data Base was accessed, and patients diagnosed between 2004 and 2013 with an advanced-stage (II–IV) MOGCT, who underwent definite surgical treatment with known status of residual disease, were selected for further analysis. Women with less than 1 month of follow-up were excluded. For analysis, two groups were formed: women who had complete gross resection (R0) and those with macroscopic residual disease (R1). Demographic and clinicopathological characteristics were compared by using the χ^2 and Mann Whitney U tests. Univariate survival analysis was performed with the log-rank test after generation of Kaplan-Meier curves, while a Cox proportional hazard model was constructed to evaluate mortality after controlling for possible confounders.

Results: A total of 312 women who met the inclusion criteria were identified. The overall rate of R0 was 75.3%; 87% for women with stage II disease compared to 75.4% and 52.5% for those with stage III and stage IV disease, respectively ($P < 0.001$). Women with R0 were more likely to undergo lymphadenectomy compared to those with R1 (77.4% vs 53.9%, $P < 0.001$). There was no difference between the two groups based on patient age ($P = 0.11$), race ($P = 0.34$), medical comorbid conditions ($P = 0.20$), receipt of chemotherapy ($P = 0.99$), and histologic subtype ($P = 0.19$). By univariate analysis there was no difference in overall survival (OS) between women who had a complete gross resection and those who did not ($P = 0.14$); 5-year OS rates were 86.1% and 82%, respectively. No difference in OS was noted following stratification by histology ($P = 0.55$ and $P = 0.17$ for dysgerminoma and nondysgerminoma tumor groups, respectively). Multivariate analysis controlling for disease stage (II vs III/IV), histology (dysgerminoma vs nondysgerminoma), and the administration of chemotherapy found that R1 was not associated with a worse mortality (HR 1.62, 95% CI 0.84, 3.14).

Conclusion: Residual disease was not associated with a worse prognosis in a cohort of women with advanced-stage MOGCT. Further research is required to evaluate the role of extensive cytoreductive surgery.

425 - Poster Session

Minimally invasive staging for apparent stage I malignant ovarian germ cell tumors.

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Objective: To evaluate the prevalence, trends, and outcomes of minimally invasive surgical staging (MIS) of malignant ovarian germ cell tumors (MOGCTs) apparently confined to the ovary.

Method: The National Cancer Data Base was accessed, and women diagnosed between 2010 and 2014 with a MOGCT apparently confined to the ovary and information on the planned surgical approach were selected for further analysis. An intention-to-treat analysis approach was selected; women who were converted to laparotomy were included in the MIS group. Demographic and clinicopathological characteristics were compared with the χ^2 and Mann Whitney U tests. Univariate survival analysis was performed with the log rank test after generation of Kaplan-Meier curves. Patients with less than 1 month of follow-up were excluded from the survival analysis.

Results: A total of 1,122 patients were identified. MIS was planned for 389 (34.7%) patients; a laparoscopic approach for 298 patients; and a robotic-assisted approach for 91 patients. Rate of conversion to laparotomy was 11.8% (46 cases); 1.1% and 15% in the robotic and laparoscopy groups, respectively ($P < 0.001$). No difference in the use of MIS was noted based on year of diagnosis ($P = 0.37$). Women in the MIS group were older (median 25 years vs 22 years, $P < 0.001$) and more likely to be of white race ($P = 0.048$) with a higher education level ($P < 0.001$). No differences between the MIS and laparotomy groups were observed based on tumor histology ($P = 0.93$) or substage ($P = 0.49$). However, women in the MIS group had smaller tumors (median 11 vs 15 cm, $P < 0.001$) and were less likely to undergo lymph node dissection (46.1% vs 52.7%, $P = 0.037$) and omentectomy (22.5% vs 29.4%, $P = 0.014$). Rate of lymph node metastasis (11% vs 6.1%, $P = 0.067$) and chemotherapy

administration (31.5% vs 25.3%, $P = 0.032$) were higher in the laparotomy group. Hospital stay following surgery was shorter for women who had MIS (median 1 vs 3 days, $P < 0.001$). The unplanned 30-day readmission rate was also lower in the MIS group (1% vs 4.2%, $P = 0.007$). No difference in OS was noted between the two groups ($P = 0.67$); 3-year OS rates were 97.9% and 99.1% for women in the laparotomy and MIS groups, respectively.

Conclusion: In the present cohort, MIS of apparent early-stage MOGCTs was less comprehensive but associated with a decreased hospital stay and unplanned readmission rate. MIS was not associated with a worse prognosis.

426 - Poster Session

Prevalence of concurrent or previous high-grade cervical intraepithelial neoplasia in women with high-grade anal intraepithelial neoplasia and or anal carcinoma

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Objective: (1) To determine the prevalence of previous or concurrent high-grade cervical intraepithelial neoplasia (CIN 2 or 3) in women diagnosed with high-grade anal intraepithelial neoplasia (AIN 2 or 3) or anal carcinoma. (2) To determine prevalence of high-risk HPV positivity in women with both CIN 2 or 3 and AIN 2 or 3 or anal carcinoma

Method: Institutional review board approval was obtained. We conducted a chart review of patients seen in the Grady Health System from January 1, 2006, to December 31, 2015. The inclusion criterion was women aged 18 years or older diagnosed with AIN 2 or 3 or anal carcinoma. We reviewed those records for any documentation of the patient's Pap smear history, colposcopic procedures, or treatment for CIN 2 or 3 including cervical excisional biopsy. Charts without a documented Pap smear, colposcopy, or cervical excisional biopsy were excluded. We also reviewed the included charts for a documented high-risk HPV test and demographic information including HIV status, age, race, and smoking status. Data analysis was completed by the Morehouse School of Medicine Biostatistics Department. Descriptive statistics were used to summarize the data. Mean with standard deviation was used for continuous variables, and frequency with percentage was used for categorical variables.

Results: We identified 53 patients with the diagnosis of AIN 2, AIN 3, or anal carcinoma during the study time period. Fifty-two patients, or 98.1%, of our study population were African-American. Of the 53 patients, 16 had a previous or concurrent diagnosis of CIN 2 or 3, for a prevalence rate of 30.2%. Of the 16 patients, nine had documented high-risk HPV testing, for a prevalence rate of 55.5%. Of the 16 patients with a history of high-grade cervical dysplasia, 87.5% were HIV positive.

Conclusion: Currently, there are no standardized guidelines for screening for anal dysplasia or carcinoma. This may be in part because to date there are no randomized clinical trials demonstrating the efficacy of any screening method. However, because of the increase in the incidence of anal carcinoma, some experts have advocated screening certain high-risk populations (such as women with prior CIN, HIV positive patients, and men who have sex with men) with anal Pap smears and high-resolution anoscopy. In our study population the majority of the women with concurrent high-grade CIN and AIN or anal cancer (87.5%) were co-infected with HIV. Thus, there is a definite role for screening HIV-positive women with CIN 2 or 3 and anal dysplasia.

427 - Poster Session

Increased risk of breast and uterine cancer among women with ovarian granulosa cell tumors

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Objective: Ovarian granulosa cell tumors secrete estrogen; thus, an increased risk of hormone-related neoplasms is speculated. We evaluated the incidence of uterine and breast cancer among women diagnosed with granulosa cell tumors (GCT) of the ovary.

Method: The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database was accessed, and a cohort of women diagnosed between 1973 and 2014 with a microscopically confirmed malignant ovarian granulosa tumor and known follow-up was selected. Personal tumor history was extracted, and women with a previous or subsequent malignant breast or uterine tumor were identified. The expected incidence of breast and uterine cancer was calculated based on the U.S age-specific rate of breast and uterine cancer per 100,000 women drawn from the SEER database. Patients were grouped based on their age at the end of follow-up to reflect the cumulative risk of breast and uterine cancer. The cumulative

expected cancer rate for each age group was calculated by adding the incidence of the previous age group. Odds ratio (OR) with 95% confidence intervals was calculated for each tumor.

Results: A total of 1,908 women diagnosed with ovarian GCTs was identified. Median age at GCT diagnosis was 52 years (range 3–94), and the majority of patients were of white race (73.1%). In our cohort, 79 (4.14%) and 53 (2.78%) women were found to have breast and uterine cancer, respectively. The expected number of malignant breast and uterine tumors in our cohort was 27 and 6, respectively. Calculated OR for breast and uterine malignancies was 2.96 (95% CI 2.34–3.68) and 8.83 (95% CI 6.61–11.56) respectively.

Conclusion: Based on data from a population-based registry, an increased incidence of breast and uterine malignancies among patients diagnosed with ovarian GCTs was observed. This may have significant implication on cancer screening and surgical planning.

428 - Poster Session

Colposcopy rates decrease among younger women without increasing overall rates of cervical cancer after implementation of 2012/2013 management guidelines

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Objective: To examine trends in referral to an academic colposcopy clinic and distribution of high-grade dysplasia and cancer as well as rates of intervention among patients with abnormal cervical cancer screening.

Method: A prospective registry of 5,804 patients seen between January 2007 and December 2016 at a specialized center for evaluation of abnormal Pap smear screening was queried to examine trends in patient characteristics, cytology results, histologic diagnoses, and interventions.

Results: Mean patient age increased significantly from 2007 to 2016 (27.0 vs 35.0 years, $P < 0.0001$), and fewer pregnant patients were served (9.8% vs 4.1%, $P < 0.0001$). High-grade cytology represented a higher proportion of the referral base in 2016 than in 2007 (13.8% vs 9.7%, $P = 0.02$), as did patients testing positive for HPV (19.2% vs 12.7%, $P < 0.0001$). Despite often-lengthened ASCCP (American Society for Colposcopy and Cervical Pathology) screening intervals, no statistical increase was observed in patients diagnosed with high-risk histologies, such as cancer, adenocarcinoma in situ, or high-grade squamous intraepithelial lesion, between 2007 and 2016 (16.1% vs 19.0%, $P < 0.14$). There was, however, a decrease in the percentage of visits involving colposcopy between 2007 and 2016 (77.2% vs 47.2%, $P < 0.0001$) and a stable relationship of visits involving interventions, such as loop electrosurgical excision procedures (6.9% vs 5.5%, $P = 0.10$).

Conclusion: Findings from this large prospective registry suggest that the ASCCP guidelines have functioned as intended in identifying high-grade dysplastic changes, minimizing unnecessary intervention, and optimizing excisional treatment decisions, especially in younger patients.

429 - Poster Session

Decentralized treatment for post-molar gestational trophoblastic neoplasia (PMGTN) is associated with increased lines of chemotherapy and longer time to remission

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Objective: Every woman who receives care for gestational trophoblastic disease at our specialty trophoblastic disease center is referred by her primary physician. U.S. and international data suggest care at a specialty center may improve outcomes. The aim of this study was to assess whether referral before or after primary postmolar gestational trophoblastic neoplasia (PMGTN) treatment affected subsequent outcomes for women diagnosed with PMGTN.

Method: Records were queried for all patients with molar pregnancy or PMGTN from 1993 to 2013. Retrospective chart review was performed to extract relevant clinical and demographic data. Parametric and nonparametric tests were utilized to compare variables. Time to remission was modeled utilizing the Kaplan-Meier method.

Results: From 1993 to 2013, 173 women were treated for PMGTN, and 65 required greater than 1 line of chemotherapy and formed the study population. The majority (75%) of this cohort required 2 lines of chemotherapy to achieve remission, and only 8% ($n = 5$) of women required 4 or more lines of chemotherapy. The women who were treated at other institutions prior to referral had a higher human chorionic gonadotropin (hcg) at the time of persistence ($P = 0.01$) and a higher World Health Organization (WHO) risk score ($P < 0.001$). A significant increase in the need for more than 2 lines of chemotherapy was noted in the cohort ($n = 18$, 28%) who had been referred after initial chemotherapy was given at an outside institution, even when controlling for age, hcg at persistence, and WHO risk score ($P = 0.03$). This translated into a prolonged time to remission (78 vs 107 days, $P = 0.01$) on univariate analysis. Treatment at an outside institution was the variable most strongly associated with prolonged time to remission in a multivariate model (HR = 0.54, 95% CI 0.27–1.07, $P = 0.08$) of age, WHO score, and hcg at persistence. See Figures 1 and 2.

Conclusion: Women who received primary chemotherapy for treatment of PMGTN at an outside institution prior to referral to our specialty center had an increased need for additional lines of chemotherapy resulting in a significantly prolonged time to remission.

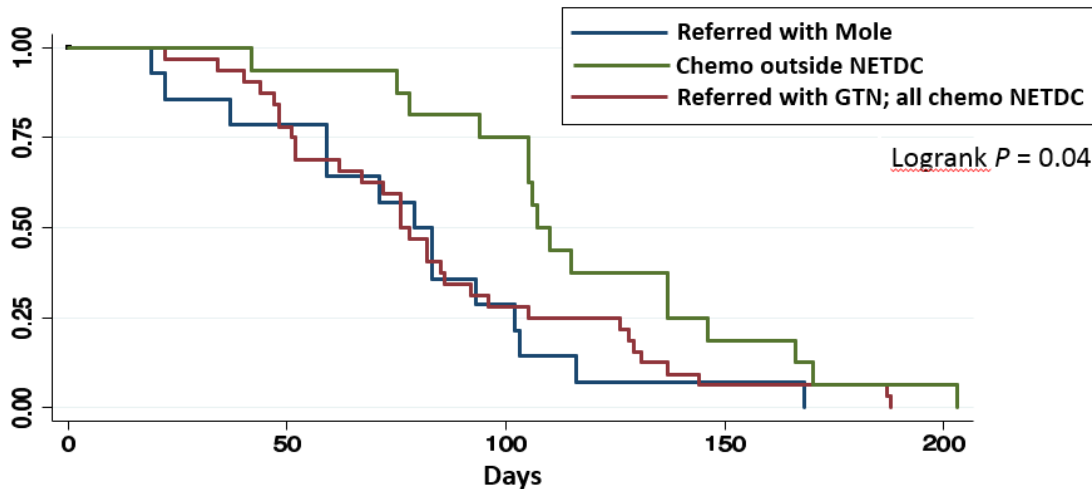


Fig. 1. Time from Molar Evacuation to Remission by Treatment Group.

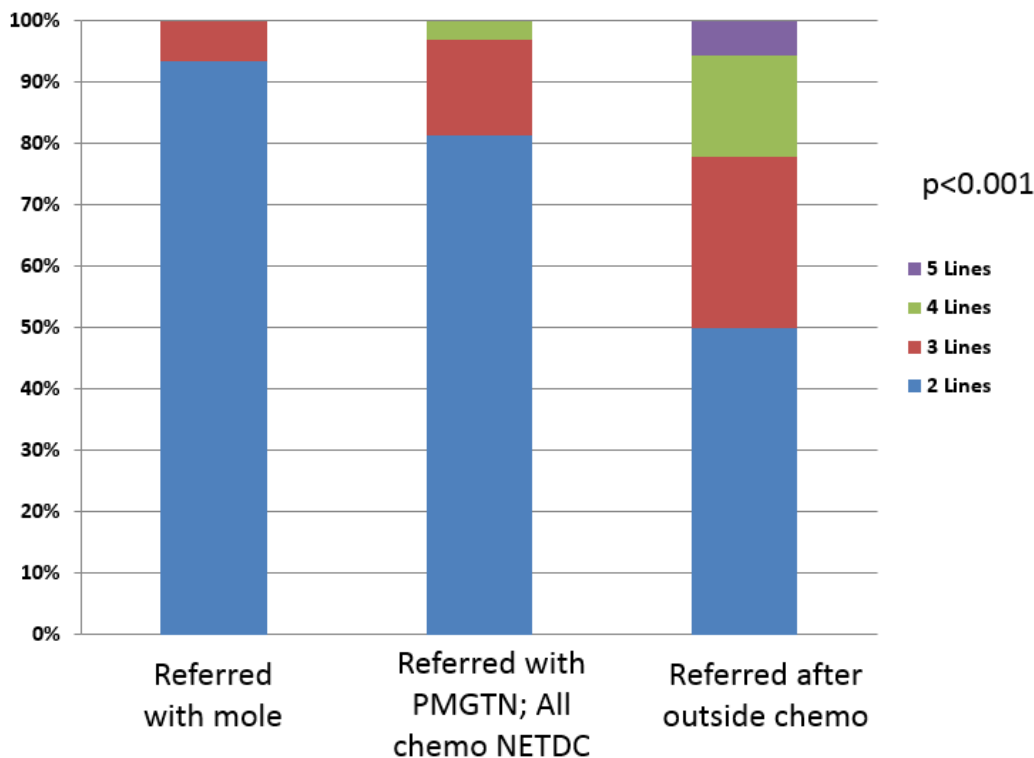


Fig. 2. Lines of Chemotherapy by Referral and Treatment Site.

430 – Poster Session

Impact of choice of chemotherapy on survival of patients with carcinosarcoma of the ovary: A retrospective review across two academic institutions

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Objectives: Ovarian carcinosarcomas (CS) are rare, accounting for less than 1% of ovarian tumors. Platinum-based chemotherapy is the standard treatment for ovarian carcinoma, whereas ifosfamide is included in the treatment regimen for sarcoma. The objective of this study is to compare the clinical outcomes of patients with ovarian CS treated with surgical cytoreduction and different combination chemotherapy regimens at two major academic centers.

Method: We queried a prospectively maintained database for a retrospective analysis of all patients with a pathologic diagnosis of ovarian CS treated between 1995 and 2016 at the two centers. Medical records were probed for demographic data, surgical stage, pathologic data, cytoreduction status, chemotherapy, date of diagnosis, date of recurrence, date of death, or last follow-up. Using the Kaplan-Meier method, we described progression-free and overall survival.

Results: A total of 57 patients with ovarian CS were identified. The median age at diagnosis was 67 years. The majority of patients presented at an advanced stage (stage III or IV) (79%) and had optimal surgical cytoreduction (82%). There was no difference in the mean age at diagnosis, stage, or cytoreduction status between the chemotherapy groups. The median progression free survival (PFS) of the entire cohort was 13.5 months, and the median overall survival (OS) was 39.7 months. Median PFS was similar with the cisplatin/ifosfamide regimen and the carboplatin/ paclitaxel q 3 weekly regimen and was the poorest in the ifosfamide/paclitaxel group (17.3 vs 15.3 vs 12.0 months, respectively, $P = 0.04$). The median OS was highest with the carboplatin/paclitaxel regimen, followed by the cisplatin/ifosfamide regimen, and then the ifosfamide/paclitaxel group (65.8 vs 38.0 vs 35.7 months, respectively, $P = 0.004$). Four patients received other chemotherapy regimens with median OS of 4.4 months, and these patients progressed almost immediately. There was no difference in PFS or OS for those patients with heterologous versus only homologous components in the carcinosarcoma.

Conclusion: Most patients with ovarian CS present with advanced-stage disease. Ovarian CS patients treated with carboplatin and taxol chemotherapy had an improved OS compared to patients treated with cisplatin/ifosfamide or ifosfamide/paclitaxel or other chemotherapy regimens.

431 - Poster Session

Does the addition of vaginal brachytherapy to adjuvant chemotherapy for stage I-II uterine serous carcinoma improve recurrence-free and overall survival?

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Objective: To evaluate the effect of adding vaginal brachytherapy (VBT) to adjuvant chemotherapy on patterns of recurrence, recurrence-free survival (RFS), and overall survival (OS) in stage I-II uterine serous carcinoma (USC).

Method: Adult women with a new diagnosis of FIGO (2009) stage I–II USC from 2001 to 2012 were identified. Women who received adjuvant chemotherapy with or without VBT were included. Those who received whole pelvic radiation were excluded. Categorical variables were compared using χ^2 or Fisher exact tests. Wilcoxon-Mann-Whitney tests were used to compare continuous variables. The Kaplan-Meier method was used to estimate RFS and OS, and log rank test was used to compare survival functions. Cox proportional hazards models were used to identify factors predictive of RFS and OS.

Results: Among 190 women with stage I-II USC, 89 received adjuvant chemotherapy with or without VBT: 46 (51.7%) in the VBT group and 43 (48.3%) in the non-VBT group. More women in the VBT group were obese compared to the non-VBT group ($P = 0.01$). There were no significant differences in demographic or other clinical/tumor characteristics (age, race, stage, lymph node dissection and count, disease confined to polyp, and lymph vascular space invasion) between groups. Median number of chemotherapy cycles was 6 for both groups. Nineteen percent of women experienced recurrence (VBT, 9; non-VBT, 8). Only one vaginal recurrence occurred in the non-VBT group. There was no significant difference in crude rate of abdominal/pelvic or distant recurrence between groups ($P > 0.99$). All patients with recurrence died of disease. Unadjusted RFS and OS survival curves showed no significant difference between two groups (Figure 1). Obesity (HR = 9.6, 95% CI 1.9–50.2) and stage II versus IA (HR = 9.3, 95% CI 1.3–68.9) were predictive of OS, but not of RFS.

Conclusion: The addition of adjuvant VBT to adjuvant chemotherapy for stage I–II uterine serous carcinoma does not appear to significantly alter patterns of recurrence or survival outcomes.

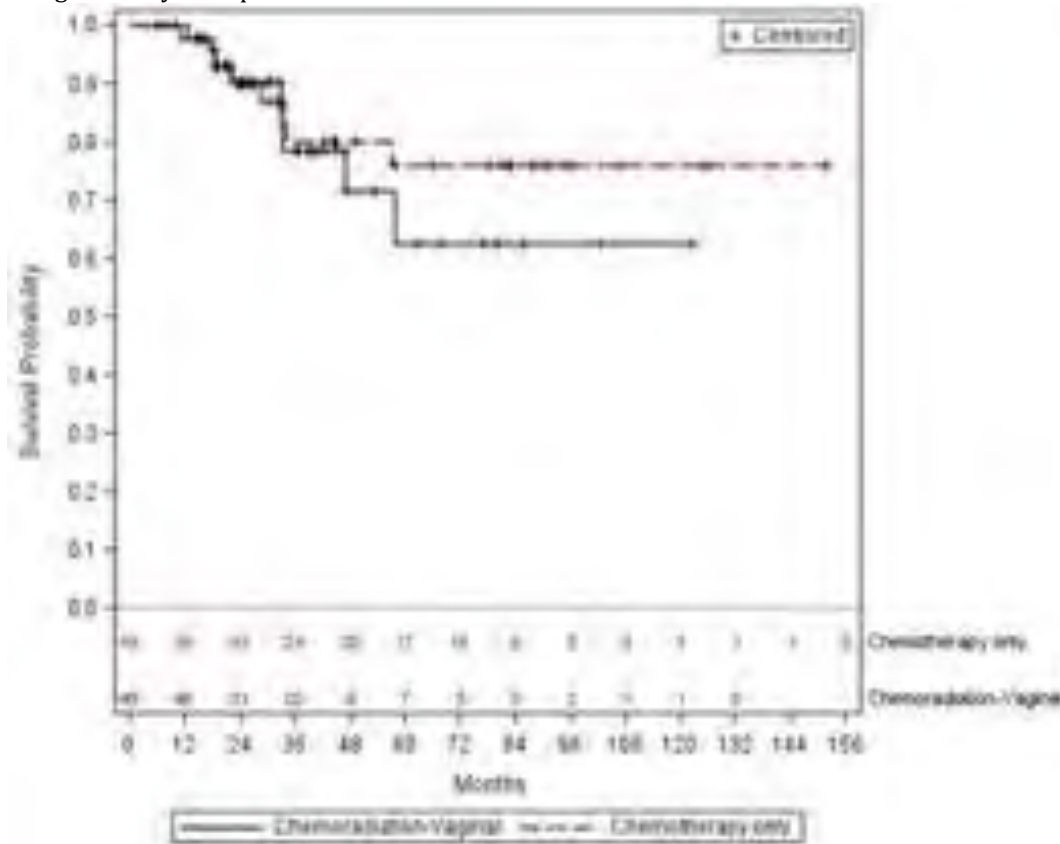


Fig. 1. Disease-free survival ($P = 0.56$).

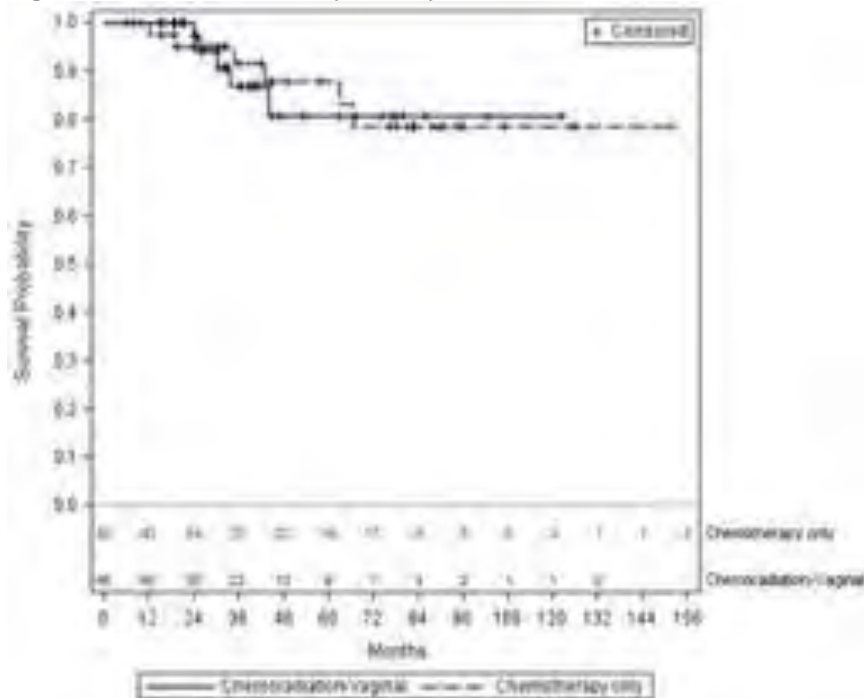


Fig. 2. Overall survival ($P = 0.89$).

432 - Poster Session

Risk of unplanned postoperative readmission after sentinel lymph node biopsy compared to complete inguinofemoral lymphadenectomy in patients with squamous cell carcinoma of the vulva

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Objective: To discern whether sentinel lymph node biopsy (SLNB) is associated with a reduced risk of unplanned readmission compared with complete inguinofemoral lymphadenectomy (IFLND) among women undergoing surgery for vulvar carcinoma.

Method: We identified women who underwent surgery for stage IB–IVA squamous cell carcinoma of the vulva from 2013 to 2014 in the National Cancer Database. We excluded women who did not receive surgical lymph node evaluation or who underwent superficial IFLND (fewer than 4 nodes identified). Patients were categorized as having SLNB by the hospital cancer registrars based on review of the operative note. We considered patients to have undergone a complete IFLND when the lymph node dissection yielded 4 or more lymph nodes and was not identified as SLNB. Outcomes of interest included unplanned readmission within 30 days of surgery and length of postoperative hospitalization. We performed univariable analyses and multivariable regression modeling to adjust for covariates, which were selected a priori, including age, race, hospital type, socioeconomic status, tumor size, lymph node involvement, bowel or bladder invasion, and Charlson comorbidity index.

Results: We identified 1,637 women who underwent IFLND and 383 women who underwent SLNB for regionally confined squamous cell carcinoma of the vulva in 2013 and 2014. The mean age at diagnosis was 64.5 years. Most women had tumors smaller than 4 cm (70.5%). Lymph nodes were positive in 23.8% of patients. Among women who underwent IFLND, 95/1,637 (5.8%) were readmitted, compared with 13/383 (2.9%) of those who underwent SLNB ($P = 0.03$). After adjusting for potential confounders, women who underwent SLNB were 43% less likely to be readmitted than those who underwent IFLND (aOR = 0.57, 95% CI 0.34–0.95, $P = 0.04$). Restricting the study population to 1,053 women with tumors larger than 4 cm and no lymph node involvement did not alter our main findings (aOR = 0.48, 95% CI 0.24–0.97, $P = 0.04$). In addition, SLNB was associated with a 1.1-day (95% CI 0.3–1.9) reduction in postoperative stay from 3.4 to 2.3 days ($P = 0.01$), a difference that remained significant in multivariable analysis ($P = 0.02$).

Conclusion: Compared with IFLND, SLNB is associated with significant reduction in postoperative readmission.

433 - Poster Session

Immune-reactive microenvironment of small cell carcinoma of the ovary, hypercalcemic type provides a rationale for evaluating immunotherapies to treat this malignancy

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Objective: Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a rare and very aggressive malignancy affecting very young women. The treatment options are limited, and survival rates remain poor. Several SCCOHT patients have received antiprogrammed death 1 (PD-1) immunotherapy with promising responses. Immunotherapies have been proven to be effective particularly in cancers that are hypermutated. Given that SCCOHT is a monogenic disease (SMARCA4 mutation is the sole alteration), SCCOHT patients' positive responses to immunotherapies are unusual. SCCOHT has not been immunoprofiled to date. Our objective was to characterize SCCOHT's immune landscape and to establish a rationale for using immunotherapies to treat SCCOHT patients.

Method: We measured the expression of PD-L1, CD3 (T cells), and CD68 (macrophages) with immunofluorescence in 11 SCCOHT patients. SMARCA4 mutation status in SCCOHT was confirmed by MSK-IMPACT and immunohistochemistry. Immune-related gene expression profiling was performed with NanoString's nCounter PanCancer Immunoprofiling panel.

Results: PD-L1 expression and T cell infiltration were detected in most tumors. PD-L1 expression was detected in both tumor and stromal cells. The majority of tumors were also infiltrated by macrophages. There was a strong association between T cell infiltration and PD-L1 expression. Gene expression profiling revealed that the high-PD-L1 group had increased PD-1 expression, as expected upon immune checkpoint activation. All immune cell types were elevated in the high- versus low-PD-L1 group, further demonstrating a correlation between PD-L1 upregulation and immune response. Cytolytic and antigen-presenting genes were also highly expressed in the high-PD-L1 group, suggesting an association between PD-L1 expression and high immune reactivity.

Conclusion: These data suggest that SCCOHT is an immunogenic malignancy with elevated PD-L1 expression and T cell infiltration. Our findings also highlight that mutational burden is not detrimental for tumor immunogenicity; SMARCA4 loss

alone may promote immune recognition of SCCOHT. Our work provides a strong rationale for evaluating immunotherapies in SCCOHT patients.

434 - Poster Session

A 16-year experience with early-stage uterine clear cell carcinoma: Are we overtreating?

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Objective: To evaluate clinicopathologic factors and adjuvant treatment effects on recurrence-free (RFS) and overall survival (OS) in early-stage uterine clear cell carcinoma (UCCC).

Method: This single-institution, retrospective review evaluates patients with stage I or II UCCC treated between January 2000 and May 2016. Central pathology review was performed, and cases of pure or mixed histology with >50% UCCC were included. Data were analyzed using the Kaplan-Meier method and Cox proportional hazards regressions. Stata/MP v15.0 (College Station, TX) was used for all analysis.

Results: A total of 112 patients were included. Median age was 65.5 years (range 34–94 years). Median follow-up was 3.8 years (range 0.28–22.14 years). Sixty percent ($n = 68$) had mixed UCCC, while 40% ($n = 44$) had pure UCCC. The majority had stage IA UCCC ($n = 73$, 66%) versus stage IB ($n = 17$, 15%) or stage II ($n = 20$, 18%). Most patients ($n = 68$, 60%) underwent lymph node assessment. Adjuvant treatment included chemotherapy (CT) + radiation (RT) ($n = 29$, 26%), vaginal brachytherapy (VBT) ($n = 30$, 27%), pelvic RT only ($n = 17$, 15%), and CT only ($n = 9$, 8%). There were 27 patients (24%) who received no adjuvant treatment and 38 (34%) who experienced recurrence, 75% distant and 25% pelvic. Median RFS was 4.32 years (95% CI 2.77–5.78). On multivariate analysis, age ≥ 70 (HR = 2.48, 95% CI 1.28–4.81, $P = 0.007$) and lymphovascular space invasion (LVSI) (HR = 2.19, 95% CI 1.15–4.18, $P = 0.010$) were associated with shorter RFS. Median OS was 9.8 years (95% CI 7.46–15.93). On multivariate analyses, age ≥ 70 years (HR = 3.57, 95% CI 1.64–7.74, $P = 0.001$) and LVSI (HR = 2.46, 95% CI 1.12–5.37, $P = 0.024$) were associated with shorter OS. Pure UCCC had a worse OS than mixed UCCC (HR = 2.41, 95% CI 1.28–4.55, $P = 0.007$). Stage and adjuvant therapy type were not associated with RFS or OS on univariate or multivariate analysis.

Conclusion: Although UCCC is an aggressive subtype of endometrial cancer, early-stage patients have an OS approaching 10 years, regardless of adjuvant treatment type. These findings suggest that only a subset of these patients may benefit from adjuvant therapy.

435 - Poster Session

Overall survival among American women with gestational trophoblastic neoplasia: A National Cancer Data Base study

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Objective: In the United States, where centralization of the initial management of gestational trophoblastic neoplasia (GTN) does not exist, outcomes may be suboptimal. We used the National Cancer Database (NCDB) to describe the real-world overall survival of American women with GTN.

Method: The 2004–2013 NCDB was queried for women with choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor using ICD-O-3 codes 9100, 9104, and 9105, respectively. Patient, disease, and treatment characteristics were described. Five-year survival estimates were calculated with the Kaplan-Meier method. Statistical analyses were performed in R using the survival package.

Results: Among 897 women with choriocarcinoma, median (IQR) age was 31 (25–38) years. Of the 52.2% (443/848) with stage III–IV disease, only 72.5% (321/443) initially received multiagent chemotherapy. Five-year survival (95% CI) was 96.8% (94.0%–99.0%) for stage I, 92.7% (83.0%–100%) for stage II, 79.5% (64.8–97.5%) for stage III, and 83.7% (80.0–87.6%) for stage IV. Among 46 women with placental site trophoblastic tumor, median (IQR) age was 30 (24–37) years. Surgery was omitted in 45.7% (21/46). Of the 54.3% (25/46) who had stage III–IV disease, only 56.0% (14/25) initially received multiagent chemotherapy. Five-year survival (95% CI) was 97.4 (92.6%–100%). Among 112 women with epithelioid trophoblastic tumor, median (IQR) age was 37 (29–43) years. Of the 37.0% (42/108) who had stage III–IV disease, only 61.9% (26/42) initially received multiagent chemotherapy. Five-year survival (95% CI) was 91.6% (82.9%–100%) for stage I disease

and 77.6% (65.2%–92.2%) for stage II–IV disease. Of all women, 90.1% (974/1,081) were reported by facilities with an average of less than 1 GTN case per year. Of all women who received any chemotherapy, only 16.2% (145/893) were referred to another facility for initial chemotherapy.

Conclusion: Most American women with a GTN received initial treatment at very-low-volume facilities that are not GTN referral centers. Compared to historical data reporting near 100% survival of women treated at GTN referral centers, American women with GTN have suboptimal survival. Requests for advice from or early referral to centers with expertise in the management of GTN prior to initiating therapy may increase survival of American women with GTN.

436 - Poster Session

Undifferentiated endometrioid carcinoma of the uterus: A National Cancer Data Base analysis of prognostic factors and treatment outcomes

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Objective: Undifferentiated endometrioid carcinoma (EC) of the uterus is a rare yet highly aggressive subtype of endometrioid EC. This study evaluates the incidence, prognostic factors, and treatment outcomes associated with undifferentiated EC.

Method: The National Cancer Database (NCDB) was queried to identify patients with undifferentiated EC who underwent definitive primary surgical treatment. Patients with nonendometrioid histology or incomplete treatment data were excluded. Recursive partitioning was used to determine cutoffs for age, tumor size, and identification of prognostic factors. Overall survival was measured from date of diagnosis. Univariate and multivariate analyses were used to determine independent prognostic factors using stepwise variable selection (with $P = 0.05$). Prognostic groups were defined by assigning points proportionate to the regression coefficients in the final model to each prognostic factor. Five-year survival was summarized using both stage and prognostic group combinations.

Results: Out of 349,404 women diagnosed with EC between 2004 and 2013, 3,994 (1.1%) met criteria for diagnosis of undifferentiated EC. The median age at diagnosis was 65 years (IQR 57–74). Fifty-eight percent of patients had early-stage disease. The median interval from diagnosis to surgery was 3.7 weeks (IQR 2.0–5.7). Adjuvant therapy was administered in 62% of patients. Five-year overall survival was $57\% \pm 1\%$. Stage was the strongest predictor of 5-year survival (with 15%–20% decrement in survival for each advance in stage). Stage, age, race, presence of comorbid conditions, and tumor size were independent predictors of survival and were used to categorize patients into prognostic groups (Figure 1). Adjuvant therapy was associated with improved survival across all disease stages and prognostic groups. Multimodal adjuvant therapy (chemotherapy and radiation therapy) was superior to unimodal adjuvant therapy particularly in advanced-stage, unfavorable and very unfavorable groups.

Conclusion: In women with undifferentiated EC, survival is primarily driven by stage, while age, race, comorbid conditions, and tumor size further modify outcomes. Despite the poor overall prognosis of undifferentiated EC, use of adjuvant chemotherapy and radiation therapy appears to extend survival particularly among patients with advanced disease and unfavorable prognosis.

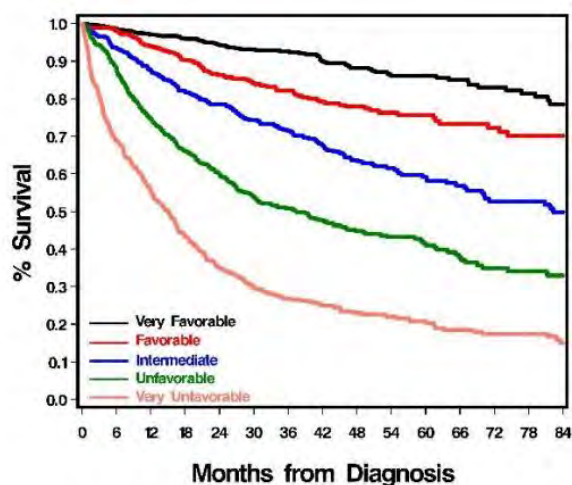


Fig. 1. 5-year overall survival based on prognostic groups in undifferentiated endometrioid endometrial carcinoma.

437 - Poster Session

Pediatric and adult dysgerminoma treatment disparities and associated outcomes: A National Cancer Data Base review

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Objective: Dysgerminomas account for less than 1% of all ovarian neoplasms in adults, but account for one-third of malignant neoplasms in adolescents. In adults, surgical staging with lymphadenectomy (LND) is recommended with rates of lymph node (LN) metastases reported as high as 28%. The approach in the pediatric population involves minimal surgery outside of removal of the primary tumor with removal of pathologic LN only. The objective of this study is to evaluate the disparity in surgical approach to dysgerminoma in adult and pediatric patients and assess factors associated with survival.

Method: The National Cancer Database was queried for all patients with ovarian dysgerminoma with complete staging information from 2004 to 2014. Overall survival (OS) was estimated by the Kaplan-Meier method; univariate comparisons were made with log-rank tests; and multivariate 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 1,206 patients were identified of whom 306 were pediatric (younger than 18 years) and 900 were adults. Survival was favorable for both groups, but worse in adults compared to pediatric (5 -year OS 94.2% vs 97.8%, $P = 0.032$). LND was performed in 54.9% of the pediatric and 69% of the adult cases ($P < 0.001$). Positive LNs were 28% for the cohort, similar to prior reports, with a high rate at apparently clinically stage I disease (1A, 14.5%; IB, 16.1%; IC, 19.7%; II, 42.7%; and III, 84.5%, $P < 0.001$). Clinicopathologic factors were otherwise similar for the both groups. Stage-specific survival was high except for stage IV disease (5-year OS: I, 97.5%; II, 95.8%; III, 93.8%; and IV, 70.4%, $P < 0.001$). On univariate analysis, increasing age, African-American ethnicity, lower income, less education, rural setting, not performing LND, and stage were associated with worse survival. On multivariate analysis, only African-American ethnicity, poor education, LN positivity, and stage had an impact on survival.

Conclusion: Stage and LN positivity have an impact on survival. With the high rate of LN metastases in all stages, lymphadenectomy should be considered part of the surgical approach as a diagnostic role to guide initial therapy.

438 - Poster Session

Central nervous system metastasis from endometrial carcinoma: A multi-institution retrospective study

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Objective: Central nervous system metastasis (CNSm) secondary to endometrial cancer (EC) is rare. As a result, data in this population are limited. In this study we evaluated the relevant clinical outcomes in patients with CNSm from EC.

Methods: Following institutional review board approval at participating institutions, hospital databases were searched to identify all patients with a diagnosis of EC and CNSm. A total of 27 patients were identified, and clinical data were retrospectively collected. Univariate analysis and log rank test were used for statistical analysis.

Results: Median age at diagnosis of EC was 58 (37–69) years. Stage at diagnosis was IV (48.2%), III (33.3%), II (11.1%), and I (3.7%). Histologic grade was 3 (74.1%), 2 (18.5%), and 1 (14.8%). Histologic types included endometrioid (77.8%), serous (44.4%), and clear cell (7.4%). Initial treatment included surgery (55.6%) or chemotherapy (37%). Of lymph nodes (LN) sampled, 42.9% of pelvic LN were positive and 41.7% of paraaortic LN were positive. Lymphovascular space invasion was present in 47.4%. Median interval between primary treatment and diagnosis of CNSm was 19.5 months (0–144). Symptoms of CNSm included headache (33.3%), altered mental status (18.5%), weakness or numbness (14.8%), nausea or vomiting (11.1%), unsteady gait (7.4%), and dysphagia (7.4%). The number of CNSm was >5 in 18.5% and ≤ 5 in 70.4%. Location of CNSm included cerebrum (74.1%), cerebellum (33.3%), and meninges (7.4%). Treatment for CNSm included radiation alone (48.2%), resection and radiation (14.8%), and resection alone (7.4%), or followed by placement of chemotherapy wafers

(3.7%). Median survival following CNSm was 5 months (0–144), while 2-year survival was 17%. Median survival with more than CNSm was 5 months, compared to 38 months with 5 or fewer CNSm ($P < 0.01$)

Conclusion: The majority of CNSm due to EC occurred in patients with advanced-stage and high-grade tumors. Although survival after CNSm was highly variable, presence of more than 5 CNSm significantly correlated with reduced survival. Our findings may have prognostic and therapeutic implications and require additional studies.

439 - Poster Session

Hormonal therapy for low-grade endometrial stromal sarcoma

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Objective: To better understand outcomes for patients treated with aromatase inhibitors (AI) or progestins as adjuvant therapy for low-grade endometrial stromal sarcomas (LGEES).

Method: We performed a single-institution retrospective review of LGEES cases from 1984 to 2017. Data were collected on patient demographics, surgical procedures, and type of adjuvant hormonal therapy (HT) administered. Rates of disease recurrence and recurrence-free survival (RFS) were assessed among patients who received AI, progestins, or no adjuvant HT.

Results: Among 39 patients with LGEES identified during the study period, 18 received progestins (megestrol acetate), 13 received AI (anastrozole), and 8 received no HT. Median age at diagnosis was 48 (range 19–76) years. Hysterectomy was performed in all patients. Thirty (76.9%) patients had stage I disease at the time of diagnosis, while 9 (23.1%) had stage II–IV disease. Seventy percent (7/10) of stage I patients who received no adjuvant HT had disease recurrence, compared with 14.3% (1/7) receiving AI, and 7.7% (1/13) receiving progestins ($P = 0.003$). In stage I patients who received AI, the mean RFS was 153.1 months (95% CI 110–195.6), compared with 306.2 months (95% CI 259.7–352.6) for the progestin group and 90.8 months (95% CI 56.8–124.9) for those who received no adjuvant HT. In stage II–IV patients who received AI, the mean RFS was 148.5 months (95% CI 148.5–148.5), compared with 120.8 months (95% CI 55.8–185.9) for the progestin group. All patients with stage I–IV disease received adjuvant HT. Among stage I patients, median follow-up time for RFS was 159.1 months for the progestin group, 52.6 months for the AI group, and 53.1 months for this who received no adjuvant therapy. Sixty-nine percent (9/13) of stage I patients taking progestins reduced or stopped the medication prematurely because of side effects. None of the 7 stage I patients taking AI discontinued the medication early.

Conclusion: HT is effective adjuvant treatment for the initial management of LGEES. AI and progestins are associated with low rates of disease recurrence and favorable RFS among stage I patients. AI is associated with decreased risk of recurrence in patients with advanced-stage or recurrent disease. Furthermore, AI is better tolerated and should be considered as primary adjuvant HT in all patients with LGEES.

440 - Poster Session

Paired tumor/germline testing for Lynch syndrome in endometrial cancers: A comprehensive testing approach

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Objectives: National guidelines recommend that all newly diagnosed endometrial cancers be universally screened for Lynch syndrome using microsatellite instability (MSI) or immunohistochemistry (IHC) analysis. In the absence of *MLH1* promoter hypermethylation or an identifiable germline mismatch repair (MMR) mutation, individuals with abnormal MSI or IHC have been managed as though they have Lynch syndrome. Recent data have shown that somatic analysis of the MMR genes in endometrial cancers may rule out Lynch syndrome in most cases. This study aimed to describe a new testing model for Lynch syndrome, whereby tumor and germline analyses are run concurrently (i.e., paired testing).

Method: A retrospective analysis was performed on data from endometrial cancer patients with abnormal IHC who underwent paired tumor/germline Lynch syndrome testing. Results of sequencing and deletion/duplication analyses of the MMR genes and *EPCAM* (del/dup only) in both tumor and germline DNA were assessed. Additional test results, including *MLH1* promoter hypermethylation testing and microsatellite instability (MSI) analysis, were evaluated when available.

Results: In total, 68 cases were included (Table 1). Fifty-three cases (78%) were informative, including 27 (40%) with double somatic alterations, 15 (22%) with germline MMR mutations, 9 (13%) with *MLH1* promoter hypermethylation alone, and 2 (3%) with likely false positive IHC results (no somatic alterations were found and MSI was stable). Fifteen (22%) of the original 68 cases were uninformative and had either 1 somatic mutation (9%) or no alterations in the tumor (13%).

Conclusion: Paired testing of both tumor and germline DNA provided an explanation for the MMR deficient endometrial cancers in 78% of cases. In this cohort, 56% of cases would have remained unexplained without the somatic testing of the Lynch syndrome genes. Adding tumor gene analysis to the testing algorithm allows for potential exclusion of Lynch syndrome and reduces the likelihood of discordant results. Combining both tumor and germline analyses reduces the number of steps needed for Lynch syndrome testing, while also providing clinicians with more comprehensive answers, which can then be used to further tailor treatment and surveillance for each patient.

Table 1. Case Details and Results.

	<i>n</i>	% Total
Total cases	68	100%
No previous germline testing	52	76%
Previous germline testing	16	24%
Meets Bethesda guidelines	9	13%
Meets Amsterdam criteria II	3	4%
Average age of cancer diagnosis in years	59	
Informative cases	53	78%
-Double somatic alterations	27	40%
-Germline mutation	15	22%
- <i>MLH1</i> promoter hypermethylation only	9	13%
-False positive IHC (no hits and MSS)	2	3%
Uninformative cases	15	22%
-One somatic mutation	6	9%
-No somatic or germline alterations	9	13%

441 - Poster Session

Vulvar sarcoma subtype influences outcome and behavior: A surveillance epidemiology and end results database review

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Objective: To identify clinical and pathologic factors associated with improved survival in patients with vulvar sarcoma and to compare outcomes between vulvar sarcoma and vulvar squamous cell carcinoma (SCC).

Method: The Surveillance, Epidemiology, and End Results (SEER) database was queried from 1973 to 2014 to identify all women with vulvar cancer. A total of 13,211 cases of SCC and 284 cases of vulvar sarcoma were identified. Demographic, clinicopathologic, surgical, and survival data were reviewed. The primary endpoint was 5-year disease-specific survival (DSS).

Result: Of the vulvar sarcoma cases, the most common histopathology was fibrosarcoma (34.8%), followed by leiomyosarcoma (24.6%), sarcoma of uncertain differentiation (22.9%), liposarcoma (5.3%), malignant fibrous histiocytoma (MFH, 5.3%), vascular sarcoma (3.5%), rhabdosarcoma (2.8%), and chondro-osseous sarcoma (0.7%). The majority of patients were treated with surgery (93.7%), with 23.5% undergoing groin lymph node (LN) dissection. Compared to women with vulvar SCC, women with vulvar sarcoma were younger (47.9 vs 66.4 years, $P < 0.001$), more likely to have a larger lesion (46.8 vs 31.3 mm, $P < 0.001$), and more likely to have high-grade disease (45% vs 19%, $P < 0.001$). Univariate analysis found a 73% 5-year DSS for SCC; 5-year DSS for vulvar sarcoma was 86%. However, the survival rate varied significantly with histologic subtype. Women with liposarcoma and fibrosarcoma had a 99% 5-year DSS, whereas women with MFH and rhabdosarcoma had survival rates of 57% and 54%, respectively. Within the sarcoma group none of the liposarcomas,

fibrosarcomas, or leiomyosarcomas had positive LNs, while rhabdosarcomas, sarcomas of uncertain differentiation, and MFH were more likely to have positive LNs (50%, 25%, and 26.2% respectively, $P < 0.001$). The 5-year DSS for women with positive LNs and vulvar sarcoma was 25%, compared to 45% for women with SCC.

Conclusion: Vulvar sarcomas are a varied group of malignancies with survival outcomes dependent on histopathology subgroup. Surgical excision is the mainstay of therapy, and regional lymphadenectomy should be considered for rhabdosarcomas, MFH, and sarcomas of uncertain differentiation, but can safely be omitted for fibrosarcomas, liposarcomas, and leiomyosarcomas.

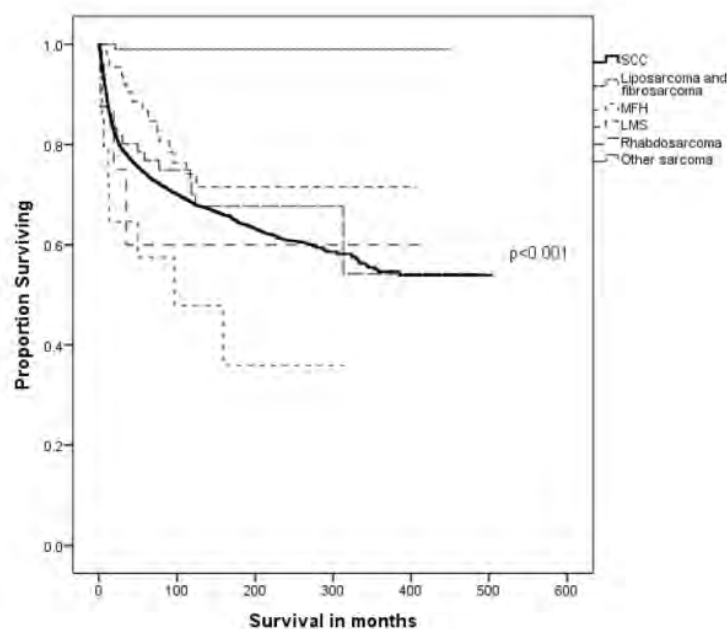


Fig. 1. Survival Curve for Vulvar Squamous Cell Carcinoma and Sarcomas, broken down by Histologic Sub-type. Abbreviations: SCC: squamous cell carcinoma, MFH: malignant fibrous histiocytoma, LMS: leiomyosarcoma.

442 - Poster Session

Placental site trophoblastic tumor: Successful treatment of 14 cases

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Objective: To review and describe the presentations, treatment, and outcomes of patients with placental site trophoblastic tumor (PSTT).

Method: We reviewed pathology and records for 14 patients with a pathologic confirmed diagnosis of PSTT referred to a trophoblastic disease center between 2003 and 2017. Patient history, laboratory values, operative reports, and pathology results were reviewed. Data collected included age, year of diagnosis, presenting symptoms, human chorionic gonadotropin (hCG) levels, type of antecedent pregnancy, FIGO stage at diagnosis, treatments, response to treatments, and length of survival.

Results: The mean age of patients was 33 (range 22–46) years. The most frequent presenting symptom was vaginal bleeding (64%). A mass was seen on ultrasound in 7 (50%) of patients. The antecedent pregnancies were normal term pregnancy ($n = 9$, 65%), elective or spontaneous abortion ($n = 3$, 21%), molar pregnancy ($n = 2$, 14%), and third trimester loss ($n = 1$, 7%). The median time from antecedent pregnancy to diagnosis was 12 (range 0–240) months. Serum hCG levels ranged from 1 to 2,606 mIU/mL with a median of 90. Most patients presented as FIGO stage I (11/14, 79%) with 1 of 14 patients FIGO stage II (7%) and 2 of 14 patients FIGO stage III (14%). All patients underwent surgery: 1 (7%) had fertility-preserving surgery (D&C), 13 (93%) underwent hysterectomy, 9 (65%) had bilateral salpingo-oophorectomy, 5 (36%) underwent pelvic lymph node dissection, and 1 (7%) had a VATS for pulmonary metastasis. Ten patients (72%) received chemotherapy for persistently elevated hCG levels (3), high-risk features (4), or metastatic disease (3), most commonly EMA/EP as initial therapy (8/10). Three patients received multiple lines of chemotherapy. No patient had a recurrence. No patients were known to be deceased with a median survival of 62.5 (range 10–167) months.

Conclusion: Complete surgical resection and multidrug platinum-containing chemotherapy, most commonly EMA-EP, given for high-risk features or metastatic disease is effective treatment of PSTT, yielding a remission rate of 100% in the present series.

443 - Poster Session

Does MMR status in endometrial cancer influence response to adjuvant therapy?

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Objective: Mismatch repair (MMR) deficiency occurs in 20–40% of endometrial cancers, but its therapeutic implication remains uncertain. Our objective was to compare recurrence rates after adjuvant therapy between MMR-deficient and -proficient endometrial cancers from a population-based study.

Method: The demographic, clinicopathological, treatment, and outcome data (with a minimum 2-year follow-up) were extracted from all cases of endometrial cancer tested for MMR deficiency from 2011 to 2017 in the Vancouver Coastal Health authority region. *P* values were calculated from Wilcoxon rank sum tests for continuous variables and Fisher exact tests for categorical variables. Patients were also stratified as having type 1 or 2 cancers.

Results: There were 461 patients who received adjuvant therapy (pelvic radiotherapy, chemotherapy, or both), including 138 (30%) and 323 (70%) with MMR-deficient and -proficient tumors, respectively. Demographic variables were similar between the two groups except MMR-deficient patients were younger (63 vs 65 years, *P* = 0.011). MMR-deficient patients had a lower proportion of type 2 cancers (19.6% vs 38.4%) but a higher proportion with LVSI (60.9% vs 51.7%) compared to MMR-proficient patients. Stage distributions were similar. Overall crude recurrence rates were 15.9% and 24.1% for MMR-deficient and -proficient tumors, respectively (*P* = 0.064). Among those with high-grade serous carcinomas, recurrence rates were 7.7% and 27.3% for MMR-deficient and -proficient, respectively.

Conclusion: Despite similar stage distributions and adjuvant therapy, women with MMR-deficient endometrial cancers may have a lower rate of recurrence compared to those with MMR-proficient cancers, suggesting that MMR status may influence response to treatment.

444 - Poster Session

Use of porphyrins for accurate intraoperative detection of lymph node metastases in an endometrial cancer model

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Objective: To establish the accuracy of intraoperative Porphyrin fluorescence image-guided resection (PYRO-FGR) for the detection of uterine tumour, metastatic lymph nodes, and abdominal metastases in a model of endometrial cancer.

Method: Rabbits were inoculated with VX2 cells via intramyometrial injection. At 30 days, Porphyrins were administered intravenously. At 24 hr the abdomen was imaged with a 675-nm fluorescence endoscope. Fluorescent tissue was resected under image guidance (PYRO-FGR). Complete pelvic and paraaortic lymphadenectomies were performed after confirming remaining lymph node tissue was fluorescence-negative. All resected tissue was examined for tumour. All pathology specimens were read by a gynecologic pathologist, and histopathology including ultrastaging was used to detect VX2 cells in fluorescent tissue. Fluorescence signal-to-background intensity ratio (SBR) was calculated, and VX2 (+) tissue compared to VX2 (–) tissue. Biodistribution was calculated, and fluorescent VX2 (+) tissue compared to fluorescent VX2 (–) and nonfluorescent VX2 (–) tissue.

Results: Eight VX2 rabbits and 2 controls were used. Eight tumours, 19 lymph nodes, and 27 abdominal metastases were fluorescence-positive on PYRO-FGR and resected (Figure 1). Of these, 8 tumours, 15 lymph nodes, and 22 abdominal metastases were VX2 (+) and 2 lymph nodes and 1 abdominal metastases were VX2 (–). Six specimens were unable to be completely assessed and were removed from analysis. Eleven negative lymph nodes were identified in the lymphadenectomy specimens, which were all fluorescence-negative. No tumour was identified on histopathology that was not fluorescent intraoperatively. Control rabbits had negative fluorescence in all lymph node basins and low uterine fluorescence. Sensitivity and specificity of PYRO-FGR for VX2 (+) tissue based on current limited samples were 100%/79% for all tissue, 100%/100%

for uterine tumour, 100%/85% for lymph nodes and 100%/92% for abdominal metastases, respectively. Increased SBR was seen in all VX2 (+) tissue ($P = 0.003$), lymph nodes ($P = 0.006$), and abdominal metastases ($P = 0.007$). Increased Porphysome uptake was seen in all fluorescent VX2 (+) tissue including tumour ($P = <0.001$), lymph nodes ($P = \text{n/a}$, 1 (-) lymph node), and abdominal metastases ($P = 0.018$).

Conclusion: Porphysomes are an intravenously administered agent that allows for accurate intraoperative detection of uterine tumour, metastatic lymph nodes, and abdominal metastases using fluorescence in a model of endometrial cancer.

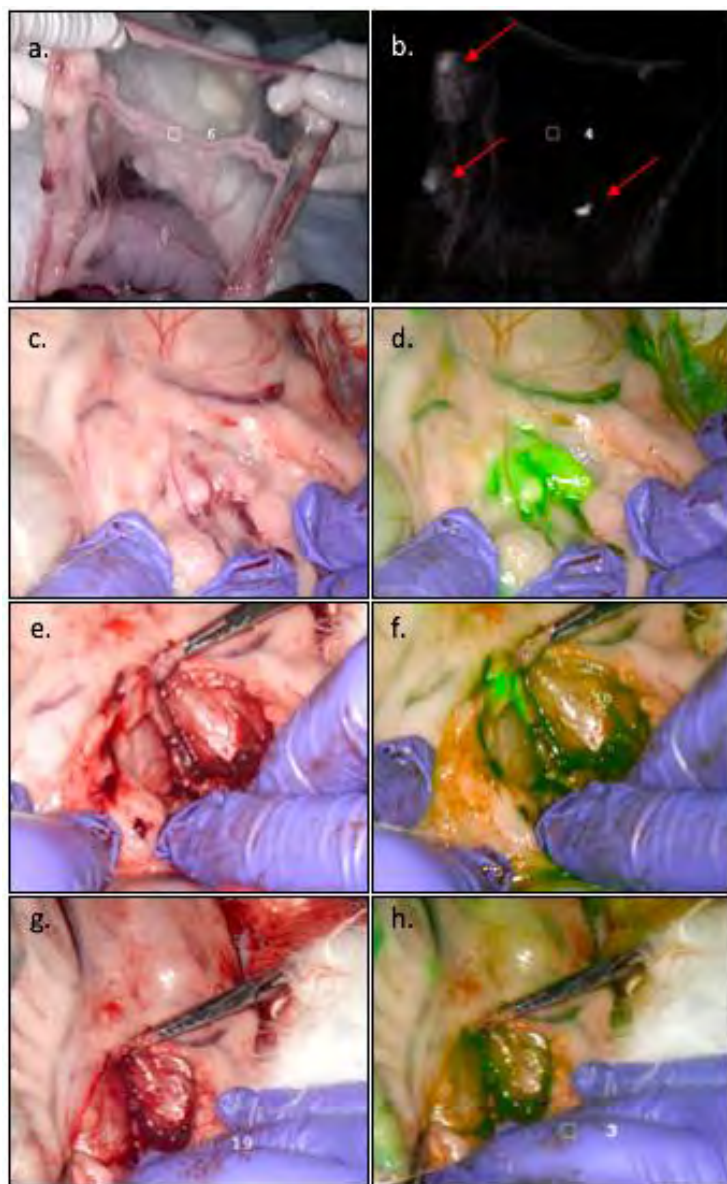


Fig. 1. Intra-operative Porphysome fluorescence image-guided resection (PYRO-FGR) **a.** Rabbit 11: Omentum, white light **b.** Rabbit 11: Omentum, 675 nm fluorescence grey scale filter identifying omental metastases (bright white, arrows) **c.** Rabbit 9: Left pelvic lymph nodes, white light **d.** Rabbit 9: Left pelvic lymph nodes, 675 nm fluorescence green filter identifying VX2+ metastatic lymph nodes **e.** Rabbit 9: VX2+ metastatic left pelvic lymph nodes, white light, initial resection **f.** Rabbit 9: VX2+ metastatic left pelvic lymph nodes, 675 nm fluorescence green filter, initial resection demonstrating remaining tumour (bright green) **g.** Rabbit 9: VX2+ metastatic left pelvic lymph nodes, white light, complete resection **h.** Rabbit 9: VX2+ metastatic left pelvic lymph nodes, 675 nm fluorescence green filter, complete resection confirmed.

445 - Poster Session

Trends in performance of sentinel lymph node mapping and its association with use of adjuvant therapy for women with uterine cancer

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Objective: Sentinel lymph node (SLN) mapping has been proposed as an alternative to lymphadenectomy for women with uterine cancer. We performed a population-based analysis to determine the utilization and predictors of SLN mapping and to examine whether use of SLN mapping was associated with changes in the prescription of adjuvant therapy for women with early-stage tumors.

Method: The National Cancer Data Base was used to identify women with uterine cancer who underwent hysterectomy in 2013–2014. Patients were stratified based on whether they underwent SLN mapping, lymphadenectomy, or no nodal assessment. Multivariable regression models were developed to determine factors associated with performance of SLN biopsy and to examine whether SLN biopsy was associated with receipt of adjuvant radiotherapy.

Results: A total of 54,039 women, including 38,453 (71.2%) who underwent lymphadenectomy, 1,929 patients (3.6%) who underwent SLN, and 13,657 (25.3%) who did not undergo nodal assessment, were identified. In 2013, 2.8% underwent SLN biopsy, while 4.3% of those in 2014 underwent SLN biopsy ($P < 0.001$). For those who had SLN mapping, 863 (45.4%) underwent only SLN biopsy, while 1,038 (54.6%) underwent concurrent lymphadenectomy. The median number of lymph nodes removed was 3 (IQR 2–4) in those who underwent SLN biopsy alone and 14 (IQR 9–21) in patients who had a concurrent nodal dissection. Among women who underwent nodal assessment, patients treated in 2014 were 60% more likely to undergo SLN biopsy than those in 2013 (aRR = 1.60, 95% CI 1.46–1.76), while those treated at a community cancer center were 72% more likely to undergo SLN biopsy than those treated at an academic center (aRR = 1.72, 95% CI 1.04–2.86). In contrast, women with more advanced stage disease, sarcomas, or carcinosarcomas and those with grade 3 tumors were less likely to undergo SLN biopsy ($P < 0.05$ for all). Among women with stage I tumors who underwent nodal assessment, there was no association between SLN biopsy (compared to lymphadenectomy) and use of radiation (aRR = 0.92, 95% CI 0.82–1.05).

Conclusion: Use of SLN biopsy for women with uterine cancer is increasing. A number of clinical and nonclinical factors contribute to uptake of SLN biopsy. Performance of SLN biopsy in lieu of lymphadenectomy is not associated with a higher rate of use of adjuvant radiation.

446 - Poster Session

A retrospective comparison of oral rivaroxaban versus subcutaneous low-molecular-weight heparin for postoperative thromboprophylaxis in women with a gynecologic malignancy

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Objective: To compare the incidence of postoperative venous thromboembolism (VTE) among women with a gynecologic malignancy who received oral rivaroxaban versus subcutaneous low-molecular-weight heparin (LMWH) as thromboprophylaxis.

Method: A retrospective study was conducted of women, without prior history of VTE, who underwent a laparotomy or minimally invasive surgery for gynecologic malignancies at our institution from 2010 through 2015 and received postoperative pharmacologic thromboprophylaxis with either rivaroxaban or LMWH. Baseline demographic characteristics, cancer type, surgical approach, method and duration of VTE prophylaxis, occurrence of bleeding complications, and occurrence of VTE were abstracted by chart review. The primary outcome was incidence of VTE within 90 days of surgery. The Fisher exact test was used to compare the incidence of VTE in each treatment group. Descriptive statistics, including χ^2 and univariate ANOVA, were used to compare secondary outcomes such as bleeding complications, surgical approach, and cancer type. A multiple logistic regression model was implemented to explore whether any of these variables had an effect on VTE rate.

Results: A total of 598 women were included, of which 147 received rivaroxaban and 451 received LMWH. Baseline demographic characteristics were well balanced between the two groups. Of the 598 patients, 12 (2.01%) developed a VTE within 90 days of surgery. Of 147 patients, 1 (0.68%) experienced a VTE in the rivaroxaban arm, compared with 11 of 451 patients (2.43%) in the LMWH arm. The 90-day incidence of VTE was not significantly different ($P = 0.31$, OR = 0.27) between the rivaroxaban arm and the LMWH arm. On multiple logistic regression analysis, the type of pharmacologic thromboprophylaxis did not have a significant effect on VTE rate. There was no difference in bleeding events requiring hospital admission between groups (2.04% with rivaroxaban compared to 0.67% with LMWH, $P = 0.32$).

Conclusion: In this retrospective analysis, we found no significant difference between rivaroxaban and LMWH upon the incidence of VTE in patients following surgery for a gynecologic malignancy.

447 - Poster Session

Diagnostic effectiveness of sentinel lymph node mapping (SLNM): Comparison with MRI, PET/CT in early cervical and endometrial cancer

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Objective: To substantiate the usefulness of sentinel lymph node mapping (SLNM) with indocyanine green (ICG) compared to preoperative imaging tools such as magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT) in early cervical and endometrial cancer.

Method: We reviewed 203 patients with early-stage cervical and endometrial cancer who underwent laparoscopic or robotic surgery with SLNM between August 1, 2015, and April 30, 2017. All patients underwent preoperative MRI and/or PET/CT, and lymphadenectomy was performed during surgery. The diagnostic exactness of MRI, PET/CT, and SLNM was evaluated with the McNemar test and logistic regression using generalized estimating equation.

Results: All patients had SLNM of at least 1 hemipelvis. Lymph nodes metastasis on permanent biopsy were found in 33 patients, and SLNM was found metastasis in 31 patients. There was no significant difference in sensitivity (45.5% vs 45.5%, $P > 0.99$), specificity (91.0% vs 92.8%, $P > 0.99$), accuracy (83.5% vs 85.0%, $P > 0.99$), positive predictive value (PPV, 50.0% vs 55.6%, $P > 0.99$), and negative predictive value (NPV) (89.4% vs 89.6%, $P > 0.99$) of MRI and PET/CT. SLNM values were more accurate at sensitivity (93.9%), specificity (99.4%), accuracy (98.5%), PPV (96.9%), and NPV (98.8%), and statistical significance was shown at all values ($P < 0.05$). In SLNM in hemipelvis, sensitivity, specificity, accuracy, PPV, and NPV were also more accurate than MRI and PET/CT.

Conclusion: SLNM using ICG is the most compatible and best way to evaluate lymph node status before conventional lymphadenectomy in early-stage cervical and endometrial cancer.

448 - Poster Session

Neoadjuvant radiotherapy and brachytherapy in endometrial cancer with gross cervical involvement: A Chirendo research group study

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Objective: Historically, radical hysterectomy followed by tailored adjuvant radiation therapy has been offered to some patients with endometrial cancer who have gross cervical involvement; however, this approach is known to carry considerable morbidity. Neoadjuvant radiation therapy followed by extrafascial hysterectomy has been proposed as an alternative treatment but has been poorly studied to date. The objective of this study is to evaluate the outcomes associated with this therapeutic strategy.

Method: A retrospective cohort study of 30 endometrial cancer patients with gross cervical involvement treated between 2006 and 2016 was carried out. Treatment protocol consisted of neoadjuvant pelvic radiation therapy and high-dose rate brachytherapy followed by interval extrafascial hysterectomy. Descriptive analyses were performed and Kaplan-Meier curves used for overall and disease-free survival data.

Results: Twenty percent of the patients were classified as clinical stage IIIB, and 43% had suspicious lymph nodes at time of diagnosis. Thirteen percent had extended-field radiation therapy, and 37% had adjuvant chemotherapy. Median follow-up time was 4 years. Ten percent had grade 3 radiation-related complications; no grade 4–5 complications were noted. On surgical specimen, 66% and 77% had a complete cervical and nodal response, respectively. Margins were negative in 93% of cases. Twenty-one percent of surgeries were done by minimal invasive technique. Grade 3–4 surgical morbidity was noted in 6.9% of cases. Five recurrences were identified, all of which had distant failure and one of which had concomitant local failure. Five-year overall survival and disease-free survival were 96.0% and 86.7%, respectively.

Conclusion: Neoadjuvant radiation therapy and brachytherapy followed by extrafascial hysterectomy offer excellent clinical and survival outcomes with low treatment-related morbidity.

449 - Poster Session

Tubal ligation and risk of highly fatal ovarian cancer: Evidence from the Ovarian Cancer Association Consortium

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Objective: While tubal ligation has been established as a protective factor for ovarian cancer, its role in the etiology of highly fatal disease has yet been determined. To assess whether tubal ligation may play a role in the duration of survival following diagnosis, we examined the association between prediagnostic tubal ligation and highly fatal ovarian cancer.

Method: Data were pooled from 12 case-control studies participating in the Ovarian Cancer Association Consortium to examine the association between prior tubal ligation and death within 18 months of diagnosis. Survival at 12- and 18-months postdiagnosis was assessed using conditional logistic regression frequency matched on 5-year age categories, interview year, and study region. The study samples included 653 patients who died within 12 months of their diagnosis matched to 2,348 controls, as well as 1,382 patients who died within 18 months matched to 4,955 controls. Age at menarche, menopausal status, prior hysterectomy, age of last pregnancy, number of full-term births, breastfeeding, family history of ovarian cancer, and hormone therapy use were also assessed as potential confounders and/or modifiers of this association.

Results: Tubal ligation was associated with a 32% reduction in the odds of death at 18 months (OR = 0.68, 95% CI 0.55–0.85) after adjusting for age, race, education, total years of oral contraceptives, and number of full-term births. We also observed increased odds for increasing age (OR = 1.07, 95% CI 1.03–1.12) and reduced odds with increasing years of oral contraceptive (P trend < 0.0001) and number of full-term births (P trend < 0.0001). There was no significant association observed with race. Similar trends were observed at 12 months; however, these findings were not significant (OR = 0.91, 95% CI 0.69–1.20).

Conclusion: To our knowledge, this is the first large, multicenter study to investigate the association between tubal ligation and risk of highly fatal ovarian cancer. These results support the current evidence of the protective effect of tubal ligation not only in the general population of ovarian cancer patients, but also for patients with highly fatal disease. Future pooled analyses should aim at replicating these findings and consider histological subtypes.

450 - Poster Session

Use of a web-based app to improve postoperative outcomes for patients receiving gynecological oncology care: A pilot randomized controlled trial

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Objective: Nearly 1 in 5 patients hospitalized for ovarian cancer surgery are readmitted within 30 days of discharge, thereby increasing 1-year mortality by at least 50%. However, some readmission may be avoided with more intensive symptom-monitoring and patient-provider communication after surgery. We conducted a randomized pilot trial to test the acceptability and feasibility of a postoperative web-based app intervention to provide real-time symptom-monitoring and improve postdischarge quality of life among ovarian cancer patients.

Method: Participants were randomized into two groups: (1) App+Reminder: had access to the app, and use was encouraged with daily and/or weekly reminders; and (2) App: had access to the app but received no reminders. The app reminded patients of their discharge instructions and asked about their symptoms. Patients' self-reported health information via the app was integrated into their electronic health records. Outcomes above a predetermined threshold triggered alerts to inform the patient's care team of trends that may need medical intervention. Eligibility included adult female patients treated at a comprehensive cancer center in Memphis, Tennessee, diagnosed or with suspected gynecological cancer who had open bilateral salpingo-oophorectomy surgery. All participants completed a questionnaire at baseline and follow-up after 4 weeks. Quality of life was measured using the SF-12. In-depth interviews were conducted to gather participant feedback.

Results: We enrolled 24 patients. Participants in the App+Reminder group had more frequent app use than the App group (P = 0.05). Using differences-in-differences (DID) analysis for quality of life, we found a relatively higher increase in the mental health composite score for the App+Reminder group (DID = 7.51, P = 0.15), but a relative decrease in the physical composite

score (DID = -7.49, $P = 0.13$). Patients reported favorable opinions of the app and reminders; weekly reminders were preferable to daily ones.

Conclusion: We found mixed results for an ovarian cancer postoperative intervention using a web-based app, promising trends for improving mental health but discouraging trends for physical health. Still, the pilot established feasibility, acceptability, and some potential benefits of a new intervention for gynecological oncology care.

451 - Poster Session

Clinical trial participation may improve survival in patients with advanced epithelial ovarian, fallopian, and peritoneal malignancies

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Objective: Our objective was to evaluate the effect of clinical trial participation on overall survival (OS) in patients with epithelial ovarian, fallopian tube, and peritoneal cancer (EOC).

Methods: An institutional review board-approved, retrospective study identified patients diagnosed with advanced or recurrent EOC between January 2004 and June 2017 who received surgery and chemotherapy at a single institution. Number of clinical trials and OS were calculated. The χ^2 , Wilcoxon, and log rank tests were used to calculate significance ($P < 0.05$).

Results: We included 236 patients with stage 3 or 4 primary or recurrent EOC with complete follow-up data. Patients were divided into two groups based on clinical trial enrollment: (1) clinical trial participants ($n = 145$) and (2) patients never treated on a trial ($n = 91$). In group 1, 94 were enrolled in 1 trial, while 51 were treated in more than 1 trial over the course of treatments. The groups were similar in age (mean 68.8 vs 68.3 years), ethnicity (75.9% vs 74.7% white), histology (87.5% vs 91.2% serous), and grade (92.4 % vs 87.9% grade 3) ($P = NS$). Median OS for trial versus nontrial patients was 52.8 months vs. 36.0 months, respectively (Wilcoxon, $P = 0.0195$; log rank, $P = 0.5146$). Clinical trial participants had improved survival during the first 5 years of treatment compared to nontrial patients (Wilcoxon, $P = 0.0011$; log rank, $P = 0.0211$; Figure 1A). In addition, those who participated in more than one clinical trial versus those who participated in a single trial had significantly improved survival rates during the first 5 years of treatment (Wilcoxon, $P = 0.0008$; log rank, $P = 0.0281$; Figure 1B).

Conclusion: This study demonstrates a survival benefit to patients with EOC treated on clinical trials. While we did not stratify for front-line versus recurrent clinical trials or positive versus negative studies, it appears that increasing clinical trial participation for patients with EOC may improve survival regardless of the study outcomes.

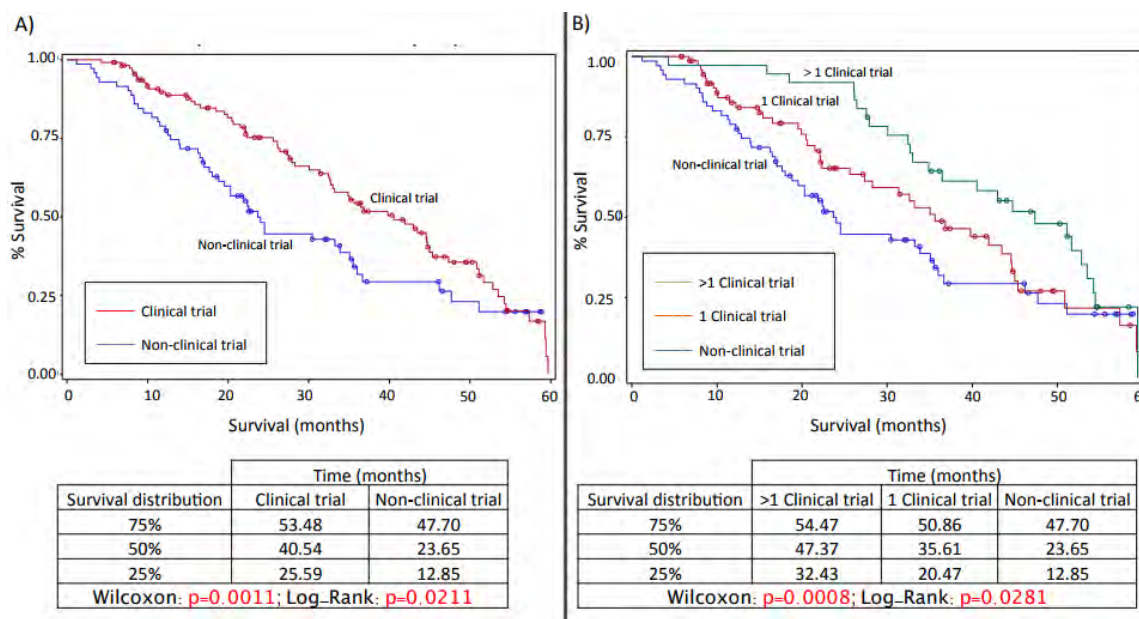


Fig. 1. 5-year survival distribution based on clinical trial participation (A) and number of clinical trials participated in (B). Clinical trial participants had a significantly improved 5-year survival distribution compared to those that did not participate (40.54 vs. 23.65 months; Wilcoxon: $P = 0.0011$; Log-Rank: $P = 0.0211$). Additionally, patients that participated in >1 clinical trial had significantly improved 5-year survival distribution compared to those that participated in a single clinical trial (47.37 vs. 35.61 months; Wilcoxon: $P = 0.0008$; Log-Rank: $P = 0.0281$).

452 - Poster Session

Variation in adjuvant therapy for stage II serous uterine cancer in the United States and its impact on survival outcome

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Objective: We sought to determine the patterns of adjuvant treatment received by women with stage II serous uterine cancer in the United States and to evaluate the impact of these variations on overall survival.

Method: The Medicare and Surveillance, Epidemiology, and End Results (SEER) database was used to identify women 65 years or older diagnosed with stage II uterine cancer from 1999 to 2011 who underwent primary surgical management via hysterectomy. Exclusion criteria included more than 1 primary cancer, history of end-stage renal disease/dialysis, and lack of activity in Medicare 1 year pre- and postdiagnosis. Adjuvant therapy including radiation (RT), chemotherapy, and sequence were collected. Demographics, surgical staging, pathology, and survival outcomes were collected. Descriptive statistics, Kaplan-Meier curves, and Cox models were used for analyses.

Results: A large portion of women with stage II serous uterine carcinoma ($n = 106$) received no adjuvant therapy 37% ($n = 39$). A large portion of the remaining women received RT alone (26%, $n = 28$) or chemotherapy alone (24%, $n = 25$). For the remaining patients, therapy included 3.8% ($n = 4$) concurrent chemotherapy and RT; 0.9% ($n = 1$) RT followed by chemotherapy; 6.6% ($n = 7$) chemotherapy followed by RT; and 1.9% ($n = 2$) sandwich chemotherapy-RT-chemotherapy. Factors associated with not receiving adjuvant treatment included old age (64% untreated age older than 80 years versus 30% age 70–79 years and 29% age 40–69 years, $P < 0.001$), higher income (50% untreated if more than \$75,000 compared to 37% if \$55,000–\$75,000, 24% if \$40,000–\$55,000, and 39% if less than \$40,000), and region (53% untreated in the West compared to 32% Northeast, 21% Midwest, and 31% South). Marital status, race, Charlson comorbidity score, and lymphadenectomy were not associated with receiving adjuvant treatment. There was no statistical difference in OS between the adjuvant treatment variations including the lack of adjuvant treatment ($P = 0.44$). See Figure 1.

Conclusion: Nearly 37% of women with stage II serous uterine cancer receive no adjuvant treatment. Factors associated with lack of receipt of adjuvant treatment included older age, higher income, and region of care. Despite these variations, there was no impact on OS. Further investigation into the use of adjuvant treatment in this population is warranted.

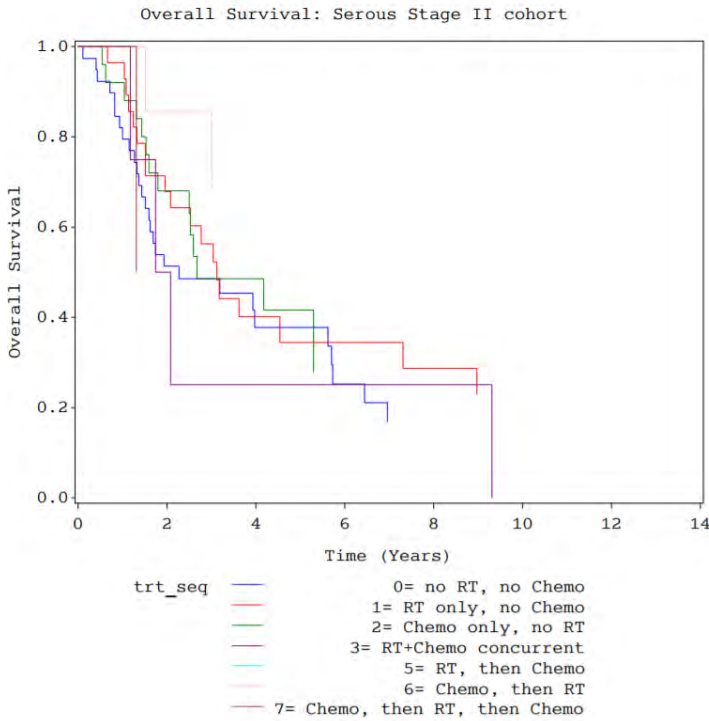


Fig. 1.

453 - Poster Session

Cervical cancer screening and goals for transition in female-to-male transgender individuals at a community health center in the southern United States

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Objective: To evaluate current cervical cancer screening practices for female-to-male (FtM) transgender individuals at a community health clinic in the southern United States.

Method: A retrospective chart review of demographic characteristics and treatment of transgender men at a single community health clinic. Patients with an ICD-10 diagnosis code for Gender Identity Disorder (GID) and female sex assigned at birth from 2013 to 2017 were included.

Results: Of the 145 individuals with codes for GID, 80 (55.2%) were classified as female and 65 (44.8%) as male. Seventy-one participants had female sex assigned at birth (i.e., biologically female). Of those, 66.2% ($n = 47$) were Caucasian and 18.3% ($n = 13$) African-American; median age was 24 years (IQR 21.5–27 years); and 33.8% ($n = 24$) had health insurance. Of 64 participants eligible for cervical cancer screening per American Society of Colposcopy and Cervical Pathology (ASCCP) guidelines, 52.4% ($n = 33$) were up-to-date; 22.2% ($n = 14$) had received past screening but were delinquent; 6.3% ($n = 4$) were never screened; and data were insufficient for 19.0% ($n = 12$). Median age of those never screened was 26 (range 22–27) years; median age for those up-to-date was 23 (range 18–38) years. Median age of coitarche was 17 years (IQR 15–18 years); and 25.4% ($n = 18$) had more than 5 lifetime partners. Participants' sexual partners were exclusively female (31.0%), male (0.3%), or both male and female (49.3%). Two had transgender partners. All participants were pursuing gender-affirming hormone therapy, with primary goals of male pattern hair growth (43.7%) and body habitus (47.9%). Three had previously procured testosterone illicitly. The majority were not planning surgery to remove their breasts, cervix, or uterus (Table 1). While there was interest in amenorrhea (21.1%) and low desire for future fertility (8.4%), only 4 were considering future hysterectomy. One already underwent hysterectomy for an alternative indication. Five participants had mastectomies with 10 considering mastectomy in the future.

Conclusion: Compliance with ASCCP guidelines for cervical cancer screening by transgender men in our community is below the national average for women. Efforts to more accurately document sex assignment at birth, gender identity, and present anatomy should be pursued to improve care in this unique population.

Table1: Goals and plans for gender affirmation ($n = 71$)

Mastectomy n (%)	
Completed	5 (7.0%)
Desires	10 (14.1%)
Hysterectomy n (%)	
Completed	1 (1.4%)
Desires	4 (5.6%)
Desires phalloplasty n (%)	1 (1.4%)
Goals of therapy n (%)	
Male pattern hair growth	31 (43.7%)
Male muscle/fat distribution	34 (47.9%)
Absence of menses	15 (21.1%)
Male voice	14 (19.7%)
Increased libido	1 (1.4%)
Outer appearance consistent with self image	7 (9.9%)
Desires future fertility n (%)	
Yes	2 (2.8%)
Maybe	4 (5.6%)
No, childbearing complete	4 (5.6%)
No desire for biological children	46 (64.8%)
Did not answer	15 (21.1%)

454 - Poster Session

Patient perceived attitudes and practice patterns regarding hormone replacement therapy (HRT) after risk reducing gynecologic surgery for Lynch syndrome

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Objective: To describe the current patient-perceived attitudes and practice patterns regarding hormone replacement therapy (HRT) in patients who undergo risk-reducing surgery for Lynch syndrome (LS). Secondary outcomes were patient-reported changes in quality of life and sexual function after risk-reducing surgery.

Method: Women with a diagnosis of LS were contacted via social media and asked to participate in an institutional review board- approved, web-based, 55-question survey regarding risk-reducing gynecologic surgery and HRT. Women were contacted by posting the survey on social media outlets specific to LS.

Results: A total of 91 women with mean age 46 years, who self-identified as being diagnosed with LS, responded to the survey. The majority were college-educated (56%) non-Hispanic white women (85.6%) with private insurance (76.7%) residing in the United States (91.1%), and were diagnosed with LS between 30 and 50 years of age (69.3%). Of the 91 respondents, 80.5% reported being referred to a genetic counselor to discuss the diagnosis of LS. Sixty-one respondents (75%) reported having undergone a risk-reducing bilateral salpingo-oophorectomy (BSO), 80% of whom were younger than 50 years at the time of surgery. Of the respondents, 66% reported that HRT was not discussed following risk-reducing surgery. Patient-reported reasons for not taking HRT included concern for increased risk of blood clots (7%), cancer (28%), HRT not being natural (2%), and inability to afford (3%). After BSO, women reported decreased sexual activity (67%), sleep (21%), mood (20%), general well-being (15%), ability to exercise (18%), and increased hot flashes (30%). The percentage of women who reported that they were not counseled about the risks of BSO on their quality of life was 30.8%. When analysis was restricted to women younger than 50 years without known contraindications to HRT (smoking, migraines, endometrial or ovarian cancer, thromboembolic disease, $n = 48$), 19% reported that HRT was not discussed and 40% that they were not offered HRT.

Conclusion: A significant number of surveyed women who received risk-reducing BSO for LS were not offered HRT despite the well-known effects of surgical menopause on quality of life. The perceived reasons patients do not choose to receive HRT

are modifiable with both patient and provider education.

455 - Poster Session

Joint exposure to smoking, excessive weight, and physical inactivity affects survival of ovarian cancer patients: Evidence from the Ovarian Cancer Association Consortium

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Objective: To evaluate the combined effect of unfavorable lifestyle factors, including smoking, obesity, and physical inactivity, on ovarian cancer prognosis.

Method: Using pooled data from 13 studies participating in the Ovarian Cancer Association Consortium, we examined the association between exposure to smoking, excessive weight, and physical inactivity and overall survival (OS) and progression-free survival (PFS) among women diagnosed with invasive epithelial ovarian carcinoma. Using age- and stage-adjusted Cox proportional hazards regression models, we estimated hazard ratios (HRs) and 95% confidence intervals (CIs) associated with joint exposure to these factors.

Results: Combined exposure to current smoking, overweight/obesity, and physical inactivity prior to diagnosis ($n = 159$) was associated with a statistically significant increased risk of mortality compared to those who never smoked, had normal BMI, and were physically active ($n = 1,403$, HR = 1.38, 95% CI 1.11–1.71). Similarly, exposure to both current smoking and overweight/obesity ($n = 269$) and current smoking and physical inactivity ($n = 183$) was also associated with increased risk of death (HR=1.27, 95% CI 1.07–1.51, and HR = 1.41, 95% CI 1.16–1.71, respectively). When excessive weight was limited to obesity only, the estimated HR remained similar to those in the main analyses. No significant associations were observed between joint exposure to any of these factors and PFS.

Conclusion: Joint exposure to smoking, excessive weight, and physical inactivity may have an impact on survival of ovarian cancer patients. These results suggest the importance of examining the combined effect of various lifestyle factors on ovarian cancer patients' survival. Moreover, clinicians may need to be aware that promoting healthy lifestyle choices among their patients can potentially improve survival outcomes.

456 - Poster Session

An educational intervention to improve human papillomavirus (HPV) and cervical cancer knowledge among African American college students

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Objective: Misinformation and lack of formal education about cervical cancer may contribute to disparities. The objective of this study was to assess the role of an educational intervention in improving knowledge about human papilloma virus (HPV) and cervical cancer among African-American female college students.

Method: We completed a total of 5 lectures at 4 different historically black colleges in North Carolina, Virginia, and West Virginia. Each 60-minute lecture reviewed basic female anatomy, HPV pathogenesis, cervical dysplasia, cervical cancer, HPV vaccination, and cervical cancer screening. Participants completed pre- and postlecture surveys assessing knowledge, attitudes, and beliefs related to cervical cancer screening, HPV, and the HPV vaccine.

Results: A total of 72 students attended the lectures, and 57 students completed the surveys. Of these students, 96% reported knowledge of the HPV vaccine; however, only 52% reported receiving the vaccine and 42% completing the 3-shot series. About 77% of students older than 21 years reported having a Pap smear. Of the 16 knowledge-based questions, correct response rates significantly increased (74% vs 91%, $P = 0.005$) with the intervention. At the completion of the intervention, 94% affirmed plans to get regular Pap smears, and 87% affirmed plans to get the HPV vaccine.

Conclusion: Primary prevention and early detection are key interventions for reducing disparities in cervical cancer incidence and treatment. Community outreach efforts play an important role in reducing inequities in cancer among high-risk groups.

The educational intervention utilized in this study was successful in improving knowledge about HPV and cervical cancer.

457 - Poster Session

Thirty-day readmissions following surgery for cancer of the ovary

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Objective: To identify diagnoses and procedures for patients readmitted within 30 days following surgery for cancer of the ovary.

Method: This study utilizes data from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. This agency is within the U.S. Department of Health and Human Services. Readmission data were abstracted from the 2014 Nationwide Readmissions Database. This database utilizes data from 22 states representing 51.2% of the U.S. population and 49.3% of hospital admissions. Index admissions were identified for patients with a primary diagnosis of cancer of the ovary, undergoing oophorectomy, hysterectomy, or other therapeutic procedure of the female organs. The subset of patients requiring readmission within 30 days from discharge was then identified. Primary diagnoses and therapeutic procedures associated with readmissions were examined.

Results: For 2014, there were 7,485 index admissions in the database for patients with carcinoma of the ovary undergoing a gynecologic procedure. There were 882 (11.8%) patients requiring readmission within 30 days of discharge; 656 (74.4%) were classified as elective and 226 (25.6%) were classified as nonelective. The most common primary diagnoses for readmission were complications of surgery or care (32% of patients), septicemia or other infection (14.7%), ovarian cancer or secondary malignancy (11.9%), and intestinal obstruction (10.3%). The most common primary procedure codes were cancer chemotherapy (18.5%), paracentesis or thoracentesis (16.7%), blood transfusion (13.2%), and vascular catheterization (10.6%). Total hospital charges were significantly higher for patients readmitted than for patients who were not readmitted ($P < 0.0001$). No patients undergoing readmission died during hospitalization.

Conclusion: As payers have focused on reducing readmissions as a cost-saving measure, 30-day readmissions are now perceived as a surrogate indicator for quality of care. Cancer of the ovary, however, is a complex disease, and postoperative care often requires management of both surgical issues and symptoms related directly or indirectly to the disease burden. Hospital readmission may be required to address patient well-being and disease control.

458 - Poster Session

Prevalence of high risk non-vaccine type HPV among U.S. women who received Cervarix or Gardasil: NHANES 2009-2014

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Objective: Since the introduction of Cervarix and Gardasil in 2006, the prevalence of vaccine-type HPV has declined. However, there is limited knowledge about the extent to which immunized women are at risk for nonvaccine genotypes, or how effective the vaccine is if one is already sexually active. The objective of this study was to assess the prevalence of vaccinated women who test positive for high-risk HPV later in life.

Method: We analyzed data for 335 women (ages 18 to 56, mean 24.67) who reported that they received either Cervarix or Gardasil in the 2009–2014 National Health and Nutritional Examination Surveys (NHANES). Participants responded to questionnaires and provided samples for Roche Linear Array Assay detection for HPV DNA. Data were analyzed using SAS statistical software.

Results: Of immunized women, 20% (67/335) tested positive for nonvaccine type high-risk HPV DNA (specifically 31, 33, 45, 52, and 58). The percentages for each HPV genotype were 2.69% (9/335) for 31, 0.30% (1/335) for 33, 4.48% (15/335) for 45, 8.36% (29/335) for 52, and 3.88% (13/335) for 58. Prevalence for these subtypes among women who were vaccinated before initiating sexual activity was found to be 13.73% (14/102), compared to 22.32% (52/233) among those who were vaccinated after becoming sexually active.

Conclusion: Despite uptake of Cervarix and Gardasil, high-risk nonvaccine subtypes are still being detected among immunized women. These data suggest use of a vaccine that protects against more subtypes (such as Gardasil 9), earlier vaccination, and barrier contraception among women who have been vaccinated.

459 - Poster Session

Identifying modifiable and non-modifiable risk factors for prolonged length of stay after hysterectomy for uterine cancer

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Objective: For hysterectomy, little is known about the influence of modifiable (intraoperative factors and complications) and nonmodifiable (clinical and demographic characteristics) factors on length of stay (LOS). The relative contribution of these factors to prolonged LOS after hysterectomy for uterine cancer was examined in a national cohort of patients.

Method: The National Surgical Quality Improvement Program (NSQIP) database was used to identify women who underwent abdominal or minimally invasive hysterectomy for uterine cancer from 2006 to 2015. The association between demographic, preoperative, intraoperative, and postoperative factors and LOS was examined. The primary outcome was prolonged LOS (>75th and >90th percentiles). Model fit statistics were used to assess the relative importance of each group of characteristics on prolonged LOS.

Results: Of 19,084 women identified, 6,082 (31.9%) underwent abdominal hysterectomy and 13,002 (68.1%) underwent minimally invasive hysterectomy. In the open hysterectomy group, the 75th and 90th percentiles for LOS were >5 and >8 days, respectively. The examined factors were able to explain 23.6% of the total variation in LOS >75th percentile (full model pseudo- R^2). Individually, demographic characteristics explained 4.0%, preoperative factors 7.0%, intraoperative factors 7.9%, and postoperative characteristics 9.7% of the variation in prolonged LOS. In the minimally invasive group, the 75th and 90th percentiles for LOS were >1 and >2 days, respectively. For minimally invasive hysterectomy, the examined factors were able to explain 16.2% of the variation in LOS >75th percentile. Demographic characteristics accounted for 6.2%, preoperative factors 4.1%, intraoperative factors 6.9%, and postoperative characteristics 1.3% of variation in prolonged LOS. Similar trends were noted for both procedures when prolonged LOS was defined as >90th percentile.

Conclusion: While postoperative complications explain a portion of the risk, nonmodifiable demographic and clinical factors also account for a substantial portion of the explained variation in prolonged LOS after hysterectomy. Overall, a significant portion of the variation in LOS is not explained by measurable patient and hospital factors.

460 - Poster Session

Reasons for emergency room visits and admissions among cervical cancer patients

K.E. Lewis and A.M. Rodriguez. *The University of Texas Medical Branch, Galveston, TX, USA*

Objective: To determine the most frequent reasons that cervical cancer patients seek treatment in the emergency room and analyze commonalities for hospital admission.

Method: Discharge data from the Nationwide Emergency Department Sample (NEDS) 2008–2012, a product of the Agency for Healthcare Research and Quality's (AHRQ) Healthcare Cost and Utilization Project (HCUP), was used to identify emergency room encounters for which the ICD-9-CM diagnosis code for cervical cancer was indicated. Descriptive statistics were calculated using SAS software version 9.4.

Results: Among the 146 million emergency room visits during the study period, 23,833 were associated with cervical cancer. Patients who had emergency room visits resulting in hospital admissions were older than those not admitted (54 vs 46 years, respectively). The rate of admission increased as age increased. Most visits occurred on weekdays (73.6%), with more than half occurring in large central or fringe metro areas (57.3%). Hospital admissions were lowest for visits in small metro and rural areas. The primary payer for more than half of the visits was Medicaid (38%) and Medicare (25%). More than half of the Medicare visits resulted in hospitalization (3,926/5,841). The top three ICD-9 diagnoses for visits were related to urinary tract infections ($n = 1,557$, 7.8%), abdominal pain ($n = 1,308$, 6.5%), and unspecified cancer issue ($n = 842$, 4.2%). The top three diagnoses for visits that resulted in hospital admission were unspecified cancer issue ($n = 813$, 7.6%), septicemia ($n = 800$, 7.4%), and urinary tract infections ($n = 788$, 7.3%). Genitourinary problems accounted for more than 17% of the top reasons

for visits and admissions. Pain control was the next most common category for visits, compared to infection, for hospital admissions.

Conclusions: This is the first study to analyze emergency room visits of cervical cancer patients. Determining the reasons for emergency room visits among cervical cancer patients may highlight gaps in cervical cancer care and management. Targeting certain patient demographics and aiming to address some of the most common complications in the clinic setting may decrease emergency room visits and potentially cut health care costs.

461 - Poster Session

Patient with *BRCA* mutations have superior outcomes after intraperitoneal chemotherapy in optimally resected ovarian cancer

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Objective: To compare the outcomes for intraperitoneal (IP) chemotherapy in *BRCA* (+) and *BRCA* (–) patients.

Method: Patients with high-grade ovarian cancer who were treated primarily with at least 1 dose of IP chemotherapy from 2005 to 2016 were identified. The outcomes were compared between patients with known *BRCA* mutations and those who either tested negative or were unknown.

Results: A total of 114 evaluable IP patients were identified. Fourteen patients were excluded because of low-grade tumors (9), not first-line therapy (3), or uterine primary (2), leaving a total of 100 patients with a mean follow-up of 51.7 months. Of these, 74 underwent *BRCA* testing, and 24 (32%) were *BRCA* positive (23 germline, 1 somatic). No difference was noted between the groups with respect to number of IP cycles, toxicity of chemotherapy, stage of disease, or residual disease after surgery. The median progression-free survival (PFS) was 38.1 months in the *BRCA* (+) patients versus 27.9 months in the *BRCA* (–) patients (HR = 0.35, 95% CI 0.18–0.69, *P* = 0.003) (Figure 1). The median overall survival (OS) was 98.1 months in the *BRCA* (+) patients versus 64.0 months in the *BRCA* (–) patients (HR = 0.29, 95% CI 0.11–0.75, *P* = 0.01) (Figure 2).

Conclusion: In this series, the rate of pathogenic *BRCA* mutations is higher than expected in optimally resected high-grade ovarian cancer patients selected for IP therapy. *BRCA* (+) patients had a dramatic benefit in PFS and OS with IP therapy, and this is greater than has been reported for *BRCA* (+) patients with IV chemotherapy. The magnitude of this benefit would suggest that the *BRCA* (+) patient population may benefit from IP therapy despite a recently reported negative randomized trial that included patients without regard to *BRCA* status.

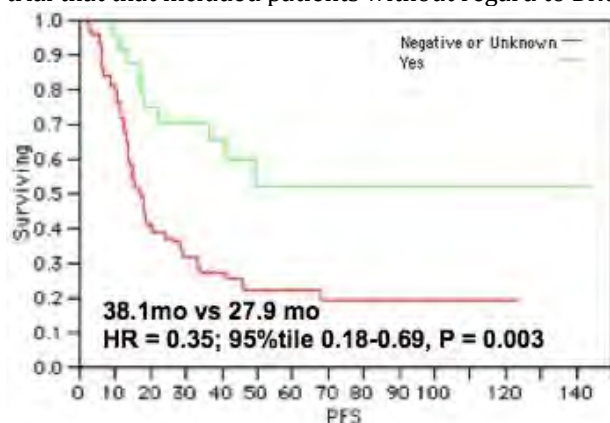


Fig. 1. Progression Free Survival.

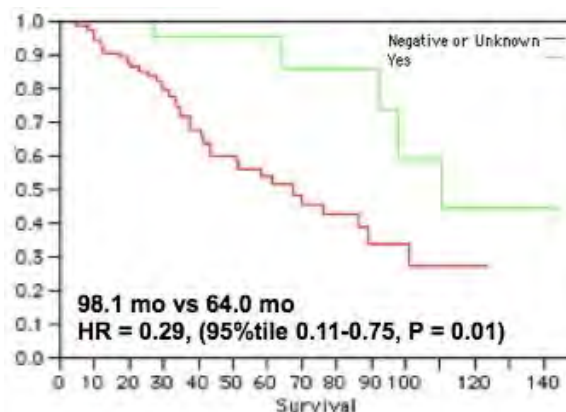


Fig. 2. Overall Survival.

462 - Poster Session

Long-term survival after intraperitoneal carboplatin chemotherapy for advanced ovarian cancer

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Objective: Multiple RCTs show increased overall survival in women with advanced ovarian cancer treated with intraperitoneal (IP) cisplatin chemotherapy compared to intravenous; however, uptake is poor because of toxicity concerns. Substitution of IP carboplatin as a viable therapeutic option was analyzed for outcomes.

Method: At a comprehensive cancer center, women with advanced epithelial ovarian/fallopian tube/primary peritoneal cancer (EOC) were offered IP chemotherapy with cisplatin or carboplatin following optimal surgical cytoreduction. Data were abstracted as to tolerability and survival, and statistics calculated using STATA.

Results: Over a 10-year period, 183 EOC patients underwent primary optimal surgical cytoreduction with IP port placement. Over 75% were high-grade serous ovarian carcinoma; 10% stage II; 75% stage III; and 13% stage 4. Twelve percent had a germline *BRCA1* or *BRCA2* mutation with 47% unknown genetic status. Surgical outcomes included 54% optimal debulking to R0 (no gross residual), 30% R1 (less than 1 cm), and 16% optimal with no designation of residual. At the time of port placement, 37% (68/183) underwent bowel surgery, of which 78% (53/68) were rectosigmoid resections. Following surgery, 72% of patients went on to receive IP chemotherapy; 37% (48/131) of patients received IP cisplatin and 63% (83/131) received IP carboplatin, both with IV taxane. Most patients (86%) had median 2 cycles of IV paclitaxel/carboplatin chemotherapy prior to initiating IP therapy. Median total number of IP cycles was 4 (range 1–6), and median total number of IV + IV/IP cycles was 6 (range 1–9). Incidence of grade 3 neuropathy was 7.7% and grade 3 nausea/vomiting, 4.2%. Thirty patients discontinued IP therapy early because of abdominal pain (5), IP port complication (8), adverse event (4), patient preference (6), and provider preference (6). Progression-free survival was 35.2 months for the entire group, 35.2 months for IP cisplatin, and 34.5 months for IP carboplatin. Median overall survival was 76.4, 74.5, and 87.3 months, respectively, with median follow-up of 43.7 months. See Figure 1.

Conclusion: Treatment of advanced ovarian cancer with IP carboplatin chemotherapy may confer long-term survival with acceptable toxicity.

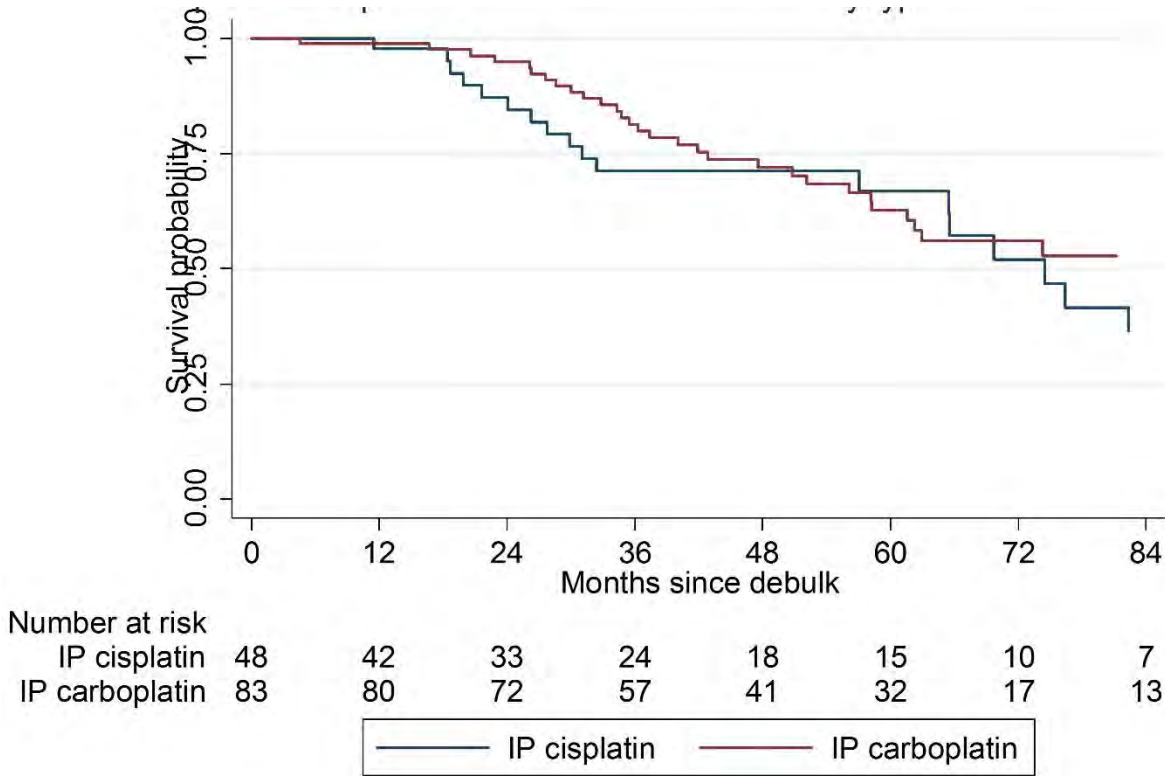


Fig. 1. Kaplan-Meier plot of overall survival stratified by type of IP chemotherapy.

463 - Poster Session

Clinical characteristics and outcomes in elderly women with *BRCA1* and *BRCA2* mutations

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Objective: Describe the clinical characteristics and risk-reducing strategies utilized by women with a *BRCA1* or *BRCA2* mutation who survive to age 75 and beyond.

Method: This is a retrospective study of women in a community-based health system with *BRCA1* or *BRCA2* mutations identified from January 1995 to August 2015. All participants lived to age 75 or older at the time of data collection. Descriptive statistics were used to analyze reason for genetic testing, age when *BRCA* mutation was identified, personal cancer history, ethnic background, surgical history, and risk-reducing strategies utilized after identification of *BRCA* mutation.

Results: There were a total of 69 women with a *BRCA* mutation who lived to age 75 or greater. The median age of the cohort at time of genetic testing was 73.5 years (range 57–92 years). The majority of women were white (81%), and 14% were Ashkenazi Jewish. At the time of genetic testing, 47 women (68%) had a personal history of breast cancer, and 27 (39%) had a personal history of ovarian cancer. Twenty-three women (33%) were tested because a *BRCA* mutation had been identified in another family member. Three out of 19 women (15.8%) with no prior history of breast cancer elected risk-reducing mastectomies (RRM) after learning their *BRCA* positive status (at ages 58, 66, and 68). Two of the 3 women who elected RRM had prior personal history of ovarian cancer. Among 30 women who had ovaries in place at the time of genetic testing, 14 (47%) of them elected to have a risk-reducing salpingo-oophorectomy (RRSO); 6 of these women were 70 years or older at time of RRSO. Three women (4%) in the cohort developed cancer after genetic testing. One woman developed breast cancer at age 67, and 2 women developed pancreatic cancer at age 76. Overall, 6 women (8.7%) had no personal diagnosis of a *BRCA*-related cancer during the study period.

Conclusion: The majority of women with *BRCA* mutations who survived beyond age 75 received their genetic test result at an older age, and most had a personal history of *BRCA*-related cancer. Almost half of the women who had their ovaries in place underwent RRSO after identification of their *BRCA* mutation. Older women are making medical decisions based on the information from *BRCA* genetic testing, and it is important that the health care needs of this cohort be acknowledged.

464 - Poster Session

Differences in overall survival associated with type and sequence of adjuvant therapy in stage I uterine carcinosarcoma

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Objective: We sought to determine patterns in adjuvant treatment and associated differences in overall survival (OS) among women with stage I uterine carcinosarcoma (UCS).

Method: A cohort study assessing adjuvant treatment among 504 women with stage I uterine carcinosarcoma between 1999 and 2011 was completed utilizing the SEER-Medicare database. Data were collected on demographics, disease factors, lymph node dissection (LND), and adjuvant treatment. Descriptive and survival analyses were performed.

Results: Among women with stage I UCS, 45.8% ($n = 231$) received no adjuvant treatment; 31.6% ($n = 159$) received radiation (RT) only; and 13.5% ($n = 68$) received chemotherapy (CHEMO) only. In addition, a smaller subset received variations of CHEMO-RT including 3.6% ($n = 18$) concurrent CHEMO-RT; 2.6% ($n = 13$) RT followed by CHEMO; 2.4% ($n = 12$) CHEMO followed by RT; 0.4% ($n = 2$) sandwich (CHEMO-RT-CHEMO); and 0.2% ($n = 1$) concurrent CHEMO-RT followed by additional CHEMO. Use of adjuvant treatment has increased in more recent years (58.2% in 2009–2011 vs 53.7% in 1999–2008, $P < 0.01$). Women who underwent LND were more likely to receive adjuvant treatment (57.9% vs 42.7%, $P < 0.01$). Younger women were also more likely to receive adjuvant treatment (65% in those age <70 years vs 38% in age >80 years, $P < 0.01$) and chemotherapy (32% in age <70 years vs 8% in age >80 years, $P < 0.01$). There were no associations between marital status, race, socioeconomic status, Charlson comorbidity index, FIGO grade, or geographic region and type of adjuvant treatment. Kaplan-Meier survival analyses demonstrated a survival benefit for those subjects receiving CHEMO alone (log rank $P < 0.01$, Figure 1). After adjusting for year of diagnosis, age, and LND, only the CHEMO alone group had significantly improved OS compared to the no treatment group (HR = 0.44, 95% CI 0.27–0.72, $P < 0.01$).

Conclusion: In this national cohort, approximately one-half of women with stage I UCS received adjuvant treatment. Of the 7 modalities of adjuvant treatment for stage I UCS, only those who underwent chemotherapy alone had improved OS compared to women who received no adjuvant therapy. Additional studies are needed to further elucidate this relationship.

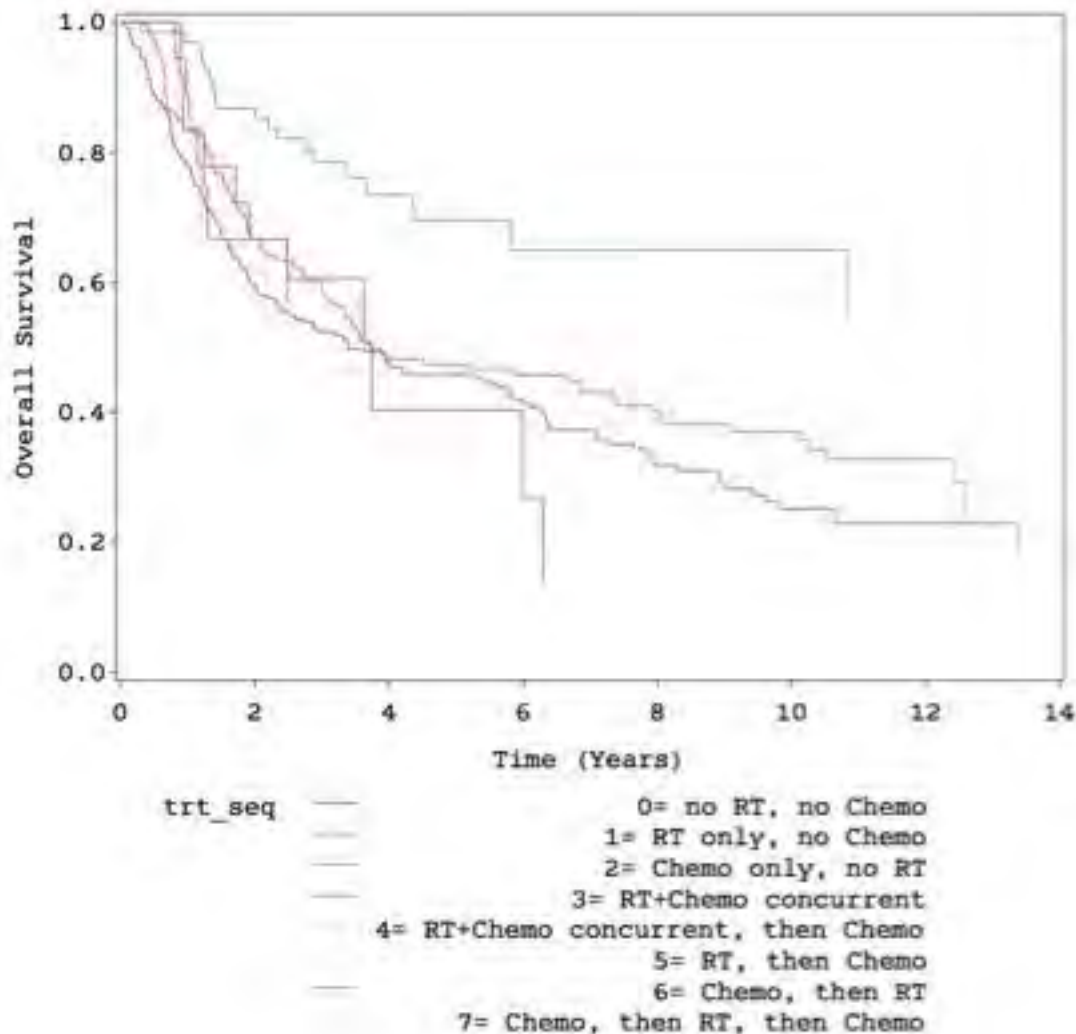


Fig. 1. Overall Survival: Carcinosarcoma Stage I cohort.

465 - Poster Session

Aggressive surgery in the elderly: National trends and outcomes associated with bowel and upper abdominal procedures in ovarian cancer surgery

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Objective: We sought to evaluate the trends in performance of surgical debulking procedures and complications in a population-based cohort of elderly women with advanced ovarian cancer, comparing patients who underwent primary cytoreductive surgery (PCS) versus neoadjuvant chemotherapy (NACT) and subsequent interval debulking.

Method: A cohort of patients older than 66 with stage III–IV epithelial ovarian cancer diagnosed between 2000 and 2013 was identified in the SEER-Medicare database. “Aggressive surgery” or receipt of small or large bowel resection, ostomy creation, and/or upper abdominal procedures (UAP) was identified using relevant codes. Demographic and clinical variables were used to develop a propensity score from a multivariate logistic regression model. Based on the propensity score, we performed a 1:1 match of NACT and PCS patients. We compared 30-day complications and use of acute care in this matched cohort.

Results: A total of 5,417 women were identified; 34% underwent bowel resection, 16% underwent ostomy creation, and 8% had UAP. While there was no change in rates of bowel surgery over time, there was an increase in upper abdominal procedures from 2000 to 2013 in patients who received PCS (5.2% vs 12.4%, $P < 0.0001$) and NACT (2.9% vs 11.3%, $P = 0.041$). Patients who received NACT were less likely to undergo bowel resection (OR = 0.50, 95% CI 0.41–0.61) or ostomy creation (OR = 0.48, 95% CI 0.42–0.56). UAP did not differ between groups. Among the PCS patients in our matched cohort, patients who received aggressive surgery were more likely to have a postoperative ICU stay (OR = 3.06, 95% CI 1.42–6.62), compared to those who didn't receive aggressive surgery. This association was not significant for patients who received NACT in the matched cohort (OR = 2.13, 95% CI 0.97–4.65). In both PCS and NACT groups, receipt of aggressive surgery was significantly associated with multiple 30-day postoperative complications, as well as higher rates of readmission and emergency room visits (see Table 1).

Conclusion: Performance of upper abdominal procedures increased in this older patient population over time. Use of NACT is associated with decreased risk of ostomy or bowel resection. In matched PCS and NACT cohorts, receipt of aggressive surgery was associated with overall increased likelihood of postoperative complications and use of acute care services.

Table 1. 30-day complications in elderly patients undergoing advanced ovarian cancer surgery.

	NACT ($n = 1,123$)			PCS ($n = 1,123$)		
	No aggressive surgery ($n = 796$)	Aggressive surgery ($n = 327$)	P value	No aggressive surgery ($n = 580$)	Aggressive surgery ($n = 543$)	P value
30-day complications, n (%)						
Wound infection	80 (10.1)	58 (17.7)	0.0004	84 (14.5)	114 (21.0)	0.0042
Pulmonary embolus/Deep venous thrombosis	92 (11.6)	37 (11.3)	0.9077	53 (9.1)	62 (11.4)	0.2079
Hematoma/hemorrhage	196 (24.6)	93 (28.4)	0.1837	135 (23.3)	147 (27.1)	0.1427
Other surgical complications*	222 (27.9)	169 (51.7)	<0.0001	217 (37.4)	320 (58.9)	<0.0001
Cardiac	106 (13.3)	61 (18.7)	0.0224	92 (15.9)	112 (20.6)	0.0385
Respiratory	136 (17.1)	101 (30.9)	<0.0001	188 (32.4)	243 (44.8)	<0.0001
Acute renal failure	31 (3.9)	25 (7.6)	0.0087	47 (8.1)	45 (8.3)	0.9106
Shock	40 (5.0)	33 (10.1)	0.0018	51 (8.8)	54 (9.9)	0.5077
Fluid/electrolyte imbalances	211 (26.5)	114 (34.9)	0.0050	178 (30.7)	202 (37.2)	0.0212
Other infections**	77 (9.7)	68 (20.8)	<0.0001	88 (15.2)	129 (23.8)	0.0003

*Peritonitis, reopening laparotomy, surgical complication NOS, injury to vessel of abdomen/pelvis, suture or laceration of ureter, foreign body, stoma complications

**pneumonia/respiratory infection, sepsis/bacteremia, urinary tract infection, clostridium difficile

Bold indicates statistical significance with a $P < 0.05$

466 - Poster Session

Opportunities for improved Lynch syndrome tumor screening in endometrial cancer patients surgically treated at an NCI-designated comprehensive cancer center

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Objective: There is no consensus on the best approach to identifying Lynch syndrome (LS) among patients diagnosed with endometrial cancer. Universal tumor testing for LS was initiated at our institution in September 2011. This study aims to describe the efficacy of universal screening of pathology specimens over a 4-year period.

Method: Women who underwent surgical treatment for endometrial cancer between September 2011 and December 2015 and had immunohistochemical (IHC) staining for mismatch repair (MMR) proteins MLH1, MSH2, MSH6, and PMS2 ($n = 418$) were identified from a clinical database maintained by the Department of Clinical Genetics. Demographic and pathologic characteristics were ascertained from the electronic medical record. In patients with abnormal expression of any of the MMR proteins by IHC, additional testing including tumor-based microsatellite instability (MSI), MLH promoter hypermethylation, and serum germ-line testing was performed to establish the diagnosis of LS. Testing results were obtained through review of the Risk Assessment Program patient record.

Results: A total of 503 endometrial cancer patients were surgically managed during this time, of which 418 (83.1%) had IHC testing on their tumor specimen. Of those screened by IHC, 115 (27.5%) patients had an abnormal result. In those with an abnormal screen, 44 (38.2%) had microsatellite instability (MSI) testing; 17 (14.8%) had MLH hypermethylation testing; and 17 (14.8%) had serum gene panel testing. Of the patients with an abnormal screen, 49 (42.6%) were documented to have been referred for genetic counseling, although only 28 (57.1%) of those patients attended their scheduled session. Ultimately, out of patients screened, 11 (2.7%) were diagnosed with LS through germline testing, and an additional 7 (1.7%) were diagnosed with clinical LS based on testing and risk factors.

Conclusion: Universal screening resulted in 2.7% of patients being diagnosed with germline mutations consistent with LS. However, despite its implementation, IHC screening was missed in 16.9% of patients, and only 44.6% of patients with an abnormal screen were referred for genetic counseling. In those referred, only 57.1% presented for follow-up. Identifying obstacles in screening and genetic consultation may allow for improvement in diagnosis and outcomes.

467 - Poster Session

Perioperative complications in elderly patients undergoing hysterectomy for gynecologic malignancies

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Objective: Perioperative morbid conditions in gynecologic cancer surgery are poorly quantified in the elderly population. This study compares the patterns of complications from hysterectomy performed for gynecologic malignancies between patients younger than and older than 80 years of age using the National Inpatient Sample (NIS) Database.

Method: Admissions of patients with gynecologic malignancies who underwent hysterectomy were identified from the 2007–2012 NIS data sets. The sample was stratified by age greater and less than 80 years. ICD-9 codes for circulatory, pulmonary, gastrointestinal, renal, neurologic, and wound-related morbidities were used to identify perioperative complications within the surgical admission. Two-sample t tests and χ^2 tests were used to compare the type of hysterectomy performed, length of stay, complication rates, and mortality rate.

Results: A total of 58,933 admissions were identified, with 4,639 patients older than 79 years of age (elderly population) and 54,294 younger than 80 years. The mean age of elderly patients was 83.9 years, compared to 59.3 years. Elderly patients had a higher rate of laparoscopic hysterectomy (25.3% vs 23.7%, $P = 0.01$). Mean length of stay was increased by 1.2 days ($P < 0.01$) in the elderly. Increased circulatory (8.9% vs 5.7%, $P < 0.01$), respiratory (13.7% vs 10.0%, $P < 0.01$), gastrointestinal (19.8% vs 16.9%, $P < 0.01$), renal (5.2% vs 2.9% $P < 0.01$), and neurologic (0.5% vs 0.2%, $P < 0.01$) complications were observed in the elderly cohort. In-hospital mortality was higher in elderly patients (1.6% vs 0.5%, $P < 0.01$). Rate of wound complications did not differ between the groups.

Conclusion: Elderly patients undergoing hysterectomy for a gynecologic malignancy have higher rates of perioperative complications, with the exception of wound complications, despite undergoing a higher proportion of minimally invasive procedures. Average length of stay and mortality are increased. Though statistically significant, the relatively low magnitude of these differences suggests that with patient counseling and proper surgical modality selection, hysterectomy has an appropriate role in management of elderly patients with gynecologic malignancies.

468 - Poster Session

Patients with a history of cervical cancer are at an increased risk of developing primary anal or oropharyngeal cancer

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Objective: HPV infection is responsible for approximately 31,500 new cancers in the United States annually. The purpose of this study is to assess the risk of primary anal and oropharyngeal cancers among women with a history of squamous cell carcinoma of the cervix.

Method: A population-based cohort of 21,060 women diagnosed with cervical squamous cell carcinoma between 1973 and 2014 was identified from the Surveillance, Epidemiology and End Results Program data (SEER 9). Standardized incidence ratios (SIR) for anal and oropharyngeal cancers were calculated to estimate the risk of a second primary HPV-related malignancy based on incidence in the general population. Results were further stratified by age (20–53, 54+ years) and latency period (2–11, 12–59, 60–119, 120+ months).

Results: Cervical squamous cell cancer survivors had a higher risk of being diagnosed with oropharyngeal cancer (SIR = 4.36, 95% CI 1.19–11.15) and anal cancer (SIR = 2.20, 95% CI 1.28–3.52). Patients diagnosed with cervical cancer between ages 20 and 53 years had an increased risk of anal cancer (SIR = 3.53, 95% CI 1.15–8.23). Age 54+ years at cervical cancer diagnosis was associated with increased oropharyngeal cancer risk only (SIR = 5.04, 95% CI 1.37–12.91). Latency stratification was significant only at 120+ months, at which time there was an increased risk of both oropharyngeal cancer (SIR = 7.97, 95% CI 2.17–20.42) and anal cancer (SIR = 2.60, 95% CI 1.34–4.54).

Conclusion: Squamous cell cervical cancer survivors have a substantially increased risk of anal and oropharyngeal cancer. Long-term screening for anal cancer with digital rectal examination and anal cytology should be considered. Development of screening methods for oropharyngeal cancers is urgently needed.

469 - Poster Session

Evaluation of postoperative mortality in octogenarians with advanced epithelial ovarian cancer

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Objective: To evaluate the role of age older than 80 years as a risk factor for postoperative mortality in patients with advanced epithelial ovarian cancer.

Method: The National Cancer Database (NCDB) was used to identify women with stage III–IV epithelial ovarian cancer diagnosed from 2004 to 2012 who had surgery as part of their initial treatment. Patients were divided into two cohorts by age (<80 years or ≥80 years). The primary outcomes were 30- and 90-day mortality. Secondary outcomes included length of stay (LOS) and 30-day hospital readmission rates. A multivariate logistic regression was performed to assess the effect of age and other demographic factors on postoperative mortality.

Results: We identified 68,000 patients with stage III–IV epithelial ovarian cancer who had surgery as part of their initial treatment. Of these patients, 13.7% were 80 years or older at time of diagnosis and were significantly more likely to have stage IV disease, nonserous histology, and a higher Charlson comorbidity index. They were also more likely to be white and insured by Medicare. The 30-day postoperative mortality rate was 2.0% for patients younger than 80 years versus 9.6% for patients 80 years or older ($P < 0.001$). The 90-day postoperative mortality rate was 5.0% in patients younger than 80 years versus 18.0% in patients 80 years or older ($P < 0.001$). A multivariate regression model showed that age 80 or older was the most significant predictor of postoperative mortality, with odds ratios of 3.2 (95% CI 2.9–3.6) for 30-day mortality and 2.9 (95% CI 2.7–3.2) for 90-day mortality. Patients 80 years or older had a longer postoperative LOS (8.0 vs 7.1 days, $P < 0.001$); however, they had lower 30-day readmission rates (3.3% vs 5.0%).

Conclusions: Patients 80 years or older with advanced epithelial ovarian cancer are at a substantially increased risk for both 30- and 90-day postoperative mortality. Age not only is an independent risk factor for postoperative mortality but also appears to be the most important risk factor.

470 - Poster Session

Multivariable analysis of association of beta-blocker use and survival in advanced ovarian cancer

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Objective: Studies have suggested improved survival in ovarian cancer patients who use beta-blockers at the time of upfront therapy. Since use of beta-blockers may be associated with use of other medications, we sought to evaluate whether this relationship is evident after adjusting for potential confounding by common medications.

Method: In this retrospective cohort study, we reviewed the discharge medication lists of all women who underwent primary or interval cytoreduction for stage IIIC–IV epithelial ovarian cancer at 2 academic hospitals from 2010 to 2014. The exposure of interest was use of beta-blockers at the time of cytoreduction. The outcome of interest was time to death or last contact. We collected demographic and prognostic variables including age at diagnosis, race, stage, grade, histology, sequence of surgery and chemotherapy, residual disease status, and Charlson comorbidity index. We also collected information about use of aspirin, metformin, statins, and clopidogrel. We used the Kaplan-Meier method and Cox proportional hazards models in survival analyses.

Results: We identified 553 women who underwent surgery for stage IIIC–IV ovarian cancer. The average age at diagnosis was 63 years, and 85.1% of women had serous carcinoma. We identified 108 women (19.5%) discharged on a beta-blocker of whom 15 (2.7%) were on a noncardioselective beta-blocker. In addition, 25 women (4.5%) were discharged on metformin, 96 (17.4%) on aspirin, 134 (24.2%) on a statin, and 4 (0.7%) on clopidogrel. We observed 236 deaths after a median follow-up of 49 months. In univariable analysis, beta-blocker users had a median survival of 40 months compared to 58 months among nonusers (HR = 1.5, 95% CI .1–2.1, $P = 0.008$). After adjustment for important demographic, clinical, and histopathologic factors, as well as use of other common medications, beta-blocker use remains associated with an increased hazard of death (adjusted HR = 1.5, 95% CI 1.1–2.2). This association appeared to be driven by users of cardioselective beta-blockers (HR = 1.6, 95% CI 1.1–2.3) rather than noncardioselective beta-blockers (HR = 1.1, 95% CI 0.4–2.7). See Figure 1.

Conclusion: In this cohort of patients with advanced epithelial ovarian cancer, use of beta-blockers proximate to cytoreductive surgery was associated with increased mortality.

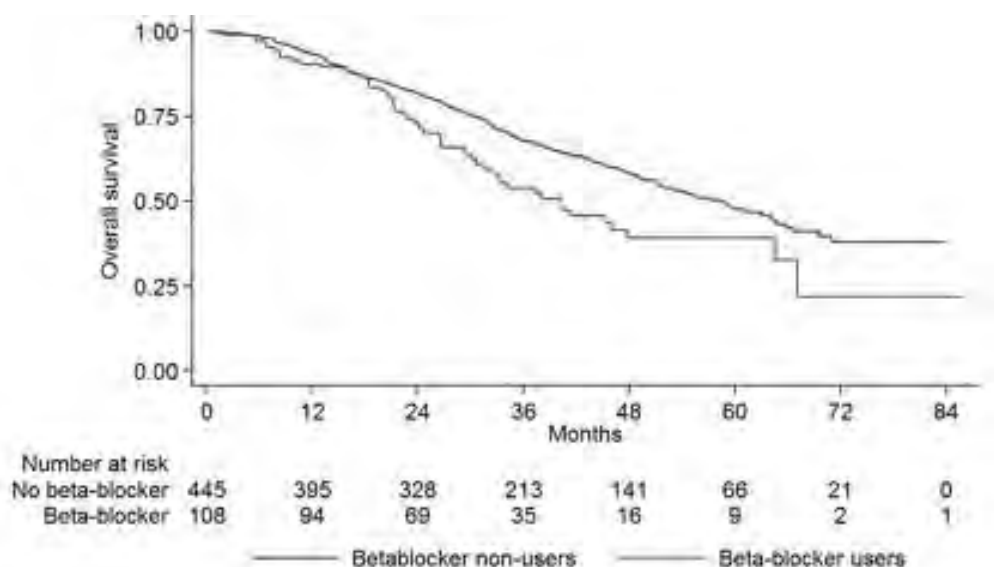


Fig. 1. Overall survival by beta-blocker use.

471 - Poster Session

Abdominal adiposity portends poor outcomes in patients with endometrial cancer

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Objective: Visceral adiposity has been established as a predictor of outcomes in various cancers; however, its role in predicting outcomes in endometrial cancer patients is unknown and unexplored. We aimed to determine the association of radiographic measurements of visceral fat with clinical outcomes in patients with endometrial cancer.

Method: After institutional review board approval, a retrospective review of endometrial cancer patients who underwent surgery between 2005 and 2009 was performed. Follow-up was continued until July 2012. Visceral fat area (VFA) and subcutaneous fat area (SFA) were assessed on preoperative computed tomography (CT) scans by a board-certified radiologist. Total fat area (TFA) is the sum of VFA and SFA. Exploratory analysis was performed to establish the optimal cutoff values for VFA, SFA, and TFA to identify patients with poor prognostic body composition. Survival rates were analyzed using Kaplan-Meier analysis, log rank tests, and Cox regression.

Results: A total of 109 patients were included. The mean age was 65.4 years, and the mean BMI was 34.7 kg/m². The majority of patients had endometrioid histology (72.5%), grade 1 (39.8%, or grade 2 (36.4%), and stage I–II (73.4%) disease. The mean VFA, SFA, and TFA were 169.2 HU, 396.9 HU, and TFA 566.2 HU, respectively. An elevated SFA (>232.5 HU) was associated with a decreased recurrence-free survival (RFS) (median 25.0 vs 31.8 months, HR = 0.35, *P* = 0.034). An increased TFA (>582.3 HU) was predictive of decreased overall survival (median 30.6 vs 34.3 months, HR = 0.39, *P* = 0.02). After adjustment for BMI, race, and histology, SFA (adjusted HR = 0.34, 95% CI 0.12–0.99) and TFA (adjusted HR = 0.28, 95% CI 0.08–0.97) were associated with a reduced overall survival.

Conclusion: Visceral fat measurements are predictive of outcomes in patients with endometrial cancer. Specifically, TFA and SFA are predictive of overall survival in this cohort. Future studies should be pursued to identify potential therapeutic targets and biological mechanisms that underlie obesity's relationship with endometrial cancer.

472 - Poster Session

Disease course and treatment patterns of unselected patients with ovarian carcinoma and germline *BRCA* mutations

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Objective: Patients with hereditary ovarian, peritoneal, or fallopian tube carcinoma (OC collectively) associated with germline *BRCA1* and *BRCA2* (*BRCA*) mutations have better 5-year survival than patients without mutations, but little has been reported on their long-term disease course. The goal of this study was to describe the cumulative treatments and outcomes of a cohort of OC patients with germline *BRCA* mutations.

Method: A retrospective study of women with germline *BRCA* mutations and OC from a database in which all patients were genotyped was conducted. Women with stage II or greater epithelial high-grade tumors, diagnosed from 2004 to 2014, and for whom complete medical records were available were included. Demographic and treatment data were abstracted; survival analysis was completed; and a Swimmer was plot used to depict disease timelines.

Results: Forty *BRCA* mutation carriers (26 *BRCA1*, 14 *BRCA2*) met inclusion criteria. Median age was 54 years (52 *BRCA1*, 57 *BRCA2*); 80% were white; 63% had stage IIIC disease; and 75% serous histology. Median follow-up was 49.3 months (IQR 33.7–85.4 months). In total, 38% received neoadjuvant chemotherapy, and the remainder had upfront surgery (56% no residual, 32% less than 1 cm, 12% suboptimal). Most (90%) were platinum-sensitive, with median first platinum-free interval 11.8 months (IQR 3.6–21.9 months). The median number of treatment lines was 3 (IQR 1–6) with a median of 2 (IQR 1–3) platinum lines. More than 7 treatment lines were administered to 18% of patients. Half (50%) received bevacizumab, and 20% received PARP inhibitors. On average, patients spent 43% (range 6%–87%) of the time after diagnosis in active treatment. The median overall survival was 77.8 months from diagnosis, 70.2 months after first-line, and 19.4 months after second-line treatment. A full 15% of women had complete responses to first-line treatment longer than 5 years. Their characteristics did not differ significantly from those of the larger group. A quantified treatment course per patient is presented in Figure 1.

Conclusion: Beyond standard first-line platinum, there was treatment and outcome heterogeneity for OC patients with *BRCA* mutations. After diagnosis, these women spent nearly half their life on treatment. Nevertheless, there was an important subset who did not recur, even without maintenance therapy.

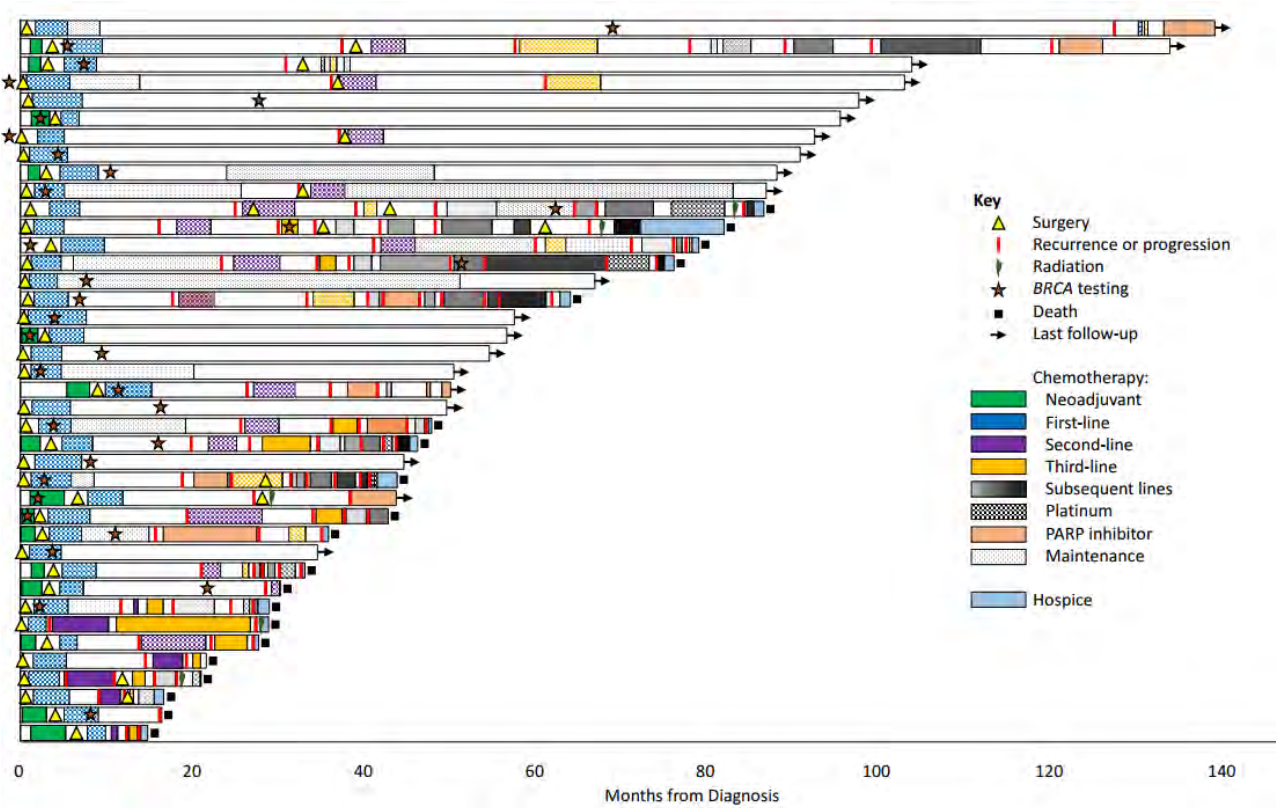


Fig. 1. Time course of ovarian cancer from diagnosis to death or date of last follow-up in women with germline *BRCA* mutations. Colored blocks represent times patients spent in treatment (details provided in key), while blank portions represent treatment-free intervals. Red lines mark times when disease progression was diagnosed (by imaging if done or Ca-125 otherwise). Times in between red lines represent progression free intervals where patients either had no evidence of disease (complete responses), partial responses, or stable disease. Cytoreductive surgeries, radiation therapy, and date of clinical *BRCA* mutation testing (if done) are denoted by specific symbols (details provided in key).

473 - Poster Session

Readability of online hysterectomy literature: Too difficult for our patients?

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Objective: Inadequate health literacy has been shown to have a negative impact on health outcomes, decrease patient satisfaction, and increase the financial burden on the health care system. The American Medical Association and National Institutes of Health have recommended that health information be published at a sixth-grade reading level, because the average adult in the United States reads at an eighth- to ninth-grade level. With more than 62% of patients now accessing health care data online, websites have become a primary source of health information. This study aims to determine the readability of online patient content about hysterectomy.

Method: Internet queries using the terms, “abdominal hysterectomy,” “robotic hysterectomy,” and “vaginal hysterectomy” were performed using a search engine. The top U.S. websites for each query were used to abstract articles specific to each route of hysterectomy. All figures, tables, links, and citations were removed prior to analysis. Readability analysis was performed with Readability Studio (Oleander Software, 2012) using nine standardized readability tests. The Tukey test was performed to determine differences between sources and routes of hysterectomy.

Results: Sixty-six articles were identified from the top search results specific to abdominal, robotic, and vaginal hysterectomy. The average readability of available online hysterectomy literature overall was that expected of a college freshman, or a grade level of 13.5 (10.4–15.5). When analyzed by route of hysterectomy, there was no significant difference ($P = 0.07$) in the average readability of abdominal (13.9, SD 1.9), robotic (13.3, SD 1.6), and vaginal hysterectomy (13.3, SD 1.7) literature. When individual websites were compared, a significant difference in average readability was noted (10.4–16.7, $P < 0.01$).

Conclusion: Readability of available online patient literature on abdominal, robotic, and vaginal hysterectomy exceeds current recommended guidelines (Figure 1). All identified sources are too difficult for the average American to read, although some are significantly easier to read than others. Available online patient health information should be modified to meet current guidelines. Providers should consider recommending specific, appropriately written online resources when counseling patients.

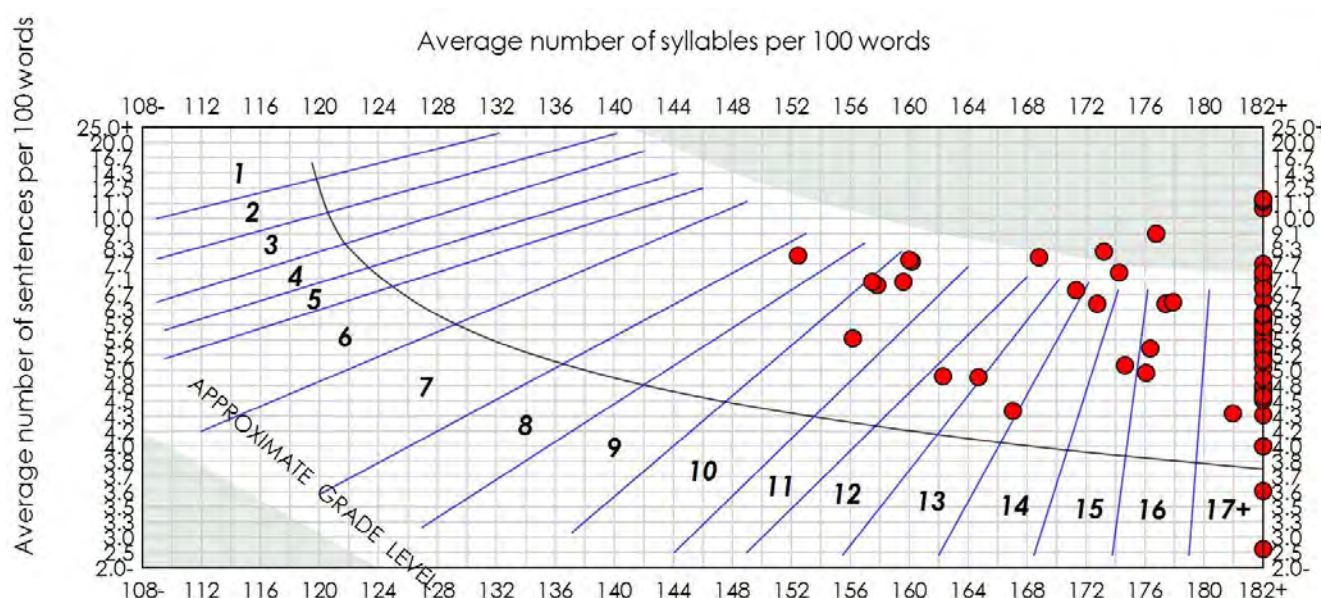


Fig. 1. Graph for estimating readability—extended. By Edward Fry, Rutgers University Reading Center, New Brunswick, NJ 08904.

474 - Poster Session

Adherence to updated cervical cancer screening guidelines at an academic health system

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Objective: To assess for over-screening for cervical cancer in women receiving care at an academic health system.

Method: We performed a retrospective cohort investigation of electronic medical records from 1998 to 2017 at a single academic health system. Date of specimen, type of test (conventional or liquid-based), use of high-risk human papilloma virus testing, age, race, and prior history of abnormal testing were collected. We identified patients with more than 1 cervical cancer screening over the study period. Number of months between these paired screening tests defined our testing interval. Patients with more than 2 cervical screenings would be identified as having more than 1 set of paired tests. Adherence was defined as screening within 12 months of the guideline-recommended interval. Over-screening was defined as more frequent testing. Guidelines were updated in 2012. Therefore, practice prior to January 1, 2012, was compared to that after January 1, 2012.

Results: A total of 214,455 women underwent 561,789 cervical cancer screenings over the study period. There were 114,196 paired samples. Cervical cancer screening performed in 11,588 patients younger than 21 years prior to 2012 was compared to that in 1,043 patients younger than 21 years from 2012 to 2017 ($P < 0.001$). Cervical cancer screening of women older than 65 years remained relatively unchanged: 15,453 versus 14,547 ($P = \text{NS}$). Mean interval between Pap smears in the paired tests

was 16.7 months prior to 2012 and 21.4 months from 2012 to 2017 ($P < 0.001$). We identified 80,463 paired co-tests (cytology and high-risk human papilloma virus testing) in patients aged 30–65 years without a history of abnormal Pap smears. Mean interval between co-tests in this population was 18.0 months prior to 2012 and 26.2 months in the period 2012–2017 ($P < 0.001$). Over-screening (retesting less than 48 months) occurred in 90% of patients (12,113/13,317) prior to 2012 and 88% (59,169/67,146) in the period 2012–2017 ($P < 0.001$).

Conclusion: With the publication of updated cervical cancer screening guidelines in 2012, there has been a 90% decrease in Pap smears in females younger than 21 years and an increase in screening interval in women overall. However, more than 85% of women aged 30–65 years who underwent co-testing without prior abnormal Pap smears were over-screened. While co-testing increases sensitivity, its inappropriate use needlessly increases costs to the health system and increases risks of unnecessary procedures to patients.

475 - Poster Session

Evaluating the impact of a history of breast cancer on outcomes in women with high-grade serous ovarian cancer

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Objective: Patients with *BRCA 1* or *2* mutations (*gBRCA*) are at increased risk of developing both breast cancer (BC) and epithelial ovarian cancer (EOC). It is not known whether patients diagnosed with EOC who have a personal history of BC have different outcomes compared to those without a prior history of BC, or whether treatment for prior BC modulates any outcomes for subsequent EOC. This study compares progression-free (PFS) and overall survival (OS) for women with EOC to determine whether there is any difference between those with and without a personal history of BC.

Method: This is an institutional review board-approved, multiinstitutional retrospective chart review. Matched patients with a diagnosis of EOC were identified, both with and without *gBRCA* and with and without a history of breast cancer. Descriptive statistics and univariate and multivariate analyses were performed in SAS v9.4.

Results: A total of 151 patients were included in this analysis, 77 (50.6%) of whom had a history of BC. Of these 151 women, 32 (21%) had *BRCA 1* and 14 (9.2%) had *BRCA 2* mutations. The average age at diagnosis of EOC for patients with and without a history of BC was 56.9 and 59.5 years, respectively. The majority of patients in both groups were Caucasian and had stage IIIc serous EOC. Twenty-three women with a history of BC underwent chemotherapy, and 22 received radiation. There was no difference in PFS (19.2 vs 26.4 months, $P = 0.26$) between women with and without a history of BC. There was also no difference in OS ($P = 0.33$), but median time to death was not estimable as the majority of patients are currently alive with disease or have no evidence of disease. Among *BRCA+* women, there was no difference in PFS (19.2 vs 26.4 months, $P = 0.6$) between women with and without a history of BC. OS was also not different ($P = 0.5$). Among *BRCAwt* women, the median PFS was 19.2 and 26.4 months ($P = 0.3$); OS was similarly not different ($P = 0.4$).

Conclusion: A prior history of breast cancer did not have a negative impact on OS or PFS in women treated for high-grade serous ovarian cancer regardless of *BRCA* status. This analysis is matched based on *BRCA* status, and so the *BRCAwt* women are younger and may have been more aggressively cytoreduced than all-comer *BRCAwt* populations. Study in this population is warranted as is study of the treatment-related toxicity among EOC patients with a prior history of BC treatment.

476 - Poster Session

The impact of clinical trial participation on overall survival in advanced ovarian cancer patients at a single-institution cancer center

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Objective: We set out to determine whether clinical trial participation positively affects overall survival in advanced-stage ovarian cancer patients.

Method: A retrospective chart review identified 500 advanced-stage (IIIC–IVB) ovarian cancer patients treated January 1, 2001, through April 1, 2014, at a single-institution cancer center at some point in their treatment course. Demographic and clinical data were extracted from electronic medical records.

Results: A total of 373 patients (75%) did not choose to enroll in clinical trials (NCT) at any stage of treatment, and a total of 127 (25%) participated in a clinical trial (CT) at some stage of their treatment. Most patients were Caucasian (97% vs 94% in CT vs NCT). Most were stage IIIC (81% vs 79% in CT vs NCT) with serous histology the most common subtype (88% vs 83% in CT vs NCT). Most had high-grade disease (97% vs 96% in CT vs NCT). Most patients had their cytoreductive surgery performed by a gynecologic oncologist (90% vs 89% in CT vs NCT), and optimal debulking status was comparable (83% vs 82% in CT vs NCT). Platinum sensitivity was uniform among the groups (72% vs 68% in CT vs NCT). Most CT patients only participated in 1 clinical trial with a total of 89/127 (79%) trials completed. The majority enrolled for treatment in a recurrent setting with 99/127 (79%) in CT. The overall median survival was 43.03 months for NCT and 57.43 months for CT ($P = 0.0435$).

Conclusion: Clinical trial enrollment and participation may confer survival benefit for patients with advanced-stage ovarian cancer in our cohort. Encouragement for clinical trials appears to be warranted.

477 - Poster Session

Outcomes in patients who refuse initial treatment for endometrial cancer

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Objective: The purpose of this study is to characterize the outcomes of patients who refuse initial treatment for endometrial cancer.

Method: A retrospective analysis of untreated endometrial cancer patients was conducted using the National Cancer Data Base. Patients diagnosed between 2004 and 2014 with endometrial cancer who refused recommended initial treatment and did not undergo other treatments (including chemotherapy, surgery, radiation, or hormone or experimental therapy) were identified. Patients who did not receive therapy because of comorbid conditions or death prior to initiation of therapy were excluded. Patients were grouped into low-risk (grade 1 adenocarcinoma) or high-risk (grade 2/3 adenocarcinoma, clear cell, or papillary serous) cohorts. Survival was analyzed using Kaplan-Meier univariate analysis. Multivariate analyses were performed utilizing Cox proportional hazard regression for overall survival to identify factors affecting survival.

Results: A total of 506 patients were identified. Median age was 67 years (range 22–90 years). Clinical stage I, II, III, and IV accounted for 27.7%, 3.4%, 5.5%, and 20.6%, respectively, with 42.8% having unknown stage. By cohorts, 38.7% and 61.3% were considered low risk and high risk, respectively. Of the low-risk patients with stage I disease, 85% were alive at 2 years and 77.3% were alive at 5 years. Of high-risk patients with stage I disease, 66.4% were alive at 2 years and 55.6% alive at 5 years. Too few low-risk patients in stage II–IV were available to comment on survival. For high-risk patients, 54.5%, 20.2%, and 7.6% of patients were alive at 2 years for stage II, stage III, and stage IV, respectively. In univariate analysis, age ($P < 0.001$), insurance status ($P < 0.001$), treatment geographical location ($P = 0.008$), histology ($P = 0.044$), stage ($P = 0.013$), and grade ($P < 0.001$) were all associated with survival. In a multivariate Cox proportional hazard regression analysis, only age ($P < 0.001$), insurance status ($P = 0.009$), stage ($P < 0.001$), and grade ($P = 0.005$) remained independently associated with survival.

Conclusion: Patients with initially untreated endometrial carcinoma have remarkably long-term survival, even those with high-risk disease. It is possible that treatment at the time of progression may contribute to the prolonged survival seen in this cohort.

478 - Poster Session

The impact of obesity on uterine size in women with endometrial cancer

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Objective: The impact of obesity on uterine size in women with endometrial cancer has not been well characterized. In addition to the challenges of operating on obese patients, operating on larger uteri can also increase surgical complexity.

Further, large uteri may be associated with larger tumors, and tumor size has been associated with increased risk of lymph node metastasis. We aimed to explore the correlation between increasing BMI and increasing uterine size and stage.

Method: We performed a retrospective cohort study of all endometrial cancer patients treated at a large tertiary academic center from 2005 to 2010. Baseline patient characteristics were collected including BMI, age, race, stage, grade, depth of invasion, tumor size, and uterine weight. The primary outcome of interest was uterine size, which was measured by documented uterine weight in grams on pathology report. The exposure of interest was obesity. A multivariate regression model was used to assess the association between increasing BMI and uterine weight and stage.

Results: Overall, 1,139 patients were identified. Mean age was 62 (± 11.6) years. In this group, 75% ($n = 855$) were Caucasian. The mean BMI was 33.6 (± 9.16) kg/m². Overall, 81% ($n = 928$) had stage I disease. For each 1 point increase in BMI, the uterine weight increased by 37 g ($P < 0.05$, $R^2 = 0.18$). After controlling for tumor grade, tumor size, depth on invasion, and stage, the relationship remained. We found that uterine weight was associated with increased risk of upstaging. After controlling for BMI, age, and race, every 50-g increase in uterine weight had 20% increased odds of upstaging by 1 stage (OR = 1.21, 95% CI 1.13–1.30, $P < 0.05$).

Conclusion: We found an association between increasing BMI and increased uterine weight. In addition, increasing uterine weight was associated with increased cancer stage. In addition to the habitus-related challenges surgeons face operating on obese patients, they should be further aware of increased risk of large uterine size. Ultrasound may be a useful preoperative study in all obese women whose uterine size cannot be adequately assessed on examination for surgical planning.

479 - Poster Session

Behind every mammo there's an MRI: Evaluation of high-risk breast cancer screening strategies in *BRCA* mutation carriers

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Objective: Recent data suggest that *BRCA* mutation carriers younger than 40 years may not benefit from mammography in addition to MRI screening. Our objective was to evaluate screening modalities utilized in a high-risk population with regard to abnormalities and outcomes.

Method: Clinicopathologic data were abstracted for patients followed in a high-risk clinic from 2007 to 2017. Descriptive statistics were calculated, and associations between categorical variables were evaluated using χ^2 tests.

Results: Overall, 631 women constituted the study population: 496 patients had no known mutation (79%); 128 (20%) had a *BRCA1* or 2 mutation; and 7 had other deleterious mutations (1 *TP53*, 1 *PALB2*, 3 *ATM*, 2 *CHEK2*). Following screening mammogram, 237/440 (53.9%) of non-*BRCA* mutation carriers had a callback; 68 patients underwent biopsies with 9 breast cancers (BC)/DCIS diagnosed (13.2% of biopsies). Among *BRCA*-positive patients, 41/91 (45%) had a callback, and 12 (29.3%) underwent a biopsy, resulting in 6 BC/DCIS diagnoses (50%). Following screening MRI, 117/305 (38.4%) of non-*BRCA* patients were called back, and 90 (29.5%) had a biopsy with 10 BC/DCIS diagnosed (11.1% of biopsies). In *BRCA* patients, 35/94 (37.2%) had callbacks, and 26 (74.3%) had biopsies, resulting in 7 BC/DCIS diagnoses (26.9%). Patients without a *BRCA* mutation were more likely to have a mammogram callback than *BRCA* carriers ($P = 0.002$), but not for MRI callback or biopsy rates. *BRCA* mutation carriers were more likely to have an MRI-diagnosed cancer ($P = 0.03$). *BRCA* patients were diagnosed with cancer ($n = 13$) at an average age of 51 years (range 29–70 years). Of the cancers diagnosed after abnormal MRI, 3 were DCIS; in all 3 cases, the patient had a normal mammogram 4–6 months prior. In those found after abnormal mammogram ($n = 6$), follow-up MRI was performed in 4 cases; all demonstrated the lesion identified on mammogram. Three patients younger than 40 years were diagnosed, 1 on mammogram and 2 on MRI. The patient diagnosed on mammogram had no prior MRI, and the lesion was seen on follow-up MRI.

Conclusion: Interval screening MRI identified DCIS in *BRCA* patients with a previous normal mammogram, and cancers diagnosed on mammogram were all identified on follow-up MRI. These findings support further evaluation of MRI alone until age 40 years in *BRCA* mutation carriers.

480 - Poster Session

Complications of vulvar reconstruction following vulvectomy: A study of a nationwide cohort

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Objective: To determine complications associated with primary closure compared to reconstruction following excision of vulvar cancer and predisposing factors to these complications.

Method: Patients undergoing excision of vulvar cancer with or without reconstruction from 2011 to 2015 were abstracted from the National Surgical Quality Improvement Program (NSQIP) database. CPT codes were used to characterize surgical procedures as vulvar excision alone or vulvar excision with reconstruction. Patient characteristics and 30-day outcomes were used to compare the two procedures. Descriptive and univariate statistics were performed. Adjusted odds ratios and confidence intervals were calculated using a logistic regression model to control for potential confounders. Two-sided alpha with $P < 0.05$ was designated as significant.

Results: A total of 2,698 patients were identified; 78 (2.9%) underwent reconstruction. There were no differences in age, race, BMI, diabetes, hypertension, tobacco use, heart failure, renal failure, or functional status between the two groups. ASA class 3 and 4 patients and those with disseminated cancer were more likely to undergo reconstruction ($P = 0.0009$). On univariate analysis, reconstruction was associated with increased risk of readmission, surgical site infection, pulmonary complications, urinary tract infection, transfusion, deep venous thrombosis, sepsis, septic shock, unplanned reoperation, longer hospital stay, need for skilled nursing or subacute rehabilitation on discharge, and death within 30 days. On logistic regression analysis, disseminated cancer, ASA classes 3 and 4, and reconstruction remained significant risk factors for readmission and any postoperative complication (Table 1).

Conclusion: Patients undergoing excision of vulvar cancer with reconstruction are at increased risk for readmission and postoperative complications compared to those undergoing excision alone. Careful patient selection and efforts to optimize surgical readiness are needed to improve outcomes. Long-term data could help determine whether these 30-day outcomes are a reliable measure of surgical quality in vulvar surgery.

Table 1. Complications of vulvar reconstruction following vulvectomy.

Univariate Analysis				Logistic regression			
Characteristics and Complications	Excision alone <i>n</i> =2,620 (97.1%)	Excision and reconstruction <i>n</i> =78 (2.9%)	<i>P</i> -value	Readmission	<i>P</i> -value	Any postoperative complication	<i>P</i> -value
				Adjusted odds ratio (95% CI)		Adjusted odds ratio (95% CI)	
ASA class							
1	286 (10.9)	1 (1.3)	0.0009	Ref		Ref	
2		26 (33.3)		2.99 (0.70-12.83)	0.1395	1.29 (0.61-2.72)	0.5004
3	1,143 (43.6)	46 (59.0)		5.43 (1.25-23.55)	0.0237	2.20 (1.03-4.71)	0.0423
4	1,105 (42.2)	5 (6.4)		6.36 (1.26-32.24)	0.0250	2.95 (1.16-7.49)	0.0227
NA	82 (3.1)	0 (0.0)					
	4 (0.2)						
Disseminated cancer	141 (5.4)	19 (24.4)	<0.0001	2.19 (1.33-3.61)	0.002	3.28 (2.21-4.87)	<0.001
Readmission	139 (5.4)	24 (30.8)	<0.0001	5.2 (3.01-8.98)	<0.0001	4.33 (2.61-7.17)	<0.001
Superficial SSI	110 (4.2)	9 (11.5)	0.0065	0.88 (0.36-2.20)	0.7915	2.23 (1.22-4.07)	0.0091
Deep SSI	36 (1.4)	6 (7.7)	0.0011	0.97 (0.94-1.01)	0.1093	0.96 (0.93-0.98)	0.0014

Organ space SSI	18 (0.7)	6 (7.7)	<0.0001	Tobacco use	1.35 (0.89-2.06)	0.1571	1.17 (0.84-1.63)	0.3567
Wound disruption	49 (1.9)	8 (10.3)	0.0002	Age	1.01 (1.00-1.02)	0.0787	1.00 (0.99-1.01)	0.5423
Pneumonia	16 (0.6)	3 (3.9)	0.0161	BMI	1.00 (0.97-1.02)	0.7681	1.01 (1.00-1.03)	0.1034
Pulmonary embolism	9 (0.3)	2 (2.6)	0.0383	Diabetes Yes	Ref		Ref	
				No	2.13 (0.84-5.42)	0.1128	0.85 (0.50-1.42)	0.5273
				Non-insulin dependent	2.13 (0.76-5.94)	0.1485	0.79 (0.42-1.46)	0.4493
Ventilator >48 hours	14 (0.5)	3 (3.9)	0.0118	NA: None assigned SSI: Surgical site infection				
Urinary tract infection	61 (2.3)	7 (9.0)	0.003					
Transfusion	223 (8.5)	49 (62.8)	<0.0001					
Deep venous thrombosis	17 (0.7)	3 (3.9)	0.0186					
Sepsis	32 (1.2)	10 (12.8)	<0.0001					
Septic Shock	10 (0.4)	3 (3.9)	0.0054					
Unplanned reoperation	50 (2.2)	12 (17.9)	<0.0001					
Mean hospital stay (days)	2.2±5.5	16.6±17.5	<0.0001					
Need for skilled nursing	94 (3.6)	21 (27.3)	<0.0001					
Need for subacute rehab	7 (0.3)	1 (1.3)	<0.0001					
Death within 30 days	3 (0.1)	1 (1.3)	<0.0001					

481 - Poster Session

Variability in body mass index (BMI) during adjuvant chemotherapy is associated with clinical outcomes among invasive ovarian cancer patients

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Objective: Efforts to elucidate novel, modifiable prognostic factors in ovarian cancer would be highly beneficial. We investigated the association between BMI plasticity and survival during adjuvant chemotherapy in primary treatment of ovarian cancer.

Method: We utilized data from a previously collected ovarian cancer cohort to examine the association of BMI plasticity during primary adjuvant chemotherapy with progression-free (PFS) and overall survival (OS). We defined BMI plasticity as the standard deviation of multiple BMI measurements taken during chemotherapy treatment. We examined the association of BMI classification (underweight, normal weight, overweight, obese) and BMI plasticity (low variability < median vs high variability > median) with clinical characteristics. ANOVA, χ^2 , Student *t*, Kaplan-Meier, and log rank tests were used as appropriate with *P* < 0.05 considered significant.

Results: We identified 527 ovarian cancer patients meeting inclusion criteria. The average number of BMI measurements was 19. Underweight and obese patients had an earlier age of onset (*P* = 0.002). Patients with high BMI plasticity had significantly lower complete response rates to chemotherapy (63% vs 77%, *P* = 0.022). Survival analyses yielded significantly worse

outcomes among patients with high BMI plasticity than patients with low BMI plasticity for both PFS (20.3 months versus 26.3 months, $P = 0.033$) and OS (42.1 months vs 69.9 months, $P = 0.006$). In multivariate analyses, BMI plasticity was associated with disease progression (HR = 1.35, 95% CI 1.02–1.78) and death (HR = 1.59, 95% CI 1.14–2.23). BMI plasticity as a continuous variable was associated with increased hazard of death (per unit BMI, HR = 1.19, 95% CI 1.01–1.41, $P = 0.035$). See Figure 1.

Conclusion: BMI plasticity during adjuvant chemotherapy is inversely associated with PFS and OS among women with ovarian cancer. Interventions to stabilize BMI and preserve lean body mass should be investigated.

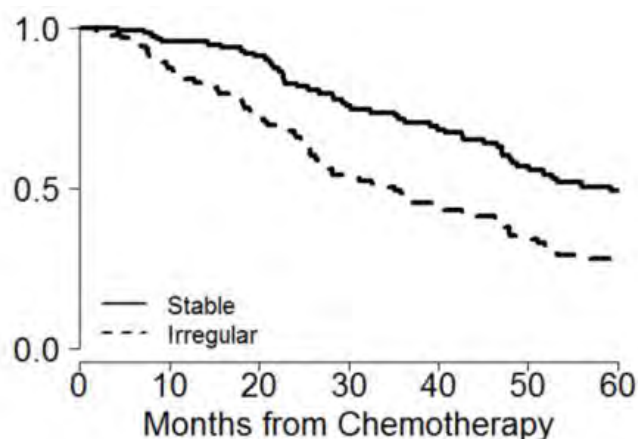


Fig. 1. Overall Survival.

482 - Poster Session

Risk prediction model for surgical site infections in patients undergoing open gynecologic cancer surgery following the implementation of a reduction bundle at a comprehensive cancer center

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Objective: A recent publication reported a significant reduction in 30-day surgical site infections (SSIs) in gynecologic cancer patients following application of a service-wide SSI reduction bundle. The objective of this study was to establish an SSI risk prediction model for patients undergoing open gynecologic cancer surgery after implementation of an SSI reduction bundle.

Method: A single institutional database was searched for patients undergoing open operative procedures for a gynecologic malignancy with colonic involvement from February 1, 2015, to July 31, 2017. Superficial, deep incisional, and organ/space SSIs within 30 days of surgery were identified and confirmed by the institution's Infection Control. Patients' preoperative and intraoperative characteristics were assessed. Boruta variable selection was performed, and Linear Support Vector Machine Learning used to model SSI prediction. The final model was internally validated using a Synthetic Minority Over-Sampling Technique (SMOTE) algorithm to account for any class imbalance or over-fitting.

Results: A total of 653 gynecologic patients were identified during the study period. SSIs were detected in 40 patients (6.13%). Type of malignancy, wound class, bowel resection, number of previous abdominal surgeries, time between room entry and surgery, operative time, time between chemotherapy and surgery, total blood loss, and number of prior admissions in the previous year were all significantly associated with SSIs on univariate analysis ($P < 0.05$). Boruta variable selection identified type of malignancy, wound class, bowel resection, and operative time as relevant variables, which were included in the model. The optimal prediction model had an accuracy of 0.72, AUC of 0.85, sensitivity of 1.0, and specificity of 0.70. After internal validation, the sensitivity remained 1.0. Figure 1 shows a predictive nomogram generated by the data.

Conclusion: This study demonstrates the development and internal validation of a risk prediction model for SSIs in patients undergoing gynecologic cancer surgery, following successful implementation of an SSI reduction bundle. Identifying patients at high risk for SSIs may facilitate individualized preoperative interventions and can be used prospectively to stratify and evaluate SSI reduction initiatives in the future.

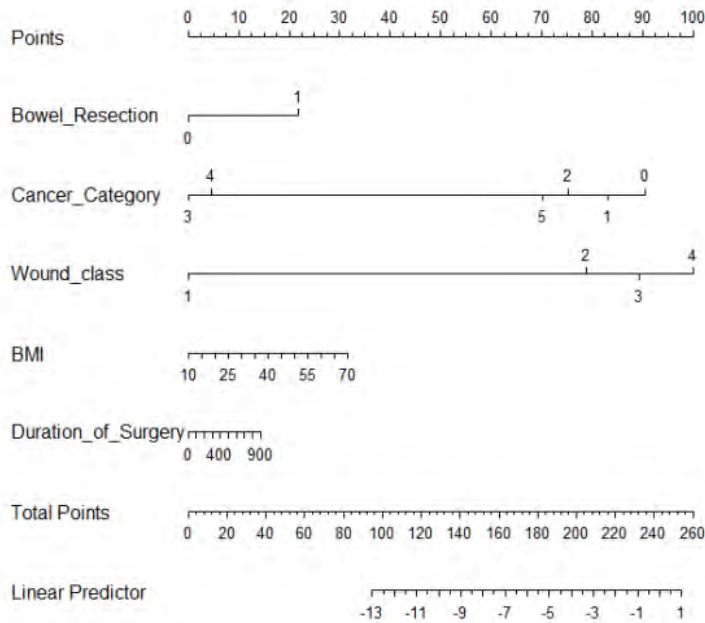


Fig. 1. SSI Risk Prediction Nomogram.

483 - Poster Session

Non-surgical patients with advanced gynecologic cancer discharged to subacute rehabilitation centers have poor prognosis and low rates of subsequent chemotherapy

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Objective: Discharge to a subacute rehabilitation center (SRC) may be recommended in the hope of improving a patient's functional status sufficiently to receive additional disease-directed therapy. We sought to characterize prognosis and rates of subsequent chemotherapy among nonsurgical patients with gynecologic cancer discharged to an SRC. If rates of subsequent chemotherapy in this population are low, this may be an appropriate population to target for advanced-care planning prior to discharge.

Method: Patients with stage III–IV or recurrent gynecologic malignancy admitted to the Kaiser Permanente Southern California health care system and discharged to an SRC over a 10-year period were included in this retrospective cohort. Patients who had surgery during their admission or who were enrolled in hospice prior to discharge were excluded. Clinical, demographic, and survival data were abstracted from the medical record. A univariate analysis was performed to identify patient characteristics that might be predictive of receiving future chemotherapy. Statistical significance was ascertained in all analyses through a Fisher exact test.

Results: A total of 35 patients met inclusion criteria. The majority were Caucasian (75%), and the median age was 70 years. The most common cancer was ovarian/peritoneal (28%), and 47% had recurrent disease. Survival after discharge ranged from 5 to 1,463 days, with a median survival of 58 days. Trends toward longer survival were seen in patients with age ≤ 75 years (60 vs 31 days, $P = 0.27$), cervical cancer (136 vs 39 days, $P = 0.11$), nonrecurrent disease (62 vs 43 days, $P = 0.69$), and a noninfectious indication for admission (62 vs 39 days, $P = 0.49$). Seven patients (20%) received additional chemotherapy after discharge. None of the examined patient or admission factors (age, primary site of malignancy, upfront vs recurrent disease, or indication for admission) was found to be predictive of future chemotherapy.

Conclusion: In this cohort of nonsurgical patients with advanced gynecologic malignancy discharged to an SRC, only 20% received additional chemotherapy, and the median survival was 58 days. This may be an appropriate population for introduction of advanced-care planning or palliative care consultation prior to discharge.

484 - Poster Session

Patient-reported outcomes in evaluation of chemotherapy toxicity in women with gynecologic malignancies

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Objective: Patient-reported outcomes (PRO) relating to treatment toxicities have been demonstrated to accurately and reliably assess adverse events in clinical trials. We assessed the feasibility, utility, and user satisfaction of implementing a focused PRO questionnaire adapted for patients with gynecological cancers undergoing chemotherapy.

Method: Patients with gynecologic cancers who are undergoing active chemotherapy were prospectively identified after institutional review board approval. We administered a novel 50-item symptoms questionnaire, adapted from the validated PRO version of the CTCAE (Common Terminology Criteria for Adverse Events), to enrolled participants at two separate treatment encounters. Following the second visit, patient/provider satisfaction was assessed with respective surveys. All data are reported by descriptive statistics.

Results: Of the 53 patients approached for the study, 45 provided consent. We report the outcome of the 6 providers and first 28 consecutive participants. The median age was 60 years (range 32–84), and patients were racially diverse: 46% Caucasian, 14% African-American, 14% Asian, and 25% other; 28% were of Hispanic origin. The majority of patients had ovarian cancer (53%), followed by uterine (21%) and cervical cancer (21%). Thirty-two percent of patients were undergoing treatment for recurrent disease, and the median chemotherapy regimen number was 2 (range 1–7). Results of the satisfaction surveys (Table 1) show 92% of patients and 100% of providers thought the PRO questionnaire addressed important symptoms, although 71% of providers thought that not all symptoms were addressed. The vast majority of patients (>90%) and 100% of providers thought the PRO questionnaire was easy to use. Importantly, 67% of patients and 100% of providers thought the questionnaire had a positive impact on clinical care; 85% of patients wished to use a questionnaire throughout treatment.

Conclusion: We have shown that adapting a focused PRO symptoms questionnaire into routine outpatient care of gynecological oncology patients undergoing chemotherapy was feasible, with a high degree of patient and provider satisfaction in content usefulness, ease of use, and perception of care improvement.

Table 1. Patient and provider responses to post-questionnaire satisfaction survey. Patient Reported Outcomes in Evaluation of Chemotherapy Toxicity in Women with Gynecologic Malignancies. Authors: Emily Webster, Hannah Ware, Bayley Jones, Reena Vattakalam, Jason D. Wright, Ana I. Tergas, William Burke, June Y. Hou. Columbia University College of Physicians and Surgeons. Columbia University Medical Center, New York Presbyterian Hospital.

Participant survey question	Participant survey response
I understood the questions asked in the survey.	
The symptoms asked about were important for me.	
Some of my symptoms were not asked about.	
The survey was easy to complete.	
The time required to complete the survey was appropriate.	
It was easy to complete the survey before I saw my doctor.	
The survey helped me talk to my doctor about my symptoms.	

The symptom survey improved my care today overall.



I would like to continue filling out this kind of symptom survey during my chemotherapy treatment.



Provider survey question

Provider survey response

The survey asked about important symptoms.



The patient had important symptoms that were not asked about.



The patient's survey results were easy to review.



The time required to review the patient's survey results was appropriate.



I had time to review the patient's survey before the visit.



The survey helped me talk to the patient about symptoms that I do not typically discuss.



The symptom survey improved my care of the patient today overall.



I would like my patients to complete a survey about their symptoms before all of their visits with me.



Green bar, strongly agree or agree. Red bar, strongly disagree or disagree. Yellow bar, unanswered or N/A.

485 - Poster Session

Insurance status does not impact surgical outcomes at a large tertiary medical center

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Objective: To determine the impact of insurance status on 30-day surgical outcomes in the treatment of gynecologic cancer.

Method: A retrospective cohort study of surgically treated gynecologic oncology patients enrolled in a large prospective cancer survivorship cohort (UNC IRB 09-0605) was performed. Patients were enrolled from May 2010 to March 2017. Inclusion criteria were (1) a diagnosis of gynecologic cancer, (2) undergoing surgical management, and (3) documentation of insurance status. The primary outcome of interest was 30-day postoperative complications, defined as Clavien-Dindo scores of 2 or higher. The exposure of interest was insurance status at time of diagnosis, classified as private (PRI), public (PUB), or no insurance/self-pay (NI/SP). Patients with multiple insurances were classified according to the best available. Logistic models were performed using SAS 9.4. Relative risks of postoperative complications were estimated using log binomial regression. Covariates of interest were hypertension, diabetes mellitus, obesity, and advanced stage.

Results: Overall, 458 patients met inclusion criteria, of which 67% ($n = 307$) had PRI; 25% ($n = 116$) had PUB; and 8% ($n = 35$) had NI/SP. Within the cohort, 17% ($n = 80$) had ovarian cancer; 66% ($n = 303$) had uterine cancer; 12% ($n = 55$) had cervical cancer; and 4% ($n = 19$) had vaginal/vulvar cancer. Median age was 59 years, and median BMI was 34 kg/m². NI/SP patients were the youngest (49 years), while PUB were the oldest (67 years) ($P < 0.0001$). All insurance types had similar rates of postoperative complications (16% PRI, 16% PUB, 14% NI/SP). Compared to PRI patients, there was no increased risk of 30-day postoperative complications with NI/SP patients (relative risk 0.99, CI 0.4–2.3, $P = 0.98$) or PUB patients (relative risk 1.03, CI 0.6–1.7, $P = 0.90$). The risk of 30-day postoperative complications was also similar between PUB and NI/SP patients (relative risk 0.96, CI 0.4–2.4, $P = 0.93$).

Conclusion: Insurance status and 30-day postoperative complications had no association in this cohort of gynecologic cancer patients treated at a large state hospital. Providing care regardless of ability to pay results in equivalent surgical outcomes, meaning payer status had no impact on quality of care. A single-payer model could provide similar equity of surgical outcomes nationally.

486 - Poster Session

Co-occurring substance use disorder: The impact on treatment adherence in women with locally advanced cervical cancer treated at an academic center

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Objective: Substance use disorder (SUD) has been suggested to have an impact on adherence to treatment and adversely affect outcomes in cancer patients. The purpose of this study is to identify the prevalence of SUD and its effect on adherence to treatment in locally advanced cervical cancer patients treated with primary radiation therapy (RT). In addition, the effect of SUD on survival was measured.

Method: This is a retrospective cohort study of all locally advanced cervical cancer patients in a single academic institution treated with RT between 2005 and 2017. SUD was identified through chart review and included treated and/or problematic use of alcohol, opiates, cocaine, or other illicit drugs. Those with SUD were compared to remaining patients for demographics, Charlson comorbidity index (CCI), treatment details, and outcomes using the Student t test and χ^2 tests.

Results: Of the 129 patients included, 12.4% were identified as having SUD. Most commonly reported substances were stimulants (87.5%), alcohol (37.5%), and opiates (18.8%). Half of those with SUD reported polysubstance use. Patients with SUD were younger (42.1 years vs 51.5 years, $P = 0.013$) and more likely to be smokers (81.3% vs 42.5%, $P = 0.004$). There were no significant differences between groups in BMI, race, insurance status, marital status, or CCI. The vast majority of patients with SUD received concurrent chemotherapy (93.8%) and brachytherapy in addition to teletherapy (81.3%). There was no significant difference in days to completion of RT between patients with and without SUD. The radiation dose received and grade 3 toxicities were similar between groups. Progression-free and overall survival (HR = 1.36, 0.69–2.68 and HR = 1.55, 0.78–3.05) for recurrence and death, respectively, were similar between groups. See Table 1.

Conclusion: In cervical cancer patients being treated with RT, SUD was not associated with longer radiation treatment times or a difference in total dose of radiation received. These data demonstrate that patients with SUD are able to adhere to complex, multimodal treatment plans resulting in similar cancer-specific outcomes compared to patients without SUD.

Table 1. Comparison of demographic and clinical characteristics by type of radiation toxicity.

Characteristic	Total cohort $n = 185$	Patients with toxicity		
		Any toxicity (AT) $n = 40$	GI toxicity (GIT) $n = 33$	GU toxicity (GUT) $n = 20$
Age (years), mean \pm SD	49.1 \pm 14.1	48.4 \pm 14.1	47.8 \pm 13.5	45.4 \pm 12.6
Body mass index (kg/m ²), mean \pm SD	27.8 \pm 9.4	24.6 \pm 8.0 *	24.4 \pm 8.2*	22.8 \pm 7.2*
Race, n (%)				
White	88 (47.5%)	25 (62.5%)*	20 (60.6%)	13 (65%)
Non-white	97 (52.4%)	15 (37.5%)	13 (39.3%)	7 (35%)
Insurance, n (%)				
Private	39 (21.1%)	10 (25%)	10 (30.3%)	2 (10%)
Federal or uninsured	146 (78.9%)	30 (75%)	23 (69.7%)	18 (90%)
Marital status, n (%)				
Married	51 (27.7%)	14 (35%)	12 (36.4%)	5 (25%)
Not married	133 (72.3%)	26 (65%)	21 (63.6%)	15 (75%)
Smoking status, n (%)				
Never or former	101 (56.1%)	16 (41%)	14 (42.4%)	8 (42.1%)
Current smoker	79 (43.9%)	23 (59%)*	19 (57.6%)	11 (57.9%)
Charlson comorbidity index quartile, n (%)				
0	71 (38.6%)	18 (45%)	14 (42.4%)	10 (50%)
1 to 2	67 (36.4%)	13 (32.5%)	12 (36.4%)	7 (35%)

3 to 4	24 (13%)	6 (15%)	4 (12.1%)	2 (20%)
≥ 5	22 (12%)	3 (7.5%)	3 (9.1%)	1 (5%)
Tumor stage, n (%)				
Early stage (FIGO stage 1A-1B1)	30 (16.3%)	7 (17.9%)	6 (18.8%)	3 (15%)
Locally advanced (FIGO stage IB2 to IVA)	144 (78.3%)	32 (82.1%)	26 (81.2%)	17 (85%)
Metastatic (FIGO stage IV)	10 (5.4%)	0 (0%)	0 (0%)	0 (0%)
Tumor histology, n (%)				
Squamous	162 (87.6%)	35 (87.5%)	28 (84.9%)	18 (90%)
Adenocarcinoma	16 (8.6%)	5 (12.5%)	5 (15.2%)	2 (10%)
Other	7 (3.8%)	0 (0%)	0 (0%)	0 (0%)
Radiation timing, n (%)				
Primary	152 (82.2%)	32 (80%)	26 (78.8%)	16 (80%)
Adjuvant	33 (18.1%)	8 (20%)	7 (21.2%)	4 (20%)
Total radiation dose (Gy), mean ± SD	75.6 ± 20.2	79.7 ± 17.5	81.2 ± 17.3*	79.9 ± 19.8
Time to complete treatment (days), mean ± SD	54.6 ± 22.5	56 ± 22.7	55.1 ± 22.9	55 ± 23.1
External beam radiation therapy, n (%)				
3-dimensional conformal therapy	113 (84.3%)	26 (89.7%)	21 (91.3%)	14 (87.5%)
Intensity-modulated radiation therapy	21 (15.7%)	3 (10.3%)	2 (8.7%)	2 (12.5%)
Brachytherapy, n (%)				
Low dose rate	77 (57.5%)	15 (55.6%)	12 (52.2%)	6 (42.9%)
High dose rate	57 (42.5%)	12 (44.4%)	11 (47.8%)	8 (57.1%)
Concurrent chemotherapy, n (%)				
Yes	158 (85.4%)	35 (87.5%)	30 (90.9%)	18 (90%)
No	27 (14.6%)	5 (12.5%)	3 (9.1%)	2 (10%)
All treatment performed with the institution, n (%)				
Yes	168 (90.8%)	32 (80%)	27 (81.2%)	15 (75%)
No	17 (9.2%)	8 (20%)*	6 (18.2%)*	5 (25%)*
Progression free survival (months)	30.8	23.2	22.9	50.5
Risk of Recurrence (95% CI)		1.34 (0.85-2.13)	1.50 (0.92-2.43)	0.85 (0.44-1.66)
Overall survival (months)	40.6	37.8	35.1	43
Risk of Death		1.40 (0.89-2.19)	1.52 (0.95-2.43)	0.98 (0.54-1.77)
*P < 0.05				

487 - Poster Session

An opportunity lost: Low rates of fertility counseling in pathogenic *BRCA* mutation carriers

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Objective: The identification of a pathogenic *BRCA* mutation can have a profound impact on family planning for women of reproductive age. Appropriate counseling, including information on family planning and the available assisted reproductive technology (ART), provides important options for patients and their families. Our institution has a large reproductive endocrinology and infertility (REI) group and is a national referral center for ART. Our objective was to evaluate the rates of fertility counseling and referrals to REI in patients with known pathogenic *BRCA* mutations at our institution.

Method: We performed a retrospective chart review of pathogenic *BRCA* mutation carriers in a single institution between August 2012 and September 2017. Exclusion criteria were history of risk-reducing salpingo-oophorectomy (RRSO), known ovarian cancer, or age older than 50 years. Statistical analyses were performed with χ^2 and Mann-Whitney *U* tests.

Results: A total of 303 women met inclusion criteria. Fertility counseling was done for 131 patients (43%), and 75 (25%) referrals were made to REI. Of these, 25 (8%) patients met with an REI provider. Gynecologic oncologists performed fertility counseling in 60% of cases, with referral to REI 32% of the time. A gynecologic oncologist was significantly more likely to discuss fertility-related issues than other specialists ($P < 0.001$). Women younger than 40 years were more likely to receive fertility counseling and REI referral than women over 40 ($P = .006$ and $P < 0.001$, respectively). Rates of fertility counseling and referral to REI were higher in nulliparous versus multiparous women ($P = 0.01$ and $P < 0.001$, respectively). See Table 1.

Conclusion: Less than half of women with pathogenic *BRCA* mutations received fertility counseling. Gynecologic oncologists were more likely to initiate these discussions with patients and to refer them to REI than other specialists. While cost and ethical issues may be barriers to ART, measures to improve provider engagement around fertility issues should be considered.

Table 1.

	Fertility Discussion		
	Yes	No	
Age <i>n</i> (%)			
<40	88 (45%)	108 (55%)	$P = 0.006$
>40	13 (23%)	44 (77%)	
Parity <i>n</i> (%)			
Nulliparous	69 (46%)	82 (54%)	$P = 0.01$
Multiparous	46 (36%)	83 (64%)	
Provider <i>n</i> (%)			
Gynecologic Oncologist	93 (50%)	92 (50%)	$P < 0.001$
Gynecologist	12 (17%)	59 (83%)	
Medical Oncologist	20 (19%)	87 (81%)	
Surgical Oncologist	9 (4%)	212 (96%)	
Number of providers seen median (range)	2 (1-4)	1.5 (1-4)	$P < 0.001$

488 - Poster Session

Variation in unplanned readmission associated with the surgical management of women with ovarian cancer

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Objective: To examine variation among hospitals in readmission rates after ovarian cancer surgery, identify potential risk factors for readmission, and assess the direct medical costs of these readmissions.

Method: We performed a retrospective cohort study of women with ovarian cancer who underwent surgery from January 2007 to March 2014 using the Premier Perspective database. The primary outcome was readmission to acute care hospitals within 90 days of discharge from the index discharge. To define planned readmission, we followed an algorithm developed by the Centers for Medicare & Medicaid Services. Diagnosis during readmission was examined with ICD-9 codes. We constructed a multivariable mixed effects logistic regression model that included clinical and nonclinical factors that were a priori considered likely to affect readmissions. Factors were considered for entry into the model on the basis of face validity and a literature search to identify factors previously shown to be associated with surgical readmissions.

Results: A total of 14,734 patients from 227 hospitals were included in the analysis. The 30-day, 60-day, and 90-day postoperative readmission rates were 8.8% ($n = 1,303$), 11.8% ($n = 1,739$), and 13.5% ($n = 1,994$), respectively. The most common diagnosis during readmission was gastrointestinal complication (18.2%), followed by infection (13.8%) and pulmonary and renal problems (both 11.7%). On the patient level, year of index admission, age of patient, comorbidity of patient, number of procedures performed during the index admission, complication score for the patient during the index admission, index admission length of stay, psychological issues for the patient, and whether a laparotomy was performed were

all significantly related. One hospital variable, geographic region, was significantly related. Without adjusting for any covariates, variation on the log odds scale was 0.17 (se 0.037, $P < 0.0001$), indicating significant variation in readmission rates among the hospitals. The final model incorporating the factors noted above reduced this variation to 0.10 ($P < 0.0001$), indicating a 38.9% reduction in variation.

Conclusion: The burden of readmissions after ovarian cancer surgery is high. Patient and hospital factors explain a substantial part of the unadjusted variation in the 90-day readmission rates.

489 - Poster Session

Role of human papillomavirus status after loop electrical excision procedure for high-grade cervical intraepithelial neoplasia

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Objective: We aimed to conduct an observational study for long-term outcomes and human papillomavirus (HPV) genotype changes after cervical loop electrical excision procedure (LEEP) for high-grade cervical intraepithelial neoplasia (HG-CIN).

Method: We conducted a prospective observational study among patients with newly diagnosed HG-CIN before LEEP (group new, N) and those who had undergone LEEP at Chang Gung Memorial Hospital without hysterectomy and were willing to participate from the point of signing informed consent (group previous, P). Cervical cytology and HPV testing were performed every 6 months. The long-term outcomes were analyzed.

Results: A total of 526 eligible patients (group N, $n = 208$; group P, $n = 318$) were enrolled between June 1, 2008, and December 31, 2014. The median age of the participants was 41.2 years (range 20–84 years). The median follow-up was 63.1 months (range 0–279.6 months). HPV was detected in 90.6% of the formalin-fixed paraffin-embedded tissue of HG-CIN. The leading HPV types were HPV16 (30.2%), HPV52 (20.1%), HPV58 (15.3%), HPV33 (8.2%) and HPV18 (7.1%). During the follow-up period, 340 women (64.6%) had at least 1 positive HPV test. Eighty-one cases had recurrences of CIN grade 2 or more severe (CIN2+); that is a 5-year cumulative recurrence rate of 13.6%. The median time between initial HG-CIN diagnosis and recurrence/progression was 19.4 months (range 3.2–209 months), with 23.5% having recurrent CIN2+ more than 5 years after LEEP. Among the 81 cases, 31 cases had HPV genotyped in paired tissues of initial diagnosis and recurrences. Fourteen (54.8%) of the 31 with paired HPV results had type-specific persistent HPV infection, while the other 17 (54.8%) had discrepant HPV types, and 6 (19.4%) harbored new high-risk HPV genotypes.

Conclusion: Late recurrences of CIN2+ after LEEP are not uncommon. Since new oncogenic HPV infections are a significant threat, vaccination against the remaining high-risk types could be considered in care of these women.

490 - Poster Session

Postoperative nomogram for the prediction of disease recurrence in lymph node-negative early-stage cervical cancer patients treated with radical hysterectomy

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Objective: The aim of the study was to develop a postoperative nomogram for the prediction of disease recurrence in lymph node-negative FIGO stage IB–IIA cervical cancer patients treated with radical hysterectomy.

Method: A total of 293 lymph node-negative FIGO stage IB–IIA cervical cancer patients who underwent radical hysterectomy with retroperitoneal lymphadenectomy between February 2000 and July 2016 were included. Disease-free survival (DFS) was defined as the clinical endpoint, and DFS probabilities were estimated using the Kaplan-Meier method. Based on the results of multivariate Cox proportional hazard regression analyses and previous studies, relevant covariates were identified. Postoperative nomogram was constructed using bootstrap cross-validation. Predictive accuracy was assessed with the concordance probability.

Results: The median follow-up time was 58 months (range, 6–202 months); 5-year DFS rate for all patients was 86.9%. Thirty-six patients (12.3%) developed a disease recurrence. FIGO stage, tumor size on magnetic resonance imaging, tumor grade, histology, parametrial margin, vaginal cuff margin, and endomyometrial infiltration were selected as nomogram

covariates. The time-dependent optimism-corrected c-index was 0.737 (95% CI 0.648–0.821), indicating accurate prediction of DFS. The DFS nomogram calibration plot appears to be relatively accurate, within the actual outcomes.

Conclusion: Based on 7 parameters, a novel statistical model to predict DFS in lymph node-negative FIGO stage IB–IIA cervical cancer patients was constructed. The nomogram assists clinicians in assessing individual patients' prognosis and follow-up strategies.

491 - Poster Session

Impact of physical inactivity on risk of developing highly fatal ovarian cancer: Evidence from the Ovarian Cancer Association Consortium

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Objective: Previous research on the etiology of ovarian cancer has largely been driven by study populations of patients who responded to front-line therapy and survived their disease for at least 2 years. In this study, we evaluated the impact of physical inactivity on the risk of highly fatal ovarian cancer in women who participated in epidemiological studies in the Ovarian Cancer Consortium Association (OCAC) across the globe.

Method: We assessed highly fatal ovarian cancer in two ways: first, we limited the patient group to those who died within 12 months from the date of diagnosis, and second, we evaluated these associations among patients who died within 18 months. Ovarian cancer patients who died within 12 months included 279 women, age-matched to 1,682 controls. Furthermore, data were available for 640 patients with ovarian cancer and 3,565 controls for the 18-month analyses. Physical inactivity was defined as those who did not engage in moderate or vigorous recreational activity. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Relative to controls for the 12-month pooled participants, those who died within 12 months had significantly higher odds of no recreational physical activity of almost 50% (OR = 1.47, 95% CI 1.22–1.92). A similar trend was observed for those who died within 18 months (OR = 1.49, 95% CI 1.24–1.80).

Conclusion: Our findings suggest that not engaging in regular recreational physical activity is associated with a highly fatal phenotype of ovarian cancer. These associations are more pronounced than those observed among the general population of ovarian cancer patients. To our knowledge, this is the first well-powered study investigating the association between physical inactivity and risk of dying from highly fatal ovarian cancer. In fact, our study not only has identified the dreadful consequences of abstinence from regular physical activity, but also has pointed to the possibility of new phenotypes of ovarian cancer that might even carry a unique etiology. More investigation is warranted to understand this phenomenon using prospectively collected data to possibly identify the level of required physical activity to minimize the risk of dying from ovarian cancer.

492 - Poster Session

The increasing incidence of uterine cancer in the United States: Who is at greatest risk?

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Objective: To determine the trend and incidence of uterine cancer in the United States and identify specific populations at risk.

Method: Data were extracted from the American Cancer Society (ACS) and the United States Cancer Statistics (USCS) from 2001 to 2014. Age-specific and -adjusted incidences and trend analyses were performed using SEER*Stat and Joinpoint regression.

Results: Based on ACS data, the estimated number of new uterine cancers has steadily increased from 38,300 in 2001 to 61,380 in 2017 with a corresponding increase in mortality from 6,600 to 10,920. Using USCS data to determine special populations at risk, we identified 607,363 patients from 2001 to 2014. Of these patients, 476,382 were white (78.4%); 59,085

black (9.7%); 45,315 Hispanic (7.5%); 18,425 Asian or Pacific Islander (3.0%); and 8,156 other/unknown (1.3%). The age-adjusted incidence (per 100,000) was highest in whites, 25.6 (vs blacks 23.1, Hispanics 20.6, and Asians 16.9, $P < 0.05$). In the overall group, the age-specific incidence (per 100,000) was highest at 98.9 in the 65–69 age group. Based on region in the United States, the age-adjusted incidence was greatest in the Northeast at 30.0 compared to the Midwest at 27.3, West at 22.9, and South at 21.3 ($P < 0.05$). In a subset analysis of whites, we found the peak age to be 65–69 years with an age-specific incidence of 100.9. Furthermore, whites had the greatest incidence at 31.5 in the Northeast compared to only 27.8, 23.8, and 21.5 in the Midwest, West, and South, respectively ($P < 0.05$). A trend analysis of the overall study group demonstrated that the annual percentage increase from 2001 to 2012 was 2.5%, 2.0%, 1.4%, and 1.0% for blacks, Asians/Pacific Islanders, Hispanics, and whites, respectively ($P < 0.05$).

Conclusion: Over the last 14 years, there has been a near 2-fold increase in the estimated number of new uterine cancers per year in the United States. Whites aged 65–69 years and residing in the Northwest appear to be at the highest risk.

493 - Poster Session

Should young obese women with endometrial cancer retain their ovaries to avoid menopausal symptoms?

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Objective: Obesity increases the risk of endometrial cancer (EC) because of increased peripheral estrogen production. However, how obesity affects menopausal symptoms after EC surgery is unknown. Our aim was to better understand the impact of BMI on symptoms of surgical menopause.

Method: After institutional review board approval, a cross-sectional review of surgically staged EC patients from January 1, 2000, through December 31, 2014, was performed. Inclusion criteria were stage I disease, age <50 years, removal of both ovaries at the time of staging, and no previous menopausal symptoms. Self-reported menopausal symptoms abstracted from the medical record included hot flashes, mood changes, fatigue/sleep disturbances, or sexual dysfunction/vaginal dryness that occurred within 12 weeks postoperatively. Symptoms were classified as severe if treatment was prescribed or mild if treatment was declined. Univariate analysis was performed with ANOVA and χ^2 tests when appropriate. Relative risks were generated from Poisson regression models. Covariates for multivariate analysis included age, BMI, and preoperative antidepressant use.

Results: We identified 166 patients. A BMI of <30, 30–39.9, 40–49.9, and ≥ 50 kg/m² occurred in 33 (19.9%), 49 (29.5%), 50 (30.1%), and 34 (20.5%) patients, respectively. There was no difference in race, age, or adjuvant treatment among the groups (Table 1). Overall, 65 (39.2%) of women reported symptoms of surgical menopause, including 19 (11.4%) mild and 46 (27.7%) severe. The most common type was hot flashes (78.5%), followed by sexual dysfunction/vaginal dryness (33.8%), mood changes (16.9%), and fatigue/sleep disturbances (9.2%). Symptom type did not differ by BMI; however, the frequency of severe menopausal symptoms decreased with increasing BMI: <30 kg/m² (45.5%), 30–39.9 kg/m² (30.6%), 40–49.9 kg/m² (22%), and ≥ 50 kg/m² (14.7%); $P = 0.002$. Multivariate analysis confirmed that compared to women with a BMI of <30 kg/m², those with a BMI 40–49.9 kg/m² were significantly less likely to experience menopausal symptoms, RR = 0.39 (95% CI 0.17–0.87). This effect was even more pronounced for women with a BMI ≥ 50 kg/m², RR = 0.24 (95% CI 0.08–0.70).

Conclusion: Women with BMI >40 kg/m² and stage I EC are significantly less likely to experience menopausal symptoms within 12 weeks after surgical staging, and these findings can assist in preoperative counseling.

Table 1. Clinicodemographic Factors.

BMI (kg/m ²)	<30 (n = 33)		30-40 (n = 49)		40-50 (n = 50)		≥50 (n = 34)		P-value
Mean Age (yr)	44.5 ±3.6		42.1 ±5.1		42 ±5.1		42.1 ±6.9		0.14
Race									
White	29	87.88%	40	81.63%	42	84.00%	29	85.29%	0.89
Black	3	9.09%	7	14.29%	4	8.00%	4	11.76%	0.76
Asian	1	3.03%	1	2.04%	0	0.00%	0	0.00%	0.52
Other	0	0.00%	1	2.04%	4	8.00%	1	2.94%	0.83

Stage									
1A	32	96.97%	46	93.88%	46	92.00%	33	97.06%	0.90
1B	1	3.03%	3	6.12%	4	8.00%	1	2.94%	0.69
Adjuvant Therapy									
Chemo	1	3.03%	0	0.00%	0	0.00%	0	0.00%	0.26
RT	1	3.03%	0	0.00%	0	0.00%	0	0.00%	0.26
Chemo / RT	0	0.00%	2	4.08%	1	2.00%	0	0.00%	0.45
Severity of menopausal symptoms									
Severe	15	45.45%	15	30.61%	11	22.00%	5	14.71%	0.005
Mild	3	9.1%	7	14.3%	6	12.00%	3	8.82%	0.16
None	15	45.45%	27	55.10%	33	66.00%	26	76.47%	0.003
Symptom Type									
Hot flashes	13	72.22%	16	72.73%	15	88.24%	7	87.50%	0.54
Mood	2	11.11%	6	27.27%	2	11.76%	1	12.50%	0.47
Fatigue / sleep disturbance	1	5.56%	3	13.64%	2	11.76%	0	0.00%	0.63
Sexual dysfunction / vaginal dryness	7	38.89%	10	45.45%	3	17.65%	2	25.00%	0.28
Recommended Treatment									
Anti-Depressant	6	40.00%	9	60.00%	6	54.55%	3	60.00%	0.55
Vaginal estrogen	5	33.33%	4	26.67%	0	0.00%	1	20.00%	0.01
Systemic estrogen	4	26.67%	2	13.33%	5	45.45%	1	20.00%	0.34

BMI: body mass index, chemo: chemotherapy, Kg: kilogram, m: meter, n: number, *P*-value: significant at < 0.05, RT: radiation therapy, yr: years

494 - Poster Session

Utilization of complementary and alternative medicine (CAM) in gynecologic oncology patients

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Objective: To assess the attitudes and beliefs about complementary and alternative medicine (ABCAM) among gynecologic oncology patients and determine whether the use of complementary and alternative medicine varies with race and socioeconomic status.

Method: A validated ABCAM instrument using a 5-point Likert-type response scale was distributed to patients with a diagnosis of a gynecologic malignancy treated at two affiliated institutions. Survey results were evaluated using χ^2 or Fisher exact tests as appropriate for category size.

Results: A total of 111 patients completed the ABCAM instrument: 45 patients with ovarian cancer; 37, uterine cancer; 20, cervical cancer; and 9, vulvar/vaginal cancer. The cohort comprised 30 white patients, 30 Hispanic, 25 Asian, 15 black, 9 other, and 2 American Indian/Alaskan. Seventy-two patients reported annual income less than \$30,000; 16 patients, \$31,000–\$50,000; 7 patients, \$51,000–\$100,000; and 16 patients, greater than \$100,000. Seventeen percent ($n = 19$) of patients reported having used complementary and alternative medicine. Non-white patients were less likely to use complementary and alternative medicine than white patients (11% vs 33%, $P = 0.01$). Age, socioeconomic status, level of education, family support, cancer type, and treatment with chemotherapy or radiation therapy were not associated with use of complementary and alternative medicine. Patients who did not have family support in dealing with their cancer were more likely to report that they did not have enough time to go to complementary and alternative medicine treatments. “Not sure” was the most commonly provided response to questions on expectations of complementary and alternative medicine and hesitancy about using it. Twenty-eight percent ($n = 37$) of patients agreed or strongly agreed that their health care providers encourage use of

complementary and alternative medicine, and 34% ($n = 45$) that their health care providers are open to complementary and alternative medicine. Patients who agreed or strongly agreed that their health care providers encouraged complementary and alternative medicine were not more likely to report using it than those patients who did not report this encouragement (47% vs 53%). See Table 1.

Conclusion: Only 17% of our population reported using complementary and alternative medicine, and utilization was even lower among non-white patients (11%). The majority of patients did not agree that their health care providers encourage complementary and alternative medicine, and its use was not higher among patients who did report encouragement by their providers.

Table1.

	Strongly disagree (N, %)		Disagree (N, %)		Not sure (N, %)		Agree (N, %)		Strongly agree (N, %)	
I expect using CAM will....										
Decrease my emotional distress	3	3	9	8	54	49	33	30	12	11
Reduce symptoms such as pain or fatigue related to cancer and its treatments	5	5	9	8	46	41	34	31	17	15
Prevent future development of health problems	5	5	6	5	60	54	24	22	16	14
Help me cope with the experience of having cancer	5	5	4	4	49	44	35	32	18	16
I am unlikely or hesitant about using CAM because...										
May interfere with the conventional cancer treatments	11	10	27	24	58	52	11	10	4	4
Treatments may have side effects	10	9	21	19	57	51	20	18	3	3
Treatments cost too much money	6	5	22	20	59	53	18	16	6	5
It is hard to find good CAM practitioners	4	4	18	16	57	51	25	23	7	6
I don't have time to go to CAM treatments	11	10	38	34	41	37	15	14	6	5
I don't have knowledge about CAM treatments	9	8	22	20	39	35	31	28	10	9
I don't have transportation to CAM treatments	10	9	35	32	40	36	16	14	10	9
Factors that influence decisions regarding CAM										
My health care providers (e.g. doctors, nurses, etc.) encourage me to use CAM	2	2	18	16	54	49	31	28	6	5
My health care providers (e.g. doctors, nurses, etc.) are open to my use of CAM	2	2	3	3	61	55	38	34	7	6
Other cancer patients think I should use CAM	3	3	10	9	80	72	10	9	8	7
My online support group encourages me to use CAM	6	5	10	9	80	72	9	8	5	5

495 - Poster Session

Hospice utilization in advanced cervical malignancies: An analysis of the national inpatient sample

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Objective: Hospice services are demonstrated to improve quality of life for patients and caretakers. The objective is to identify factors associated with in-hospital death versus hospice discharge in patients with advanced cervical cancer.

Method: Admissions of patients with a diagnosis of cervical cancer who either were discharged to hospice or died in-hospital were identified from 2007 to 2011 in the National Inpatient Sample. Monte Carlo simulation and logistic regression models were used to examine the differences in demographic and clinical factors between these two groups. Variables considered include age, race, primary payer, hospital region, hospital control (public vs private), admission type, hospital bedsize, hospital teaching status, and Elixhauser comorbidity index score.

Results: A total of 2,084 admissions with a diagnosis of cervical cancer resulting in hospice discharge ($n = 1,292$) or in-hospital death ($n = 792$) were identified. The Monte Carlo simulation identified 5 variables with nonrandom outcome distribution: age, hospital bed size, race, hospital region, and Elixhauser comorbidity index score. Logistic regression with dummy coding was performed. For categorical variables, the largest group was set as a reference including white ethnicity, large hospital bed size, location in the southern United States, and age range 51–60 years. The odds ratio (OR) of in-hospital death in the western United States was 5.14 (95% CI 3.50–7.55) and 1.52 in the Northeast (95% CI 1.13–2.04) compared to the South. Women age 41–50 years had an OR of 0.638 (95% CI 0.45–0.90) of in-hospital death. Per increase in Elixhauser comorbidity score, OR of hospital death decreased by a factor of 0.853 (95% CI 0.79–0.92). Primary payer status, public or private hospital, and hospital teaching setting did not have a statistically significant impact on disposition.

Conclusion: The modalities of care in terminal cervical cancer vary geographically with comparatively lower rates of hospice usage among patients in the northeastern and western United States, as well as among a younger and healthier patient population. These data underscore the continued push for improved end-of-life care among all cervical cancer patients, and can guide clinicians in appropriate targeted counseling to increase utilization of hospice resources.

496 - Poster Session

Weight Loss 4 Wellness: A weight loss pilot study in a predominantly breast and gynecologic cancer survivor population

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Objective: Patient-centered lifestyle interventions are a necessity to combat obesity in cancer. The purpose of the study was to evaluate the effect of an intense group-based lifestyle intervention on promoting weight loss and positive changes in quality of life and body image perception in a predominantly breast and gynecologic cancer survivor population.

Method: The 6-month lifestyle intervention titled Weight Loss 4 Wellness (WL4W) was implemented in 2014 at our local Cancer Wellness Center. WL4W meetings were held weekly for the first half of the program and subsequently every other week. The schedule of lectures and activities is listed in Table 1. Participants' weights were logged weekly; daily exercise/food logs were maintained. Quality of life surveys (FACT-G) and body image surveys (Social Physique Anxiety Scale [SPAS]) were completed at the beginning, middle, and end of the program. Traditional statistical analyses were used to evaluate changes in quality of life and body image and to evaluate weight loss.

Results: A total of 49 cancer survivors participated in 1 of the 4 programs in 2014 and 2016. The median age was 65 years. Half of the patients had early-stage disease. Nearly half of the participants were breast cancer survivors, and 14 (28.6%) were survivors of a gynecologic cancer. Median weight gain during treatment was 10–20 pounds, and median desired loss was more than 30 pounds. The dropout rate was 14 (28.6%). Participants who lost weight (57.1%) experienced a mean weight loss of 9.3 pounds (range 0.1–35.6 pounds). Of those who lost weight, 58.6% lost 5 or more pounds; 34.9% lost at least 5% of their body weight. Weight loss was positively associated with number of sessions attended ($P = 0.0349$). For those who lost weight, Hart score improved from a mean of 41.0 to a mean of 38.2 ($P = 0.0407$), and FACT-G score improved from a mean of 75.3 to a mean of 77.6 ($P = 0.0478$).

Conclusion: WL4W participants lost weight, which was correlated with consistent program attendance. Weight loss was associated with improvements in wellness (Fact-G) and body image (SPAS). An intensive weekly or biweekly group session lifestyle intervention can promote weight loss, create a positive change in quality of life, and alter body image perception in breast and gynecologic cancer survivors.

Table 1. Weight Loss 4 Wellness Curriculum/Schedule.

Session	Topic
Session 1	Introduction to Program *Surveys*
Session 2	Exercise for Cancer Class-Wear exercise clothes
Session 3	Oncology Dietitian
Session 4	Planning and Scheduling- Field Trip to Grocery Store
Session 5	Mindfulness, Triggers and Highjackers
Session 6	Sleep and Weight Management
Session 7	Mindful Walking *meet at Northbrook Court*
Session 8	Metabolism
Session 9	Yoga class-wear comfy clothes
Session 10	Special Event: Evening of Wellness* Surveys*
Session 11	Emotional Eating
Session 12	Stress Reduction
Session 13	Telling Others and Staying Strong
Session 14	Socializing Successfully – Eating Out/Field trip
Session 15	Exercise for Cancer class- Wear exercise clothes
Session 16	Culinary Tips
Session 17	Slip Ups and Relapses – Navigating the Holidays Healthfully
Session 18	Plateaus
Session 19	Outdoor (or Indoor) Walking
Session 20	Keeping the Momentum *Surveys*

There was a total of 20 sessions. Each session involved information on ways to help with weight loss/management and overall wellness. Meetings were held weekly for the first half of the program and then biweekly for the remainder of the program. Recognition was given for weight loss and attendance goals. Interaction among group members during and between sessions was encouraged.

497 - Poster Session

Do we understand patients' supportive care needs? Validation and results of a novel needs assessment tool for gynecologic oncology patients

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Objective: Understanding supportive care needs of women with gynecologic malignancies is essential. Providers may assume knowledge of these patients' specific needs, and there are minimal data for this population. The purpose of this study is to assess supportive care needs of gynecologic oncology patients by creating and validating a novel survey instrument.

Method: A 40-item self-administered survey instrument was created. Institutional review board permission was obtained, and 100 surveys were administered at 1 site over 1 year to determine face validity. The surveys were then modified and reviewed by a licensed social worker, psychologist, and integrative medicine physician. Surveys were then administered to a cross-sectional sample of patients from 3 diverse academic gynecologic oncology practices for 6 months. Baseline age, disease site, and treatments given were collected from the medical record for comparison.

Results: Surveys were given to 279 patients (during survivorship or active treatment visits) at 3 sites. The response rate was 65%–94% depending upon site. Most patients correctly identified their disease site (201 of 260, 77%) and treatments utilized (225 of 257, or 87%, identified surgery and chemotherapy; 236 of 257, or 91%, reported radiation correctly). However, only 144 of 255 patients (56%) identified their stage correctly. With respect to symptoms, only 32 of 264 patients (12%) had pain, but 107 of 223 (48%) admitted to inadequate pain control. Patients reported significant worry about recurrence (118 of 264, 45%). They were less likely to admit to any sexual dysfunction including pain during sex or decreased sex drive and were less likely to utilize mind-body techniques. Most patients did not report utilizing support groups (94%), and only 47 of 263 (17.8%) were interested in going to a support group. Dietary changes and supplement use were highly reported across all

sites (133 of 256, 52%, and 93 of 249, 37.3%, respectively), and there was significant interest in supplements (36%) and nutrition evaluations (36%).

Conclusion: There is an unmet need in patient education for women with gynecologic cancers regarding treatment course and disease process. Educating these women on diet, nutrition, and optimal use of supplements is also needed. Developing interventions to address fears of recurrence and orienting patients to cancer support services are also critical.

498 - Poster Session

Acceptability and feasibility of wearable fitness technology for endometrial cancer survivors

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Objective: Endometrial cancer survivors are the least physically active of all cancer survivor groups, and up to 70% are obese. In addition to their risk for additional cancers, these patients are at increased risk of cardiovascular disease and poor health-related quality of life. Past studies examined physical activity interventions in this population and demonstrated improved physical function, self-efficacy, and body composition. The purpose of this study was to evaluate the acceptability and validity of wearable fitness technology for endometrial cancer survivors.

Method: After institutional review board approval, 30 endometrial cancer survivors were recruited during gynecologic oncology visits and given Fitbit activity trackers to wear for 30 days. Participants answered the Godin Leisure-Time Exercise Questionnaire, Technology Acceptance Questionnaire, and qualitative prompts. Median step counts were correlated with demographic factors, BMI, and Godin Leisure-Time Index, using Stata 13.0.

Results: Twenty-five (83%) survivors completed the study and had evaluable data. Mean age was 62 ± 9 years (range 41–81 years). Mean BMI was 32 ± 9 kg/m² (range 19–52 kg/m²). Self-identified race/ethnicity was 36% Hispanic, 36% non-Hispanic white, 16% non-Hispanic black, and 12% Asian. Most (54%) had been treated for stage I cancer. Participants wore the activity trackers on 93% of the possible days, and median daily steps were 5,325 (range 1,186–17,892 steps). Mean Technology Acceptance score was 2.82 (SD = 0.53). There was a significant correlation between steps taken to age ($r = -0.61$, $P = 0.001$) and employment status ($P = 0.031$). There was no correlation ($r = 0.06$) between steps and Godin Leisure-Time Index. Most free responses reflected positive experiences. See Table 1.

Conclusion: The activity trackers were highly accepted in our population of endometrial cancer survivors, and most were compliant with daily use. Younger age and employment correlated with higher median daily steps. Self-reported physical activity did not concur with steps recorded. Median steps were well below the recommendations for older adults of 7,000–10,000 steps. Future studies are needed to determine optimal timing and intervention to improve health-related metrics in the endometrial cancer survivor population.

Table 1. Subjects grouped by demographics and activity as determined by Fitbit device.

	Entire cohort <i>n</i> (%)	Median Steps	Range	> 6000 Steps <i>n</i> (%)	<6000 Steps (%)	<i>P</i> value
Age	N = 25					0.01
< 65	15 (60)	6891	2436-17892	60%	40%	
≥ 65	10 (40)	3802	1186-10569	10%	90%	
Education						
High School Degree	12 (46)	4536	1186-10140	25%	75%	
College Graduate	13 (50)	6087	1209-17892	54%	46%	
Noreponse	1					
Employment						
Employed	10 (38)	8252	3502-17892	80%	20%	0.03

Retired	12 (46)	3802	1189-10569	17%	83%	
Other	3 (12)	4239	3482-5325	0%	100%	
noresponse	1					
Hispanic						
Yes	9 (35)	5362	2436-12070	44%	56%	
no	17 (65)	5266	1189-17892	35%	65%	
Race						
NonHispanic White	14 (54)	4884	1186-12070	36%	64%	
NonHispanic Black	6 (23)	4536	1209-17892	33%	67%	
Other	3 (12)	10454	5325-10569	67%	33%	
Noresponse	3					
Stage						
1	15 (58)	3843	1186-12070	33%	67%	
2	5 (19)	9432	4238-17892	80%	20%	
3	4 (15)	5314	1209-10454	25%	75%	
Unknown	2 (8)	4667	4502-4833	0%	100%	
Treatment(s)						
Surgeryalone	14 (54)	4913	2436-12070	36%	64%	
Surgeryand adjuvant radiation	10 (38)	5725	1186-17892	50%	50%	
Surgeryan adjuvant chemotherapy and radiation	2 (8)	3237	1209-5266	0%	100%	
Timefrom treat						
≤1 year	6 (23)	4339	1186-9432	17%	83%	
>1 year	20 (77)	5521	1209-17892	45%	55%	
BMI						
Normal Weight (BMI 19-						
Overweight	5 (19)	10140	3843-12070	60%	40%	
Obese	10 (38)	4239	1186-17892	36%	64%	
Morbidly Obese						
Godin Index						
Sedentary	8 (31)	4554	1186-10454	25%	75%	
Moderately Active						
Active	8 (31)	5521	3482-10140	38%	62%	
Godin Moderately						
>30 min	12 (46)	5883	3482-17892	50%	50%	

499 - Poster Session

A retrospective assessment of risk for opioid misuse among women with gynecologic malignancies

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Objective: The risk for opioid misuse among women with gynecologic malignancies has been neither extensively nor systematically investigated. The present study demonstrates the prevalence of women at high risk of opioid misuse and associated factors.

Method: Retrospective chart review identified a cohort of all women with gynecologic malignancies who received an opioid prescription from their gynecologic oncologists between March 1, 2016, and February 28, 2017. Women who received prescriptions solely for immediate postoperative pain were excluded. The Opioid Risk Tool (ORT) is a validated screen used to categorize risk of opioid misuse by assessing for personal and family history of substance abuse and psychiatric diagnoses. Data from the state-run prescription-monitoring program were reviewed for dosing, prescriber, and pharmacy data for the year prior to and including the study interval. Student *t*, χ^2 , and Wilcoxon-Mann Whitney tests were used as appropriate.

Results: In the cohort of 129 women, 6 (4.6%) were categorized as high risk for opioid misuse, 15 (11.6%) as moderate risk, and 108 (83.7%) as low risk. Women at low risk were significantly younger (58 vs 66 years, $P = 0.01$) than those at moderate or high risk. Sixty percent of women were white, and 38% were black. Ovarian cancer was the most prevalent (32%), ahead of uterine (31%), cervical (28%), vulvar (5%), and other (4%) cancer types. Women with cervical cancer were more likely to be at high risk (11.1% vs 2.2%, $P = 0.03$) compared to other cancers. Nineteen percent of women had a history of chronic noncancer pain and were more likely to be at moderate or high risk (43% vs 15%, $P = 0.03$). For women at high risk, there was no difference in the morphine equivalence per prescription than those at moderate or low risk ($P = 0.99$). Women at high risk had more associated prescriptions ($P = 0.039$), prescribers ($P = 0.048$), and pharmacies ($P = 0.048$). See Table 1.

Conclusion: For women with gynecologic cancer who received an opioid prescription for indications other than immediate postoperative pain, 83.7% were at low risk for opioid misuse. While patients at high risk of opioid misuse had more opioid prescriptions, prescribers, and pharmacies, there was no difference in the morphine equivalence per prescription. Gynecologic oncologists must be aware of appropriate and responsible opioid-prescribing practices.

Table 1. Demographics.

	Low Risk <i>n</i> = 108 (83.7%)	Moderate or High Risk <i>n</i> = 21 (16.3%)	<i>P</i> -Value
Age (years)	58.1	65.8	0.01*
Race			0.22
White	61 (57)	16 (76)	
Black	44 (41)	5 (24)	
Other	3 (3)	0 (0)	
Cancer Type			0.40
Cervical	30 (28)	6 (29)	
Ovarian	32 (30)	9 (43)	
Uterine	37 (34)	3 (14)	
Vulvar	5 (5)	2 (10)	
Other	4 (4)	1 (5)	
History of Chronic Non-Cancer Pain			0.03*
Yes	16 (15)	9 (43)	
No	92 (85)	16 (57)	

* Statistically significant per *P*-value <0.05

500 - Poster Session

Preoperative factors associated with unsuccessful palliation following surgery for malignant bowel obstruction in patients with recurrent ovarian cancer

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Objective: Malignant bowel obstruction (MBO) is a common sequela of progressive ovarian cancer, although there is little evidence to guide the decision on whether to attempt palliative surgery. We sought to identify preoperative factors associated with unsuccessful palliation in patients with recurrent ovarian cancer (ROC) who underwent attempted surgical correction of MBO.

Method: We retrospectively analyzed the records of patients with ROC who underwent surgery for MBO from June 1, 2004, to May 31, 2017. Successful palliation was defined as a patient tolerating at least a soft oral diet 60 days after surgery. Various clinicopathologic data were collected, and appropriate statistical tests were performed.

Results: A total of 103 ROC patients underwent surgery for MBO. The median time from initial cancer diagnosis to MBO was 31.7 months (range 3.3–215.6 months); median age was 60 years (range 37–87 years); median BMI was 24.6 kg/m² (range 15.7–37.5 kg/m²); and median preoperative albumin (Alb) was 3.4 g/dL (range 2.1–4.9 g/dL). Seventy-four patients (72%) had a small bowel obstruction; 22 (21%) had a large bowel obstruction; and 7 (7%) had a combination. Fifty patients (49%) had a prior admission for MBO. Median prior lines of chemotherapy (PLC) was 4 (range 1–15). Eighteen patients (17%) had grade 3–5 30-day secondary surgical events, and median length of postoperative hospital stay was 10 days (range 3–74 days). Seventy (68%) achieved successful palliation; these patients were more likely to resume chemotherapy (63, 90% vs 9, 27%, $P < 0.001$) and had better median survival after surgery (13.4 vs 2.0 months, HR = 0.26, 95% CI 0.13–0.50, $P < 0.001$). On univariate analysis, Alb <3.2 ($P = 0.02$) and >3 PLC ($P = 0.05$) were associated with unsuccessful palliation. On multivariate logistic regression, preoperative variables predictive of unsuccessful palliation were Alb <3.2 (OR = 3.5, 95% CI 1.2–11.0, $P = 0.03$), >2 prior cancer surgeries (OR = 4.7, 95% CI 1.1–22.6, $P = 0.04$), and >3 PLC (OR = 4.6, 95% CI 1.5–16.6, $P = 0.01$) (Table 1).

Conclusion: Successful palliation of MBO symptoms in ROC patients is feasible for most selected for surgical correction. Factors associated with unsuccessful palliation were Alb <3.2, >2 prior cancer surgeries, and >3 PLC. Further studies are needed to confirm these findings and develop a prediction model to best identify appropriate cases for surgical intervention.

Table 1. Preoperative factors associated with unsuccessful palliation following MBO surgery.

Variable	Odds Ratio (95% CI)	P-Value
Age (years)	1.00 (0.951-1.056)	0.945
ASA 2	1	
ASA 3	2.04 (0.193-54.338)	0.600
ASA 4	0.98 (0.058-31.184)	0.875
KPS ≤ 70	1	
KPS 80	1.02 (0.282-3.852)	0.975
KPS 90	0.35 (0.073-1.579)	0.175
Preoperative Serum Albumin	3.52 (1.192-11.012)	0.025
>2 Previous Cancer Surgeries	4.66 (1.063-22.611)	0.045
>3 Previous Lines Chemotherapy	4.60 (1.479-16.630)	0.012
Prior Admission for MBO	2.240 (0.768-6.948)	0.147

501 - Poster Session

Outpatient opioid prescribing after gynecologic oncology surgery: Need for individualization

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Objective: To describe patterns of opioid prescription after gynecologic oncology surgery by patient, provider, and surgical characteristics.

Method: Retrospective chart review of 306 gynecologic oncology surgeries over 1 year at a single institution was performed. Patient, provider, and surgical characteristics, as well as opioids prescribed at discharge (number of tabs) were abstracted from medical records. High pill count was determined to be ≥60 tabs and was compared to low count (<60 tabs). The Mann-

Whitney *U* test was used to compare medians to determine associations between prescribing characteristics and high pill volume. Logistic regression confirmed positive associations at a *P* value of 0.05 using SPSS 23.0.

Results: Median age was 55 years. Open surgery was most common (49%), followed by minimally invasive (33%) and minor (18%) cases. The median (range) opioid tabs prescribed by surgical approach was open 60 (20–240), minimally invasive 30 (10–75), and minor 20 (10–120) (*P* < 0.001). Twenty-two percent of patients had an active opioid prescription before surgery. None of the examined patient characteristics (age, race, chronic pain, or active opioid prescription prior to surgery) was significantly associated with higher pill volume. The following factors were significantly associated with higher pill volume: surgery type, longer length of stay, trainee prescriber, and malignant disease (Table 1).

Conclusion: The range of postoperative opioid prescription volume was wide. More than 20% of patients were on an opioid prior to surgery. None of the examined patient factors predicted prescribing patterns. In other surgical specialties, younger age, pre-existing pain disorder, and prior opioid use have been associated with higher volume or persistent use and greater risk of misuse. The surgery literature also suggests that only approximately 30% of opioids prescribed postoperatively are used, suggesting prescription volumes may be reduced while maintaining adequate postoperative pain control. Consideration of individual patient factors may be 1 path to reducing the volume of unused opioids and associated risks of misuse and diversion.

Table 1.

Characteristic	<i>n</i> (n%)	Median # (range) of Opioid Pills Prescribed at Discharge	<i>P</i> -value
Age			
>70	41 (13%)	40 (10-90)	0.893
<70	265 (87%)	40 (10-240)	
Race			
White, non-Hispanic	233 (76%)	40 (10-240)	0.540
Other	73 (24%)	40 (10-180)	
Surgery			
Open	149 (49%)	60 (20-240)	<0.001
MIS	102 (33%)	30 (10-75)	
Minor procedure	55 (18%)	20 (10-120)	
Suspected malignancy at time of discharge			
Yes	202 (66%)	40 (10-240)	<0.001
No	104 (34%)	30 (10-180)	
Length of Stay			
<24hrs	91 (30%)	30 (10-60)	<0.001
1-4 days	162 (53%)	40 (10-180)	
5+ days	53 (17%)	60 (10-240)	
Prescriber			
Trainee	264 (86%)	40 (10-240)	0.02
Attending	42 (14%)	30 (10-180)	
Prescriber gender			
Female	140 (46%)	40 (10-240)	0.658
Male	166 (54%)	40 (10-120)	
History of chronic pain			
Yes	68 (22%)	40 (10-240)	0.082

No	238 (78%)	40 (10-180)	
On opioid prior to surgery			
Yes	67 (21%)	40 (10-240)	0.527
No	239 (79%)	40 (10-180)	

502 - Poster Session

Germline mutation rate in African-American women in Arkansas with a personal and/or family history of breast cancer

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Objective: African-American women, particularly in the southern United States, are poorly represented in genetic studies. Our objective was to investigate the germline mutation rate in African-American women in Arkansas with a personal history and/or family history of breast cancer using the multiplex BROCA panel.

Method: A biorepository with more than 26,000 saliva samples donated for breast cancer research at community events across Arkansas was accessed after institutional review board approval. Saliva samples from patients (African-American women with a personal history and/or family history of breast cancer) or controls (African-American women older than 60 years with no personal and/or family history of breast cancer) were submitted to the University of Washington to undergo analysis of 48 genes, some of which are implicated in breast cancer. Results were compared to the FLOSSIES ancillary study of the Women's Health Initiative (AS538). Missense variants in these African-American patients were assessed and compared to those for 7,324 Europeans and 2,559 African-American FLOSSIES as well as our own controls. Abnormal BROCA results on saliva samples are being confirmed by additional samples.

Results: Among 976 eligible patients, 174 (17.8%) completed a phone interview and returned a signed consent form. Only 15.5% of those contacted declined to participate. Another 212 patients were included anonymously, while 403 controls were included. Of the 786 tested, 277 had a personal history and 109 had a family history of breast cancer. Forty-three damaging mutations were found in 42 of the 786 women tested (5.3%) 13 known or suspected breast cancer genes (Table 1); 1 woman with a personal history of breast cancer had both a *BRCA2* and an *ATM* mutation. Six women (0.7%) carried a damaging mutation in 4 uncertain genes (*ATR*, *CTNNA1*, *GEN1*, *SLX4*). Of the 43 damaging mutations in known breast cancer genes, 30 (67.4%) were in personal history women, 2 (4.7%) in family history women, and 11 (25.6%) in controls. Approximately 800 different missense variants were seen in our cases and controls, 40 of which occurred in known breast cancer genes, were seen in patients only, and had a PolyPhen-2 score >0.9.

Conclusion: This unique biorepository allowed a large number of African-American women with a personal and/or family history of breast cancer and controls without a personal and/or family history of breast cancer to be assessed for many genes implicated in breast cancer. Data from subjects who volunteered at community events in a relatively rural southern state provide valuable information about mutation rates in this underserved population.

Table 1. Damaging mutations.

Gene	PH BC (n = 277) (%)	FH BC (n = 109) (%)	Controls (n = 403) (%)	Total mutations (n = 43) (%)
<i>BRCA2</i>	7 (2.5)	-	1 (0.2)	8 (18.6)
<i>BRCA1</i>	7 (2.5)	1 (0.9)	1 (0.2)	9 (20.9)
<i>CHEK2</i>	2 (0.7)	-	2 (0.5)	4 (9.3)
<i>BRIP1</i>	2 (0.7)	-	1 (0.2)	3 (7.0)
<i>PALB2</i>	2 (0.7)	-	1 (0.2)	3 (7.0)
<i>RAD51C</i>	3 (1.1)	-	-	3 (7.0)
<i>XRCC2</i>	2 (0.7)	-	1 (0.2)	3 (7.0)
<i>RAD51B</i>	1 (1.1)	-	1 (0.2)	2 (4.7)
<i>ATM</i>	2 (0.7)	-	-	2 (4.7)

<i>NBN</i>	1 (1.1)	-	1 (0.2)	2 (4.7)
<i>RECQL</i>	-	-	2 (0.5%)	2 (4.7)
<i>MRE11a</i>	1 (1.1%)	-	-	1 (2.3)
<i>FANCM</i>	-	1 (0.9%)	-	1 (2.3)
Total	30 (10.8%)	2 (1.8%)	11 (2.7%)	

503 - Poster Session

Women with breast and uterine cancer are at increased risk for hereditary cancer predisposition

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Objective: The purpose of this study is to explore the germline mutation spectrum and prevalence among women with breast and uterine cancer (BUC) who were clinician-referred for multigene hereditary cancer panel testing.

Method: Clinical histories for patients who underwent multigene panel testing at a single commercial laboratory (Ambry Genetics, Aliso Viejo, CA) were retrospectively reviewed to select cases with a history of both breast and uterine cancer (with no additional cancers). Patients underwent comprehensive analysis of 23–67 genes, depending on the panel ordered. Gene-specific mutation frequencies were calculated. The combined frequency of mutations in breast and uterine cancer genes was compared between BUC cases and 3 control groups with (1) no personal cancer history, (2) breast cancer only, and (3) uterine cancer only using χ^2 analysis.

Results: A total of 767 women with BUC were identified from July 2013 to December 2016. The majority of the patients were Caucasian (70.7%, 542/767). The average age at first breast cancer diagnosis was 55 years (range 27–92 years), and the average age at uterine cancer diagnosis was 57 years (range 22–84 years). Breast cancer was diagnosed prior to uterine cancer in 52.3% ($n = 401$) of BUC cases. Fifteen percent ($n = 115$) of BUC cases tested positive for mutations in breast and uterine cancer genes. Analysis of gene-specific mutation frequencies revealed that *MSH6* (2.5%), *CHEK2* (2.1%), *BRCA1* (1.8%), *BRCA2* (1.8%), *ATM* (1.8%), *PMS2* (1.3%), *PALB2* (1.2%), and *MSH2* (0.9%) were most frequently mutated among BUC cases. All these most commonly mutated genes have published management guidelines to guide clinical care. BUC cases were significantly more likely to test positive for breast and/or uterine cancer gene mutations than breast cancer-only controls (9.6%, OR = 1.66, 95% CI 1.35–2.03, $P < 0.05$), uterine cancer-only controls (11.9%, OR = 1.30, 95% CI 1.01–1.69, $P < 0.05$), and unaffected controls (7.0%, OR = 2.34, 95% CI 1.91–2.88, $P < 0.05$).

Conclusion: In this multigene panel testing cohort, women with BUC are at greater risk of hereditary cancer gene mutations; therefore, expanded genetic testing should be considered for these women. Most mutations found via multigene panel testing in women with BUC have accompanying published management guidelines and significant implications for clinical care.

504 - Poster Session

Pathogenic mutations other than the *BRCA1/2* founder mutations in Ashkenazi Jewish patients undergoing genetic testing

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Objective: People of Ashkenazi Jewish descent have a 2.5% risk of carrying 1 of the 3 *BRCA1/2* founder mutations. Because of this risk, Ashkenazi Jewish patients often undergo founder mutation evaluation as the first step in genetic assessment and, based on these results, make a decision with their physician about reflex evaluation of the complete *BRCA1/2* genes or a larger panel of *BRCA1/2* and multiple other cancer-associated genes. We sought to evaluate the prevalence of pathogenic mutations other than founder *BRCA1/2* mutations in Ashkenazi Jewish patients.

Method: Genetic results for all Ashkenazi Jewish patients presenting for counseling and testing at a single institution between January 2013 and December 2016 were reviewed. Founder mutations were classified as 185delAG (also known as 187delAG or c.68_69delAG) and 5382insC (also known as 5385insC or c.5266dupC) in *BRCA1* and 6174delT (also known as c.5946delT) in *BRCA2*.

Results: Seven hundred and thirty Ashkenazi Jewish patients underwent genetic testing. Fifty-three percent (390) of patients had a personal cancer history, and 87% (637) had a family cancer history. Ninety-seven patients (13%) had a pathogenic mutation, 40 (6%) VUS and 2 (0.2%) mutation and VUS. Two patients carried two mutations. Among the 101 identified mutations, 80 (79%) were in *BRCA1/2* and 21 (21%) in non-*BRCA1/2* genes (Figure 1). Among the 47 *BRCA1* mutations there was 1 (2%) nonfounder mutation, and among the 33 *BRCA2* mutations there were 3 (9%) nonfounder mutations. Of the patients with nonfounder pathogenic mutations, 58% (14) had a personal history of cancer, and 100% had a family cancer history.

Conclusion: Genetic testing among the Ashkenazi Jewish patients in our population identified 25 pathogenic mutations (25% of all identified mutations) that would be missed with *BRCA* founder mutation testing alone. This emphasizes the utility of multigene panel testing in Ashkenazi Jewish patients and the need to reevaluate our current practice of genetic testing in this population.

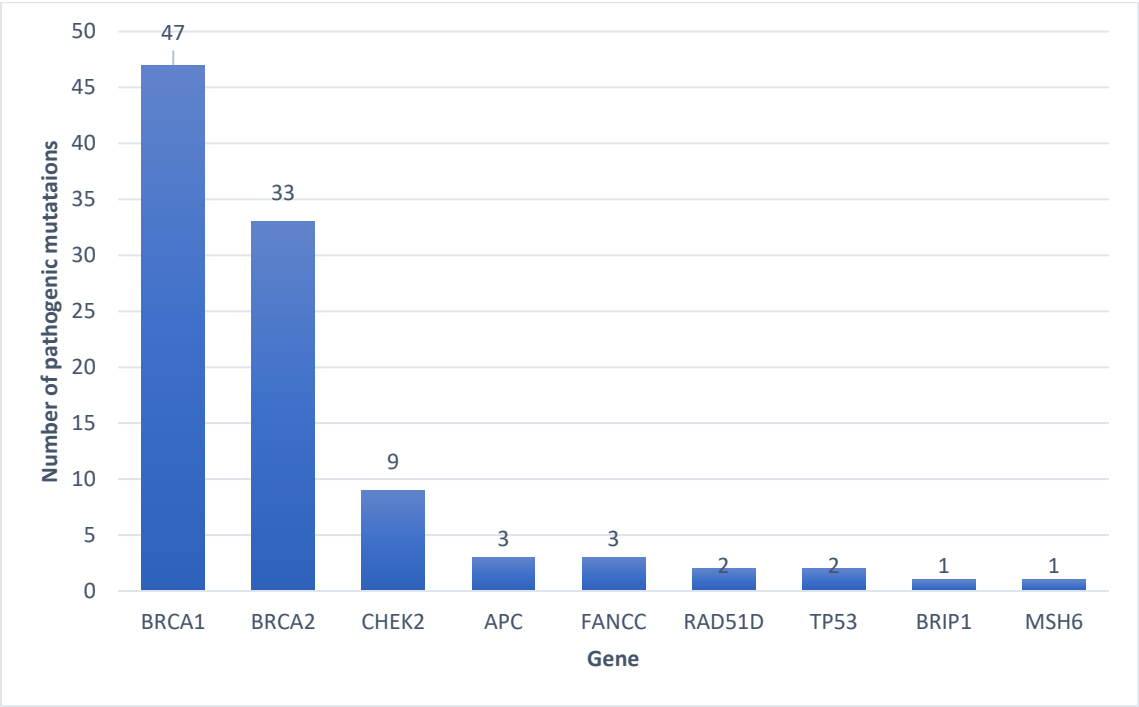


Fig. 1. Genes with pathogenic mutations. Pathogenic mutations other than the *BRCA1/2* founder mutations in Ashkenazi Jewish patients undergoing genetic testing.

505 - Poster Session

Variation in modality of adjuvant therapy for advanced stage endometrial cancer and impact on associated survival outcomes

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Objective: To examine differences in patterns of adjuvant treatment (AT) among patients with stage III endometrial cancer (EC) and the impact on their survival by treatment type.

Method: The SEER-Medicare database was used to examine AT patterns among patients with stage III endometrioid EC from 1999 to 2011 (*n* = 1,287) who underwent primary surgical management via hysterectomy. Stage IIIA–IIIB (*n* = 894) and stage IIIC1–IIIC2 (*n* = 393) were analyzed separately. Demographic factors, surgical staging, pathology, and adjuvant treatments were assessed, followed by overall survival (OS). Descriptive, Kaplan-Meier, and Cox multivariable modeling were performed.

Results: Within stage IIIA–B, AT was significantly associated with increased age (47% untreated vs 32%; 14% chemo v 30% if age >80 vs <80 years), later years of diagnosis (2009–2011 vs 1999–2008: 42% untreated vs 34%; 37% chemo vs 23%, and 21% RT alone vs 42%), respectively. Those who underwent lymph node dissection also received more AT (67% vs 56%).

Those residing in the West had the most untreated (43%), whereas those in the South had the most receiving RT alone (46%) or chemo alone (15%). No associations were noted for substage, grade, comorbid conditions, or socioeconomic status. Similar trends were seen for stage III patients, with those age >80 years receiving less AT (23% untreated vs 36%). Chemo-based treatments (46% vs 30%) were more common than RT alone (15% vs 33%) in later years. Within stage IIIA–B, compared to no treatment, an adjusted model OS was significantly improved in all of the following modalities: RT alone, chemo alone, concurrent RT/chemo, and sequential RT-chemo or chemo-RT. Those who had sequential RT-chemo had the greatest improvement in OS (Table 1). Within stage IIIC, OS was significantly improved in those receiving chemo alone, concurrent RT-chemo, sequential chemo-RT, or sandwich therapy compared to no treatment, with the greatest death reduction in sandwich therapy (Table 1).

Conclusion: AT for stage IIIA–B and IIIC endometrioid uterine carcinoma vary by age, grade, region, and year of diagnosis. In an adjusted model, OS was most significantly improved in all modalities involving chemotherapy over RT alone for stage IIIA–B, with the best found in sequential RT-chemo. For stage IIIC, OS was significantly improved with chemo-based treatment and not with radiation alone, with sandwich therapy representing the best OS.

Table 1. Overall survival by treatment type in Stage IIIA/IIIB and Stage IIIC Endometrioid Endometrial Adenocarcinoma.

Table 1: Overall survival by treatment type in Stage IIIA/IIIB and Stage IIIC Endometrioid Endometrial Adenocarcinoma.								
	STAGE IIIA/IIIB			STAGE IIIC				
Treatment Type	HR ¹	(95%CI)		P value	HR ¹	(95%CI)	P value	
No Treatment	1.00	(ref)			1.00	(ref)		
RT only	0.80	(0.66,	0.96)	0.02	0.79	(0.60,	1.04)	0.10
Chemo only	0.55	(0.40,	0.75)	0.0002	0.62	(0.45,	0.85)	0.003
RT/Chemo (conc.)	0.59	(0.40,	0.89)	0.01	0.53	(0.36,	0.79)	0.002
RT->Chemo (seq.)	0.43	(0.21,	0.87)	0.02	0.82	(0.36,	1.90)	0.64
Chemo->RT (seq.)	0.57	(0.32,	0.99)	0.05	0.53	(0.29,	0.96)	0.04
Chemo->RT->Chemo (seq.)	N/A				0.28	(0.10,	0.76)	0.01

¹Adjusted for age, grade, race and region

RT = radiation therapy; conc. = concurrent; seq. = sequential; HR = Hazard ration; CI = confidence interval

506 - Poster Session

Association of obesity with survival in patients with non-endometrioid endometrial cancer

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Objective: Obesity confers an overall increased risk for development of endometrial cancer. However, there are conflicting reports regarding the effect of obesity on patients' overall and disease-specific survival. The purpose of this study was to evaluate the effect of obesity on survival in women with endometrial cancer.

Method: After institutional review board approval, records of women with diagnosis and treatment of endometrial cancer from 1999 to 2016 were abstracted for histopathological, treatment, and demographic data. Death was confirmed by query of the Social Security Death Index. Kaplan-Meier survival curves and Cox regression modeling was performed with Stata version 14.0 (StataCorp. 2015).

Results: Of 1,732 evaluable patients, there were significant differences in age at diagnosis, histology (endometrioid versus nonendometrioid), stage, race, grade, hypertension, hyperlipidemia, diabetes, and treatment between normal weight, overweight, obese, and morbidly obese patients ($P < 0.01$). There was a linear association of younger age at diagnosis with increasing obesity ($P < 0.01$; $R^2 = 0.04$). While there were differences in survival by obesity categories using Kaplan-Meier analysis (log rank $P < 0.001$), there was no difference in overall hazard of death associated with obesity after multivariable modeling. Younger age, endometrioid histology, lower stage, and statin use were independently associated with decreased hazard of death ($P < 0.01$). However, in stratified analysis of only nonendometrioid histologies, for patients with stage III–IV disease older than 65 years, there was a survival benefit for women associated with obesity ($P = 0.02$).

Conclusion: Obesity is associated with younger age at diagnosis and lower stage disease. Obesity was associated with improved disease-specific survival in a subgroup of nonendometrioid endometrial cancers.

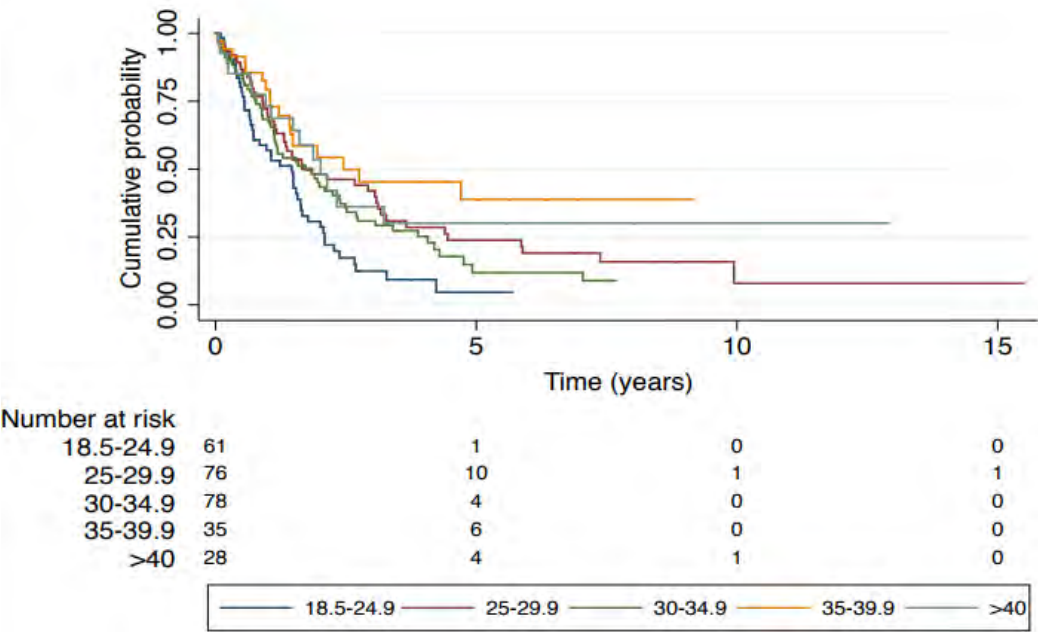


Fig. 1. Kaplan Meier survival estimates for subgroup of women with nonendometrioid histology restricted to Stage 3 and Stage 4 disease.

507 - Poster Session
Evaluating outcomes for weekly paclitaxel and carboplatin dosing in patients with primary advanced or recurrent endometrial cancer
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Objective: To examine patient outcomes and response with weekly paclitaxel compared to standard 3-weekly paclitaxel regimen in patients with primary advanced or recurrent endometrial cancer.

Method: Patients with stage III–IVB or recurrent endometrial carcinoma who were treated with weekly (q1w) or 3-weekly (q3w) paclitaxel with carboplatin from 2005 to 2016 were included and analyzed within 2 treatment groups: paclitaxel q3w (175 or 135 mg/m²) with carboplatin q3w ($n = 108$), and paclitaxel q1w (60, 70, or 80 mg/m²) with carboplatin q3w ($n = 48$). Kaplan-Meier estimates were used for survival statistics and RECIST 1.1 criteria for disease response.

Results: Of 156 patients identified, the median age was 64.3 years, and 47.4% were endometrioid histology. Thirty-one patients (19.9%) had prior recurrence before treatment, while 125 patients (80.1%) were stage III–IVB. At start of treatment, 69.4% of q1w versus 34.8% of q3w patients were stage IV ($P = 0.008$). BMI, tumor grade, number of recurrences, and prior radiation (RT) or chemotherapy (CT) did not differ between groups. Bevacizumab was utilized in 12.8% ($n = 6$) of q1w and 8.3% ($n = 9$) of q3w patients, respectively ($P = 0.39$). RT was given with CT in 43.7% of q1w and 59.2% of q3w patients ($P = 0.73$). Of 68 patients with measurable disease, overall response rate (RR) was 54.4%, complete RR was 33.8%, and partial RR was 20.6%, with median duration of response 10.8 ± 9.5 months. Ten patients had stable disease (14.7%), and 21 (30.9%) had disease progression overall. There was no significant difference in overall RR between groups. Three-year overall survival (OS) and progression-free survival (PFS) for the cohort was 70.1% and 74.2%, respectively. OS and PFS did not increase significantly for q1w versus q3w at 1-, 3-, or 5-year intervals (OS, $P = 0.34$; PFS, $P = 0.098$). On multivariate analysis adjusted for age, stage, grade, and histology, the difference between the groups was unchanged for PFS (HR = 0.90, 95% CI 0.29–2.85, $P = 0.86$) and OS (HR = 0.80, 95% CI 0.28–2.27, $P = 0.68$). On subgroup analysis of primary advanced and recurrent patients independently, there was no difference in OS and PFS between q1w and q3w groups. Three-year OS and PFS for primary advanced versus recurrent group was 70.9% and 77.7% versus 64.8 and 60.1%, respectively.

Conclusion: In this analysis, there was no significant difference in outcome between weekly and 3-weekly paclitaxel dosing in patients with advanced-stage or recurrent endometrial cancer.

508 - Poster Session

Relationship between body mass index (BMI) and gene expression profiles of cervical cancer in the cancer genome atlas (TCGA) project

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Objective: Obesity has been associated with increased risk for and greater mortality from cervical cancer (CC). Thus, we evaluated differences in gene expression profiles of patients with squamous cell CC based on BMI using The Cancer Genome Atlas (TCGA) Project database.

Method: Expression measurements for 19,712 genes were available from the TCGA database. Differential expression analyses for a model including age, race, stage, smoking status, and BMI were conducted using DESeq2 to assess the effect of BMI, adjusting for confounding effects of other covariates in the model. Subjects were included only if a complete case analysis of the covariates was available. To account for multiple testing, a Benjamini-Hochberg correction was conducted at an alpha = 0.05 level.

Results: A total of 160 subjects with squamous cell CC were evaluated from the TCGA database. For those 160 patients, median BMI was 26.8, and 39% of patients were obese (BMI > 30). The expression of 287 genes was found to be significantly altered with increasing BMI, even when controlling for all other variables. Many of the differentially expressed genes were related to lipid biosynthesis, glucose metabolism, and insulin sensitivity. Downregulated genes included hydroxysteroid 17-beta dehydrogenase 2 (0.91-fold change per unit BMI increase), LDL receptor-related protein 2 (0.90), and protein tyrosine phosphatase, nonreceptor type 20 (0.49). Upregulated genes included cytochrome P450 family 4 subfamily F member 2 (1.13-fold change per unit BMI increase), protein phosphatase 1 regulatory inhibitor subunit 1A (1.10), hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2 (1.08), fructose-bisphosphatase 1 (1.04), phospholipase A2 group IID (1.06), hexokinase 3 (1.04), and lipocalin 12 (1.06).

Conclusions: Differential patterns of gene expression were found with elevated BMI in squamous cell CCs in the TCGA database, including metabolically relevant pathways. These results suggest that the metabolic consequences of obesity may contribute to CC pathogenesis. Further work will focus on identifying obesity-dependent biomarkers as well as potential novel targets of treatment that may be specific to obesity-driven CCs.

509 - Poster Session

Intratutural environment of premenopausal endometrial cancers in South Texas Hispanic patients

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Objective: There is a high incidence of endometrial cancer (EC) in young Hispanic women residing in south Texas. EC is a devastating disease in young women who desire childbearing. Medical management with progestin therapy is rarely effective. Recent evidence has shown that cancers have a unique intratumoral environment that allows them to make their own growth factors. In this study we sought to characterize the intratumoral environment of EC in a cohort of premenopausal patients.

Method: The study included 114 surgical specimens from women aged 25 to 50 years, 74 of whom had a diagnosis of EC and 40 benign pathology (controls). Clinical data were abstracted from the electronic medical records. Immunohistochemistry was used to evaluate expression of estrogen receptors (α and β), progesterone receptors A and B, progesterone receptor B alone, aromatase, TNF- α , IL-6, IGF-1, and IGFR-1. Scores were assigned for proportion (0–5) and intensity of staining (0–3), and then a total score was determined (0, 2–8). Statistical analysis was carried out using Kendall rank correlation coefficient and Kruskal-Wallis test as appropriate. $P \leq 0.05$ was considered significant.

Results: All patient were of Hispanic ethnicity. Average age was 42 years with a mean BMI of 40 kg/m². The majority of cancers were type 1. Figure 1 shows that all markers were expressed in both cancers and controls. ER- α and β had high levels of expression in cancers, 68.5% and 60.5%, respectively. TNF- α had increased expression in the cancers compared to controls, $P = 0.001$. Furthermore, TNF- α expression was positively correlated with the expression of aromatase and ER- β , $P = 0.02$ and 0.05 , respectively. IL-6 expression was also positively correlated with the expression of ER- β , $P < 0.001$.

Conclusion: EC in this young, obese cohort has high levels of expression of hormone receptors, aromatase, and the inflammatory cytokines TNF- α and IL-6. Over-expression of intratumoral TNF- α may be a driver of carcinogenesis through induction of aromatase and subsequent increase in local estrogen production. Expression of both TNF- α and IL-6 correlated with increased expression of ER- β . Increased levels of ER- β have been associated with good prognosis in EC, suggesting a possible antiproliferative effect. The role of ER- β agonists in the treatment of premenopausal EC is an area of active research.

510 - Poster Session

Outcomes of patients with uterine carcinosarcoma and low-volume lymph node metastases

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Objective: To compare survival in uterine carcinosarcoma patients with uterine-confined disease and negative nodes (N– cohort), low-volume nodal metastases (isolated tumor cells [ITCs] and micrometastases [mM], LVN+ cohort), and macrometastases ([MM], N+ cohort).

Method: Patients with newly diagnosed uterine carcinosarcoma who underwent surgical staging at our institution from May 1994 to December 2016 were identified. Patients with disease outside the uterus were included if disease was in the cervix, lymph nodes, or cytology. All other metastatic disease was excluded. Low-volume nodal disease included ITCs (tumor cells and/or clusters of <0.2 mm or <200 cells); mM (tumor cells and/or clusters of 0.2–2 mm); and MM (tumor cells and/or clusters of >2 mm). The LVN+ cohort was confirmed on both pan-cytokeratin and H&E slides. Overall survival (OS) was measured from date of diagnosis to death. Appropriate statistical tests were used.

Results: Of 172 patients, 143 were N–, 7 LVN+, and 22 N+. Six (86%) of 7 LVN+ patients had ITCs only. There was no difference in median age ($P = 0.85$), median BMI ($P = 0.65$), or presence of heterologous elements ($P = 0.78$) among the groups. Cytology was positive in 23/143 (16%) of the N– cohort, 3/7 (43%) of the LVN+ cohort, and 5/22 (23%) of the N+ cohort ($P = 0.22$). Lymph-vascular space invasion (LVSI) was noted in 45/143 (31%) of the N– cohort compared with 7/7 (100%) in the LVN+ and 18/22 (82%) in the N+ cohorts ($P < 0.001$). Median OS in those with and without LVSI was 63.6 months (95% CI 39.4–87.7) and 103.4 months (95% CI 65.4–141.4), respectively ($P = 0.17$). Adjuvant therapy was given to 125/139 (90%), 7/7 (100%), and 20/20 (100%) patients, respectively ($P = 0.23$). The most commonly administered adjuvant therapy was chemotherapy \pm radiation in 96/143 (67%), 7/7 (100%), and 19/22 (86%) patients, respectively. Median OS was 121.7 months (95% CI 72.8–170.6), 36.0 months (95% CI 29.2–42.9), and 52.0 months (95% CI 15.8–88.1), respectively ($P = 0.008$) (see Figure 1). After controlling for cytology, lymph node status retained independent association with OS ($P = 0.013$).

Conclusion: Despite similar adjuvant therapy in all groups, OS was worse in patients with lymph node metastases of any size compared to those with negative lymph nodes. Low-volume lymph node metastases are of clinical significance in uterine carcinosarcoma.

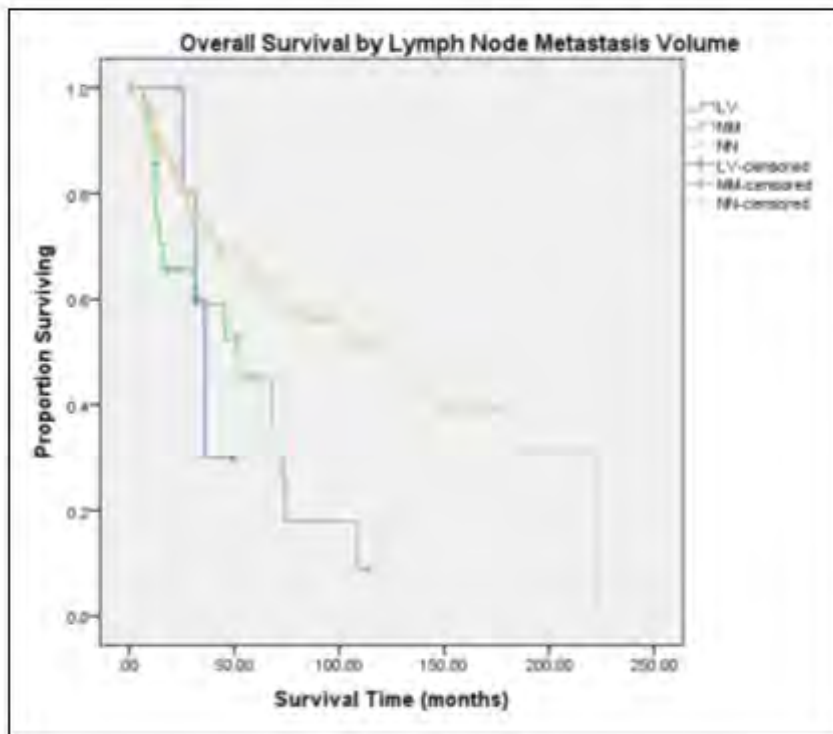


Fig. 1. Overall Survival by Lymph Node Metastasis Volume.

511 - Poster Session

Baseline activity level and 30-day surgical complications in gynecologic cancer patients: Who is fit for surgery?

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Objective: Moderate physical activity is recommended to optimize health. We sought to determine the association between baseline physical activity level and surgical outcomes in gynecologic cancer patients.

Method: We identified women enrolled in a prospective cohort study of cancer survivors from 2010 to 2017 who had gynecologic cancer surgery. Demographics and the Global Physical Activity Questionnaire (GPAQ) were completed at enrollment, prior to surgery. Surgical complications, BMI, disease site, and stage were obtained from the medical record. Baseline physical activity of at least moderate activity (MOD+) was defined as a GPAQ score of moderate or high. The primary outcome was 30-day surgical complication, defined as a Clavien-Dindo score ≥ 2 . Multivariable logistic regression models were used, including age, disease site, and BMI, to test the association between GPAQ score and complications.

Results: Overall, 516 patients were identified with a median age of 60 years (range 26–93) and BMI of 32.3 kg/m² (range 17–79). The majority of patients were white (82%). Disease site was 19% ovarian cancer (OVCA, $n = 99$), 64% uterine cancer (UTCA, $n = 330$), 12% cervical cancer (CXCA, $n = 61$), and 5% vulvar/vaginal (VUVA, $n = 26$). Minimally invasive surgery (MIS) was performed in 65% of cases. Patients with MOD+ were younger (56.6 vs 60.7 years, $P < 0.001$), more educated ($P = 0.001$), employed (44.9% vs 55.1%, $P = 0.003$), and thinner (BMI 32.6 vs 34.8, $P = 0.012$). UTCA patients were less likely to be MOD+ (35%) than OVCA (45%), CXCA (61%), and VUVA (56%) ($P < 0.001$) patients. MOD+ patients had similar incidence of complications to MOD- patients (21% vs 21%, $P = 0.92$). OVCA patients were less likely to have a complication if MOD+ (34 vs 28%, $P = 0.48$). UTCA complications were similar for MOD+/- (15 vs 16%, $P = 0.86$). In multivariable modeling, MOD+ patients had 14% lower odds of complication (OR 0.86, CI 0.54–1.38), although not statistically significant. After MIS surgery, MOD+ patients had a trend toward more complications (12% vs 18%, $P = 0.12$). After open surgery, MOD+ patients had a trend toward fewer complications (33% vs 25%, $P = 0.326$).

Conclusion: Baseline physical activity of gynecologic cancer patients varies by age, BMI, and disease site. Low baseline physical activity was not associated with increased complications in this predominantly MIS cohort. A trend toward fewer complications in MOD+ OVCA patients should be further explored in a large cohort of open surgery.

512 - Poster Session

Readmissions among advanced ovarian cancer patients treated with neoadjuvant chemotherapy as compared to primary debulking surgery

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Objective: To compare perioperative characteristics, morbidity, and postoperative readmissions among patients with advanced-stage ovarian, fallopian tube, or primary peritoneal cancers who underwent primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS).

Method: Retrospective chart review of patients with stage IIIC–IV epithelial ovarian, fallopian tube, or primary peritoneal carcinoma between January 1, 2010, and December 31, 2014, was conducted. Patients who underwent PDS were compared to those who received NACT-IDS.

Results: A total of 553 patients were identified; 260 (47%) patients underwent PDS and 293 (53%) patients underwent NACT-IDS. Patients undergoing NACT-IDS were older (64 vs 62 years, $P = 0.02$) and more likely to have stage IV disease (15% vs 44%, $P < 0.001$). NACT-IDS patients were also more likely to have a lower EBL (445 vs 737 mL, $P < 0.001$), to have decreased operative time (184 vs 228 minutes, $P = 0.002$), to achieve no residual disease (60% vs 38%, $P < 0.001$), and to have a shorter length of stay (6.12 vs 8.51 days, $P < 0.001$). NACT patients were also less likely to receive a blood transfusion (17% vs 28%, $P = 0.001$), to develop postoperative pneumonia (2% vs 8%, $P = 0.001$), to develop postoperative ileus (6% vs 18%, $P < 0.001$), and to require ICU admission (5% vs 10%, $P = 0.01$). NACT-IDS patients were less likely to be readmitted to the hospital within 30 days (9% vs 17%, $P = 0.005$). PFS and OS tended to be lower among patients who were readmitted within 30 days, although these differences did not reach statistical significance (21.6 vs 45.1 months, $P = 0.14$, and 39.4 vs 62 months, $P = 0.48$ respectively). See Table 1.

Conclusion: Patients with advanced-stage ovarian, fallopian tube, or primary peritoneal carcinomas who underwent NACT-IDS had less morbid procedures, fewer postoperative complications, and were less likely to require readmission within 30 days.

Table 1.

	PDS	NACT-IDS	P-Value
Age (yrs), Mean	62	64	0.02
Pre-Op CA-125 (U/mL), mean	1348	293	<0.001
Stage, n (%)			
3	221 (85%)	163 (56%)	<0.001
4	39 (15%)	130 (44%)	
Operative Time (min), Mean	228	184	0.002
Complete surgical resection, n (%)	99 (38%)	176 (60%)	<0.001
EBL (mL), Mean	737	445	<0.001
LOS (days), mean	8.51	6.12	0.001

Post op ICU admission, n (%)	27 (10%)	14 (5%)	0.014
Post op pneumonia, n (%)	20 (8%)	5 (2%)	0.001
Post op ileus, n (%)	48 (18%)	18 (6%)	<0.001
Readmission within 30 days, n (%)	45 (17%)	27 (9%)	0.005
PFS (months), mean	45.1	21.6	0.14
OS (months), mean	62.0	39.4	0.47

513 - Poster Session

The post-anesthesia care unit experience to enable successful and safe same-day discharge following robotic hysterectomies

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Objective: Same-day discharge (SDD) following minimally invasive hysterectomy has been shown to be safe. Preoperative and intraoperative factors associated with successful SDD have been reported, but little is known about the immediate postoperative factors while in the operating room and in the postanesthesia care unit (PACU) that enable SDD. We sought to evaluate the immediate postoperative experience following robotic hysterectomy (RH).

Method: The majority of our patients are planned for SDD after RH directly from the PACU. Records of all patients undergoing RH from 2013 to 2016 were consecutively reviewed. Comparative analysis was performed with χ^2 , Mann-Whitney U tests, and multivariate analysis.

Results: During the study period, 1,103 patients underwent RH; of these, 699 (63.4%) were SDD and 404 (36.6%) were admitted. SDD patients were younger and had shorter operative times, lower blood losses, and earlier start times. Their surgery was less likely to be performed for a cancer indication and performed by a gynecologic oncologist (Table 1). SDD patients had longer PACU times compared to admitted patients (median 292.0 minutes vs 234.5 minutes, $P < 0.0001$). More SDD patients had their urinary catheters removed (97.6% vs 87.4%, $P < 0.0001$) while in the operating room at the conclusion of RH. Of these, 98.1% were able to void prior to discharge during a median time period of 230.0 minutes. In the PACU, more SDD patients received an intravenous fluid bolus compared to admitted patients in order to expedite their void (42.4% vs 29.6%, $P = 0.02$). Often, voiding was the last milestone reached prior to discharge. There were no differences in reoperations, readmissions, or emergency room visits. There were lower rates of postoperative complications (POC) in SDD patients (12.5% vs 24.9%, $P < 0.0001$). After controlling for other factors, admission after RH remained independently associated with POC.

Conclusion: Despite intraoperative factors that may increase the likelihood of admission, SDD remains a safe and feasible option for patients undergoing RH. In order to achieve SDD, the PACU must be capable of allowing patients to recover for at least 6 hours so that patients can meet discharge milestones. Given that admission is an independent risk factor for POC, planning for longer PACU stays to enable SDD should be considered for patients undergoing RH.

Table 1. Patient characteristics between same-day discharge and admitted patients.

Patient characteristic	Same-day discharge patients (n = 699)	Admitted patients (n = 404)	P value
Age, median \pm SD (years)	49.0 \pm 9.9	53.0 \pm 12.2	< 0.0001
Body mass index, median \pm SD	27.0 \pm 6.5	27.8 \pm 7.7	0.2

American Society of Anesthesiologists score, n (%)			0.0002
1	91 (13.0%)	46 (11.4%)	
2	516 (73.8%)	265 (65.6%)	
3	92 (13.2%)	91 (22.5%)	
4	0 (0.0%)	2 (0.5%)	
Cancer indication, n (%)	168 (24.0%)	170 (42.1%)	< 0.0001
Surgery by gynecologic oncologist, n (%)	312 (44.6%)	245 (60.6%)	< 0.0001
Procedure start time after 6PM, n (%)	18 (2.6%)	94 (23.3%)	< 0.0001
Operative time, median \pm SD (minutes)	176.0 \pm 57.9	227.5 \pm 77.0	< 0.0001
Estimated blood loss, median \pm SD (mL)	100.0 \pm 112.2	150.0 \pm 246.9	< 0.0001

514 - Poster Session

Impact of enhanced recovery after surgery (ERAS) protocol on the gastrointestinal tract in gynecologic oncology patients undergoing laparotomy

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Objective: The objective of this study was to evaluate the impact of an enhanced recovery after surgery (ERAS) protocol on postoperative ileus rates in gynecologic oncology patients.

Method: This retrospective cohort study included gynecology oncology patients undergoing elective laparotomy from October 2016 to June 2017 managed on an ERAS protocol. Patients were given clear liquids on day of surgery and regular diet on the morning of postoperative day 1. A control group with a restricted diet was identified from the year prior to ERAS implementation. The primary outcome was rate of postoperative ileus, defined as nausea and vomiting requiring nothing-per-mouth or nasogastric tube (NGT) placement. Secondary outcomes included length of stay (LOS) and readmission. Statistical analysis was performed using SPSS Statistics v. 24.

Results: A total of 376 patients met inclusion criteria; 197 in the control group and 179 in the ERAS group. Patient demographics, including age, BMI, primary diagnosis, and Charlson comorbidity index, were similar between groups. Estimated blood loss was similar; however, surgical complexity score was significantly higher in the control patients (2.7 vs 2.5, $P = 0.04$). Control patients received significantly more intravenous fluids (IVF) intraoperatively (2,272 mL vs 1,986 mL, $P = 0.01$). Ileus rate was significantly lower in the ERAS group (2.2% vs. 15.7%, $P < 0.001$), and fewer patients in the ERAS group required postoperative NGT placement (2.8% vs 7.1%, $P = 0.06$). A multivariate logistic regression demonstrated that ERAS remained independently associated with decreased ileus rates when controlling for other patient and surgical factors (OR = 0.1, $P < 0.001$, 95% CI 0.03–0.34). Increased Charlson comorbidity index was associated with increased ileus rates (OR = 1.3, $P = 0.008$, 95% CI 1.07–1.31). Other factors, including surgical complexity and IVF administration, were not independently associated with ileus. LOS was significantly decreased in the ERAS group (2.9 vs 4.0 days, $P = 0.04$). The 30-day readmission rates were similar between groups (10.1% vs 10.7%, $P = 0.62$).

Conclusion: Implementation of an ERAS protocol significantly decreases the risk of postoperative ileus in gynecologic oncology patients undergoing laparotomy. ERAS also reduced postoperative LOS by 1 day compared to pre-ERAS controls.

515 - Poster Session

Comparative study of survival outcomes following robotic-assisted laparoscopic versus abdominal surgery in the management of ovarian cancer

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Objective: To evaluate and compare survival outcomes following robotic-assisted and abdominal surgery in patients with ovarian cancer.

Method: Preoperative, perioperative, and follow-up data were collected from medical records of consecutive ovarian cancer patients who had been seen by a single surgeon between January 2008 and March 2016. Patients presented with epithelial ovarian cancer requiring staging, a pelvic mass diagnosed as ovarian cancer, or debulking following neoadjuvant chemotherapy. Robotic surgery was offered when tumors were smaller than 15 cm. All other patients, including those requiring multiple major procedures, underwent laparotomy. Differences between the surgical groups were analyzed using two-sided Student *t* tests and χ^2 statistics with significance set at $P < 0.05$. Kaplan-Meier survival curve differences were compared using the Mantel-Cox log rank test.

Results: Patients who received the robotic approach ($n = 122$) were similar to those who had abdominal surgery ($n = 49$) on age, BMI, uterine weight, parity, prior pelvic surgery, and intra- and postoperative complications ($P > 0.05$). Findings indicated that more robotic-assisted cases (vs abdominal) had neoadjuvant chemotherapy (47.5% vs 24.5%, $P = 0.004$), were FIGO stage I (37.7% vs 20.4%, $P = 0.03$), and had no evidence of residual disease after surgery (79.5% vs 40.8%, $P < 0.001$). In early-stage cancer (I–II), optimal debulking (no or <0.5 cm residual disease) was achieved in 98.1% and 80.0% of robotic-assisted versus abdominal surgeries, respectively ($P = 0.27$). In advanced cases (stage III–IV), optimal debulking was attained in significantly more robotic than abdominal surgeries (85.3% vs 61.8%, $P = 0.009$). Comparison of survival distributions by surgical technique showed robotic surgery patients had better overall survival ($P = 0.02$), but only for early-stage cancers ($P = 0.003$) and not advanced cancers ($P = 0.38$) (Figure 1). There were no differences in progression-free survival by surgical approach either overall ($P = 0.56$) or by early ($P = 0.63$) or advanced-stage ($P = 0.73$) disease (Figure 1).

Conclusion: Overall and progression-free survival were at least as good in patients who underwent robotic-assisted compared to abdominal procedures, at all stages of ovarian cancer. Continued follow-up and further studies are needed to substantiate these encouraging findings.

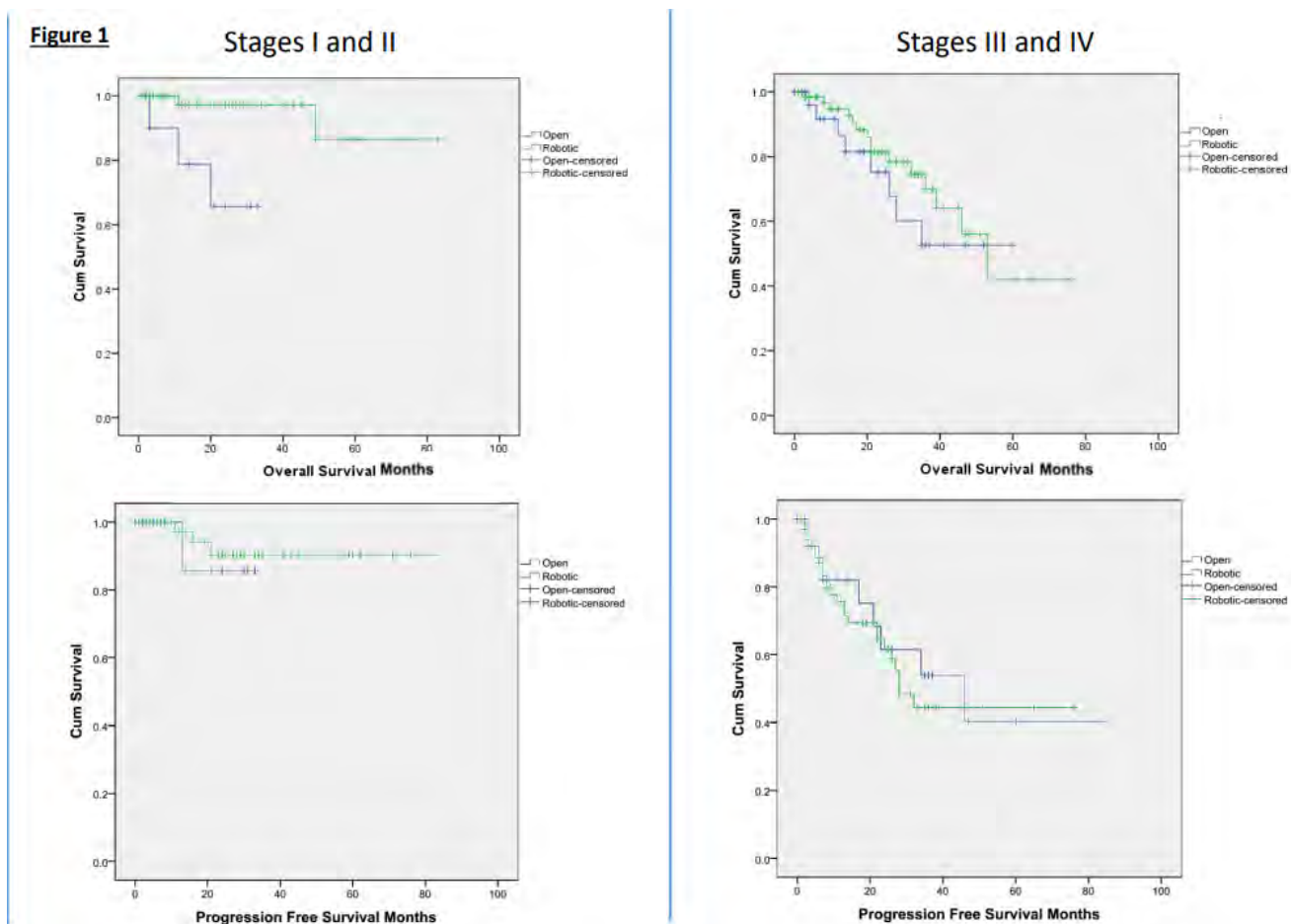


Fig. 1.

516 - Poster Session

How much is enough? Narcotic prescribing practices and patient-reported outcomes from a single institution quality improvement project

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Objective: To ascertain whether the postoperative narcotic-prescribing practices of gynecologic surgeons is in alignment with outpatient patient narcotic usage and to evaluate patient-reported prescription storage and disposal patterns.

Method: A convenience sample was identified including all patients who underwent oncologic and benign gynecologic surgery between June 1 and August 31, 2017. Demographic, operative, and clinical information was abstracted. The state-managed prescription drug database was queried to confirm prescription quantities. Patient calls were conducted by a single provider using a standardized script at 6–10 days following surgery and at 12–20 days if patients were still using narcotics. Descriptive statistics and univariate and multivariate analyses were performed.

Results: A total of 253 patients underwent surgery, and 146 were included in the survey analysis (58% response rate); 32.9% ($n = 48$) underwent open abdominal surgery (including hysterectomy, oncologic debulking, or myomectomy), while 67.1% ($n = 98$) underwent minimally invasive (MIS) or minor procedures (minimally invasive hysterectomy/myomectomy or adnexal surgery and cervical or vulvar surgery). Patients with laparotomy were prescribed a median of 30 (IQR 30–40) pills, while MIS/minor surgery patients were prescribed 22.5 pills (IQR 15–30, $P = <0.001$). A total of 21.9% of patients were still using narcotics at 6–12 days (29.2% of patients with major surgery vs 18.4% of patients with MIS/minor surgery, $P = 0.138$) and 14.8% at the second call with a median of 17 pills remaining. There was a significant difference between number of pills remaining and surgical approach ($P = 0.002$). There were a variety of storage and disposal plans, with the majority stored unlocked (88.4%) with no plans for secure disposal (43.1%). In multivariable analysis, incision type ($P = 0.032$) and use of IV Toradol inpatient ($P = 0.01$) predicted the number of remaining pills. See Table 1.

Conclusion: Despite use of an inpatient ERAS pathway to minimize narcotics, the amount of narcotics prescribed upon discharge is significantly above what is utilized by patients for gynecologic surgeries. Adjusting prescribing practices and providing guidance for safe storage and disposal may help in an effort to more broadly reduce overprescribing medicines that contribute to the opioid epidemic.

Table 1. Patient Demographics.

	Surgical cohort ($n = 253$)	Survey cohort ($n = 146$)	p-value
Age (years) (median [IQR])	46 (33-61)	47 (38-66)	0.7368
<u>Surgical Procedure (% [n])</u>			
Debulking/Hysterectomy/Myomectomy	34.5% (87)	32.9% (48)	0.07
MIS/Vaginal Hysterectomy	30.0% (76)	33.6% (49)	
Laparoscopic/Adnexal	26.5% (67)	26.7% (39)	
CKC, LEEP Hysteroscopy/Vulvar Surgery	9.1% (23)	6.8% (10)	
<u>Narcotic Type at Discharge</u>			
Percocet	35.9% (79)	35.9% (52)	0.6973
Dilaudid	15.9% (35)	14.5% (21)	
Oxycodone	42.7% (10)	44.8% (94)	
Codeine	4.5% (10)	4.1% (6)	
Number of pills at Discharge (Median [IQR])	30 (16-40)	30 (20-40)	0.2519
Recorded pain at discharge ¹ (Median [IQR])	4 (0-6)	4 (0-6)	0.3737
<u>Still Using Narcotics</u>			
Yes	--	21.9% (32) 2 nd call: 14.8% (4)	--
No		78.1% (114) 2 nd call: 85.2% (23)	
Reported pain at survey ¹ (Median [IQR])	--	2 (1-4) 2 nd call: 2 (1-3)	--

Number of pills remaining (Median [IQR])	--	17 (8-27) 2 nd call: 5 (0-16)	--
<u>Locked location for Narcotic Storage:</u>			
No		88.4% (122)	
Yes		11.6% (16)	
<u>Storage Location:</u>			
Bedroom		48.2% (67)	
Bathroom		30.9% (43)	
Kitchen		14.4% (20)	
Other		6.5% (9)	
<u>Disposal Plan:</u>	--		--
Keep in the house		35.4% (46)	
Police station		6.2% (8)	
Flush in the toilet		9.2% (12)	
Trash		9.2% (12)	
Pharmacy		23.1% (30)	
Undecided		7.7% (10)	
Doctor's office		9.2% (12)	

1. Pain scale 0-10.

517 - Poster Session

Surgical outcomes of superobese women treated for endometrial intraepithelial neoplasia and endometrial cancer

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Objective: The rising incidence of obesity has been associated with an increase in the incidence and mortality of endometrial cancer. Obese patients are at increased risk of surgical complications, particularly as the degree of obesity increases. We assessed surgical outcomes of women with endometrial intraepithelial neoplasia (EIN) or endometrial cancer (EC) and superobesity.

Method: We performed a retrospective analysis at a single institution between July 1, 2007, and May 1, 2017. We compared the outcomes of patients with superobesity, defined as BMI ≥ 50 kg/m², undergoing surgery for EIN or EC by the abdominal (TAH), laparoscopic (LH), or vaginal (TVH) approach. Medians were compared by the Kruskal-Wallis test, and means were compared by ANOVA. Statistical analyses were performed using GraphPad Prism 7.0.

Results: Among 83 patients identified, the preoperative diagnosis was EIN in 24 (29%) and EC in 59 (71%). Median follow-up was 21.8 months (range 0.8 to 119.8 months). Surgery was TAH in 29 (35%), LH in 25 (30%), and TVH in 29 (35%). Median BMI was 54.5 kg/m² (range 50–73 kg/m²) and did not differ among the groups. The median Charlson comorbidity index was 4 (3–10) and did not differ by surgical approach. Patients undergoing TAH had a higher mean estimated blood loss, 549 ml (range 150–1,250 ml), compared to patients undergoing TVH, 208 ml (range 25–700 ml) or LH 161 ml (range 10–500 ml) ($P < 0.0001$). The mean \pm sd operative time in minutes was significantly shorter in the TVH group compared to TAH or LH, 120 \pm 74.5 versus 257 \pm 91.1 versus 256.6 \pm 101.1 ($P < 0.0001$), respectively. Among women undergoing TVH, ovaries were removed in 5 (18%) of 28 women with ovaries in situ. Pelvic lymph node dissection was performed in 7 (28%) patients undergoing LH and 8 (28%) patients undergoing TAH. Complications occurred more commonly with TAH 24 (83%) compared to LH 13 (52%) or TVH 14 (48%). Among patients with EC, there were 2 recurrences each in the TAH and LH groups and 1 recurrence after TVH.

Conclusion: Among patients with superobesity undergoing surgical treatment for EIN or EC, surgical complications were more common in patients undergoing TAH than LH or TVH. Staging was performed in less than one-third of TAH or LH patients. The risk of recurrence was low in all groups, although the median follow-up was short. TVH may be an option for selected patients with superobesity and EIN or EC, who are poor candidates for abdominal surgery.

518 - Poster Session

Operative time is a major modifiable risk factor impacting surgical outcomes in patients undergoing pelvic exenteration for gynecologic malignancy

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Objective: The purpose of this study is to identify perioperative modifiable risk factors associated with surgical outcomes in patients undergoing total pelvic exenteration for gynecologic malignancy in a large national dataset.

Method: We inspected the National Surgical Quality Improvement Program (NSQIP) database from 2005 to 2014 for all patients undergoing total pelvic exenteration for gynecologic malignancy (CPT 58240). The primary outcome measure was diagnosis of surgical site infection (SSI) within 30 days of surgery. An a priori model of expected interaction was performed to identify factors contributing to SSI that are available in the dataset including age, BMI, smoking status, American Society of Anesthesiology (ASA) class, preoperative laboratory values (hematocrit, platelet count, creatinine, albumin), operative time, length of hospital stay (LOS), history of hypertension (HTN), chronic obstructive pulmonary disease (COPD), and diabetes (DM). Variables were compared using the χ^2 test, Fisher exact test, and ANOVA with a nominal value of $P < 0.05$ as a test for significance.

Results: We identified 401 patients in the dataset who underwent total pelvic exenteration for gynecologic malignancy, and the 30-day SSI rate was 20.7%. Among all the perioperative factors available in NSQIP, length of operative time, obesity, and LOS were found to be significant modifiable risk factors for SSI. Other factors such as age, race, smoking tobacco, history of HTN, DM, COPD, ASA class, and preoperative laboratory values did not significantly increase the risk for SSI. Patients with SSI had on average 103 more minutes of operative time compared to those without SSI ($P < 0.001$). A linear model of operative time was performed and adjusted for age and BMI, and patients undergoing 6 hours or more of surgical time were 3 times more likely to experience SSI (11% vs 30% $P = <0.001$). Obesity significantly increased the rates of SSI (26%, $P = 0.04$). LOS was longer by an average of 5 days in the SSI group ($P < 0.001$).

Conclusion: The overall rate of SSI in patients undergoing total pelvic exenteration for gynecologic malignancy is 20.7%. Obesity and LOS are both significant risk factors; however, longer operative time has the largest effect on SSI. Thus proper surgical planning and coordination of experienced surgical teams can significantly improve surgical outcomes.

519 - Poster Session

Postoperative outcomes in gynecologic oncology patients using a multimodal analgesia regimen with liposomal bupivacaine

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Objective: To assess the impact of a multimodal analgesia regimen with liposomal bupivacaine compared to an opioid-based patient-controlled analgesia (PCA) regimen on postsurgical outcomes in gynecologic oncology patients undergoing laparotomy.

Method: A retrospective chart review ($n = 183$) was conducted to compare a multimodal analgesia regimen including intraoperative administration of liposomal bupivacaine to an opioid-based PCA regimen in gynecologic oncology patients undergoing exploratory laparotomy. The primary outcome measure was postsurgical opioid consumption in morphine equivalents until 72 hours postoperatively. Statistical analysis was performed using Wilcoxon two-sample test with two-sided P values, Fisher's exact test with two-sided P values, χ^2 test, and Mann-Whitney U test where applicable.

Results: The multimodal analgesia regimen was associated with a significant decrease in opioid use at 0–24 hours postoperatively (24.9 mg vs 51.7 mg, $P < 0.001$) and 24–48 hours postoperatively (21.4 mg vs 38.7 mg, $P = 0.001$) (Figure 1), and days to flatus (mean, 2.4 days vs 2.9 days, $P = 0.01$). There was no significant difference in opioid use 48–72 hours postoperatively (28.6 mg vs 35.1 mg, $P = 0.18$); average pain scores 0–24 hours postoperatively (5.7 vs 5.9, $P = 0.25$), 24–48 hours postoperatively (4.4 vs 4.5, $P = 0.58$), or 48–72 hours postoperatively (4.9 vs 4.3, $P = 0.25$); postsurgical length of stay (LOS) (96.1 hours vs 97.5 hours, $P = 0.67$), postoperative emesis at 0–24 hours postoperatively (8.6% of patients vs 10.9% of patients, $P = 0.66$) or 24–48 hours postoperatively (9.9% of patients vs 10.9% of patients, $P = 0.86$); or the incidence of postoperative ileus or SBO (8.6% of patients vs 10.9% of patients and 1.2% of patients vs 1.8% of patients respectively, $P = 0.89$). There was a 33-minute increase in operating room time with the multimodal regimen (209.9 minutes vs 177.2 minutes, $P = 0.0004$). The medication cost was \$539.06 greater for the multimodal regimen.

Conclusion: A multimodal analgesia regimen including intraoperative administration of liposomal bupivacaine appears to improve postsurgical outcomes by significantly reducing opioid use in the first 48 hours postoperatively and decreasing time to flatus without significantly affecting postoperative pain scores.

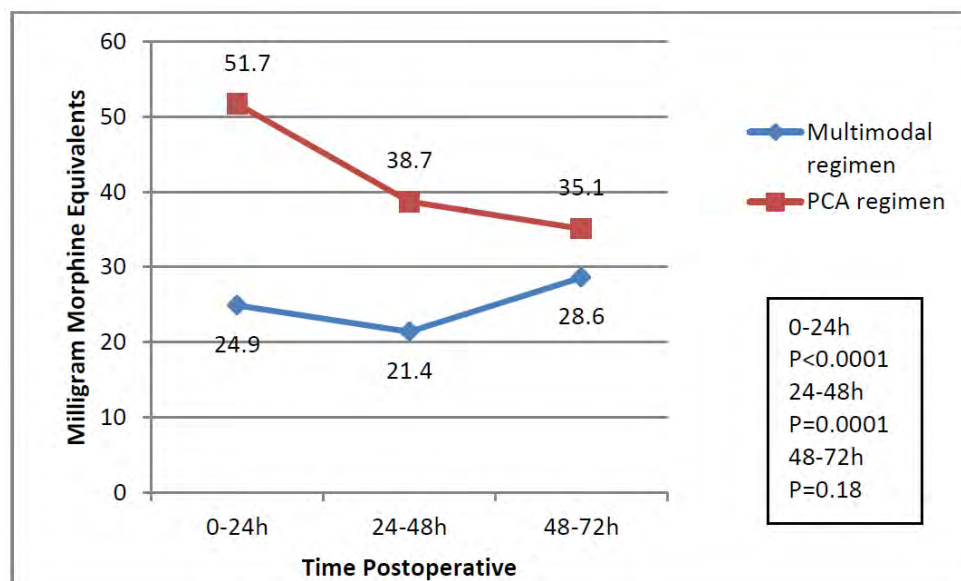


Fig. 1. Postoperative opioid use.

520 - Poster Session

Specimen fragmentation and outcomes of loop electrosurgical excision procedures (LEEP) and cold knife cone biopsies (CKC) for cervical dysplasia at a large, underserved public hospital

J. Grubman, S.S. Meinhardt, A. Nambiar and J.S. Lea. *The University of Texas Southwestern Medical Center, Dallas, TX, USA*

Objective: Surgical technique for loop electrosurgical excision procedures (LEEP) and cold knife cone biopsies (CKC) emphasizes an unfragmented, uniform cone-shaped specimen, but sequelae of specimen fragmentation have not been well studied. We aimed to evaluate outcomes between fragmented and unfragmented excisional biopsy specimens.

Method: A total of 9,900 LEEP and CKCs done at Parkland Hospital from January 2010 to October 2013 were identified via CPT codes. We reviewed pathology, operating room reports, and clinic notes. Exclusion criteria were AIS, cancer, and repeat procedures during the study period (included in follow-up). Cases were analyzed for specimen integrity (fragmented vs unfragmented), margin and endocervical curettage (ECC) status, and grade of dysplasia. Indeterminate margins included dysplasia at unidentifiable margin or in detached fragment and inconclusive or unevaluable margin. Outcomes involving residual or recurrent disease, repeat LEEP/CKC, and hysterectomy for dysplasia within 3 years were also evaluated. The χ^2 test was used for statistical analysis.

Results: Of 772 cases analyzed, 318 (41.2%) were fragmented and 454 (58.8%) unfragmented; 343 cases were LEEPs and 429 CKCs. LEEPs were more likely to be fragmented (64.5% vs 35.5%), even excluding LEEPs with tophat ($P < 0.0001$). Fragmented specimens were significantly more likely to have any positive margin ($P = 0.0034$) and indeterminate margin ($P < 0.0001$). There was no significant difference in rates of positive, insufficient, and high-grade ECC ($P = 0.97, 0.68$, and 0.51 , respectively). There were 71.1% of patients with fragmented specimens and 76.2% with unfragmented who had appropriate follow-up per the American Society for Colposcopy and Cervical Pathology ($P = 0.13$). Although there was no significant difference in rate of high-grade dysplasia in initial LEEP/CKC (61.5% of fragmented vs 67.8% of unfragmented, $P = 0.17$), patients with fragmented specimens had higher rates of high-grade dysplasia in the future ($P = 0.03$). However, there was no difference in rate of repeat LEEP/CKC or hysterectomy for dysplasia between groups ($P = 0.52$).

Conclusions: Fragmentation of LEEP and CKC specimens is associated with adverse outcomes of higher rates of positive margins, recurrent high-grade dysplasia, and indeterminate margins with consequent diagnostic uncertainty. These require closer follow-up and burden patients with increased visits and studies, which is especially difficult for our underserved population. Specimen fragmentation should be avoided.

521 - Poster Session**Design and implementation of an enhanced recovery after surgery (ERAS) protocol for gynecologic oncology patients undergoing minimally invasive surgery**

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Objective: Enhanced recovery after surgery (ERAS) protocols in gynecologic oncology have resulted in improved outcomes for patients undergoing laparotomy. We sought to develop and implement an ERAS protocol for patients undergoing minimally invasive (MIS) gynecologic oncology surgery with a goal of minimizing postoperative pain and nausea and maximizing rates of same-day discharge.

Method: An ERAS protocol intended for patients undergoing MIS gynecologic surgery was developed by a multidisciplinary team at our institution (Table 1). The protocol was designed using evidence-based interventions to address issues specific to patients undergoing MIS surgery and is distinctly different from the ERAS protocol utilized for patients undergoing laparotomy. All gynecologic oncology patients who underwent a MIS hysterectomy from July 21, 2017, to December 1, 2017, were included. Demographic, surgical, and pathologic information was abstracted from patient medical records. Statistical analysis is descriptive.

Results: A total of 235 patients were identified. Common surgical indications included endometrial hyperplasia (14%), endometrial cancer (53%), or pelvic mass (15%). There were 137 (58%) discharges on the day of surgery. Of those patients not discharged on the day of surgery, reasons for admission included urinary retention (22%), medical comorbid conditions (39%), extent of surgery (14%), nausea (1%), and pain (3%). For 19 patients, no reason was documented for admission, and the majority of these patients were meeting all goals for discharge on the day of surgery. Twelve (5%) patients were readmitted within 30 days of surgery: 7 were discharged originally on the day of surgery, and 5 were discharged on or after postoperative day (POD) 1. Of patients requiring readmission, 4 of the 7 patients in the same-day discharge group were readmitted for nausea/vomiting or pain compared to 1 of the 5 patients who were discharged on or after POD 1.

Conclusion: Implementation of an ERAS protocol for MIS gynecologic oncology cases was feasible and resulted in a high rate of same-day discharge with low rates of readmission for pain and nausea. Readmission rates remained low among patients discharged home the same day. Optimizing home health care resources and formalizing criteria for medical comorbid conditions that require admission will allow continued improvement to the same-day discharge rate.

Table 1. Enhanced Recovery After Surgery (ERAS) Protocol for Minimally Invasive Gynecologic Surgery.

Preoperative Surgical Clinic	<ul style="list-style-type: none"> Assess for comorbid conditions and optimize prior to surgery Screen for tobacco and alcohol abuse and encourage cessation Encourage protein and carbohydrate rich foods the week prior to surgery Encourage pre-operative walking program of 30 minutes/day
Preoperative Diet	<ul style="list-style-type: none"> Minimize use of mechanical bowel preparation Regular diet until midnight the night prior to surgery May ingest clear liquids until 3 hours prior to surgery Encourage carbohydrate rich drink prior to surgery
Preoperative Analgesia and Nausea/Vomiting Prophylaxis	<ul style="list-style-type: none"> Acetaminophen 1g PO Celebrex 400mg PO <60 years, 200mg PO ≥60 years Morphine sulfate ER 30mg PO <60 years, 15mg PO ≥60 years If morphine intolerant Oxycontin 20mg PO <60 years, 10mg PO ≥60 years Perphenazine 8mg PO
Intraoperative Anesthetic Management	<ul style="list-style-type: none"> Propofol on induction and total intravenous anesthetic (TIVA) maintenance Lidocaine 1mg/kg ideal body weight on induction and q1 hour Ketamine 10mg on induction and q1 hour (avoid in final hour) Dexamethasone 4-5mg IV Maintenance of euvoemia with IVF rate of 2mL/kg actual body weight Lung protective ventilation Muscle relaxant as clinically indicated Avoid opiates unless indicated on emergence Ondansetron 4mg IV on emergence from anesthesia Remove Foley prior to emergence if clinically indicated
PACU Management	<ul style="list-style-type: none"> IV hydromorphone with transition to PO oxycodone at discretion of Anesthesiologist Ketorolac and/or acetaminophen at the discretion of the surgical team Advance diet as tolerated IV fluids at 40mL/h until tolerating PO intake Discharge to home if meeting criteria Void as per specifications of surgical team Criteria for admission include: poor pain control with patient reported pain score >5, nausea/vomiting, failed voiding trial, patient not oriented x3, unable to perform activity as prior to surgery
Postoperative Management for Patients not Discharged Same Day	<ul style="list-style-type: none"> Regular diet IV fluids at 40mL/h until tolerating PO Oxycodone 5/7.5/10mg PO q4h prn Acetaminophen 1000mg IV q6h x2 doses then 650mg pO q6h, exclude if significant hepatic dysfunction Ketorolac 15mg IV q6 hours x4 doses, exclude if renal insufficiency Ibuprofen 600mg PO q6h to start 6h after last ketorolac dose Ondansetron 4mg IV/PO q8h prn Out of bed to chair the night of surgery and all meals in chair Ambulate with assistance the night of surgery Ambulate in halls at least 4x daily

522 - Poster Session

ERAS improves timely return to intended oncology therapy among gynecologic oncology patients undergoing interval cytoreductive surgery after neoadjuvant chemotherapy

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Objective: To examine whether an Enhanced Recovery After Surgery (ERAS®) program could reduce the time to resumption of chemotherapy within 28 days of surgery.

Method: We conducted a single-center retrospective cohort study of gynecologic oncology patients undergoing interval cytoreductive surgery via laparotomy after neoadjuvant chemotherapy. The pre-ERAS® cohort underwent surgery between 2010 and 2014. The post-ERAS® cohort underwent surgery in 2017 after full implementation of the ERAS® program.

Results: The final study population included 150 pre-ERAS patients and 27 post-ERAS patients. The post-ERAS group was a higher risk cohort as indicated by significantly higher BMI, surgical complexity, and rates of bowel surgery when compared to the pre-ERAS group. At 28 days postoperatively, 81% of patients had resumed chemotherapy in the post-ERAS cohort compared to only 64% in the pre-ERAS cohort (OR = 2.98, 95% CI 1.14–7.79, $P = 0.03$). (See Figure 1.) Length of stay in the post-ERAS group decreased from a mean of 4.73 ± 2.64 days to 3.93 ± 1.54 days ($P = 0.13$). There were no significant differences noted in rates of postoperative complications.

Conclusion: ERAS resulted in significant improvement in resumption of chemotherapy within 28 days of surgery after interval cytoreductive surgery despite a higher risk surgical population. With no difference in postoperative complications, we suspect that more timely resumption of chemotherapy is driven by faster return to normal function.

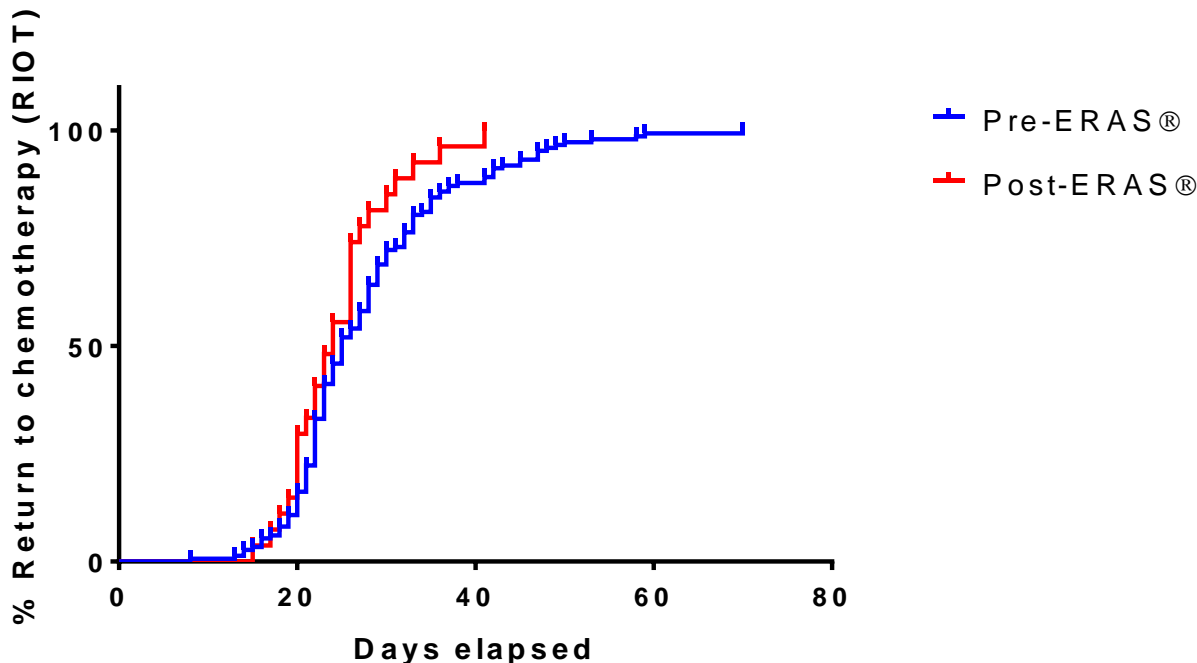


Fig. 1.

523 - Poster Session

Trends in use and survival associated with trachelectomy for young women with cervical cancer

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Objective: Trachelectomy has emerged as a fertility-sparing option for young women with cervical cancer. We performed a population-based analysis in young women with cervical cancer to determine the trends in use of trachelectomy and to examine the association of the procedure with survival compared to hysterectomy.

Method: Data were collected on women younger than 50 years with stage IA2–IB2 cervical cancer between 2004 and 2014 treated with hysterectomy or trachelectomy using the National Cancer Data Base. We examined the association of patient and hospital demographics and tumor characteristics with use of trachelectomy. After propensity score matching, we used Cox proportional hazard models to examine the association between treatment and survival.

Results: A total of 15,150 patients, including 14,714 (97.1%) who underwent hysterectomy and 436 (2.9%) who underwent trachelectomy, were identified. As shown in Figure 1A, trachelectomy rates increased from 1.5% in 2004 to 3.8% by 2014 ($P < 0.001$). The trend was most pronounced in women younger than 30 years (4.6% in 2004 to 17.0% by 2014, $P < 0.001$) (Figure 1B). Among women who underwent trachelectomy, 29.6% had tumors >2 cm in diameter. In a multivariable model, younger women and those more recently diagnosed were more likely to undergo trachelectomy, while Medicaid recipients (RR = 0.39, 95% CI 0.28–0.54) and the uninsured (RR = 0.67, 95% CI 0.45–1.00) were less likely to undergo trachelectomy. Women with

larger, more advanced stage and higher grade tumors were less likely to undergo trachelectomy, whereas those with adenocarcinomas were 48% more likely than women with squamous cell tumors to undergo trachelectomy (RR = 1.48, 95% CI 1.19–1.85). After propensity score matching, there was no association between trachelectomy and the risk of mortality (HR = 1.24, 95% CI 0.70–2.22). Similarly, 5-year survival rates were similar between trachelectomy and hysterectomy for all the stages examined.

Conclusion: Use of trachelectomy for early-stage cervical cancer has increased substantially in the United States, particularly in women younger than 30 years. Within this population, survival is similar for trachelectomy and hysterectomy.

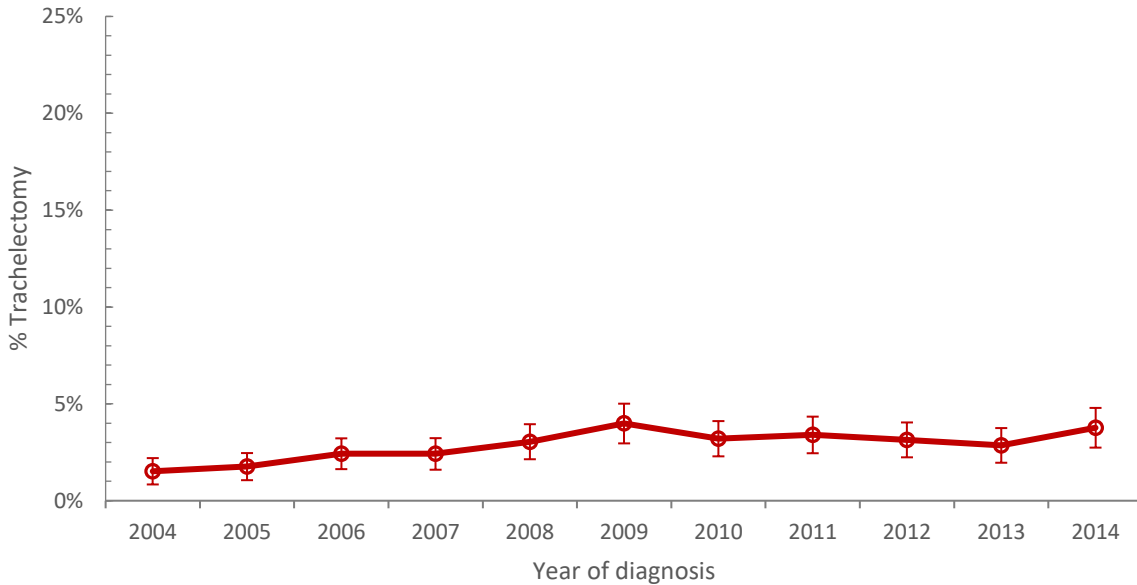


Fig. 1A. Rates of trachelectomy.

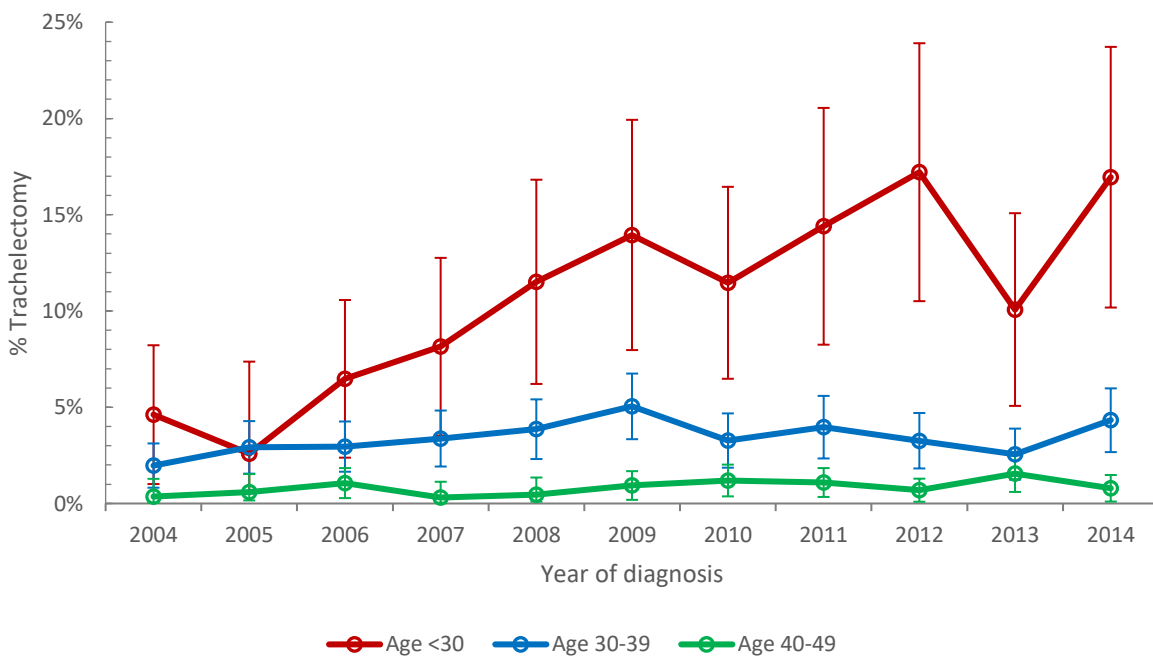


Fig. 1B. Rates of trachelectomy, stratified by age group.

524 - Poster Session

Comparison of outcomes of primary mucinous ovarian cancer patients receiving either an adjuvant gynecologic or gastrointestinal chemotherapy regimen

B. Schlappé, Q. Zhou, R. O'Cearbhaill, A. Iasonos, R.A. Soslow, N.R. Abu-Rustum and J.J. Mueller. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objective: To compare progression-free survival (PFS) and overall survival (OS) in primary mucinous ovarian cancer (PMOC) patients receiving an adjuvant gynecologic (GYN cohort) versus gastrointestinal (GI cohort) chemotherapy regimen.

Method: Patients diagnosed with PMOC from 1994 to 2016 were identified. Gynecologic pathologists used strict pathologic/clinical criteria to determine a PMOC diagnosis. Those who received adjuvant chemotherapy were included. Adjuvant therapy was coded to be either a GYN regimen (e.g., carboplatin/paclitaxel) or a GI regimen (e.g., 5-fluorouracil/oxaliplatin) based on standard agents and schedules used in these diseases. Clinical, pathologic, and treatment characteristics were recorded. The Wilcoxon rank sum test was used for continuous variables and Fisher exact test for categorical variables. Survival rate was calculated using the Kaplan-Meier method by applying landmark analysis.

Results: Twenty-one of 62 patients received adjuvant chemotherapy; 14 received a GYN regimen and 7 a GI regimen. Median age at diagnosis was 59 years (range 25–68 years) in the GYN cohort and 38 years (range 32–54 years) in the GI cohort ($P = 0.08$). Median BMI at first postoperative visit was 25 kg/m² (range 18–40 kg/m²) in the GYN cohort and 25 kg/m² (range 20–31 kg/m²) in the GI cohort ($P = 1.00$). Seven (50%) of 14 patients in the GYN cohort and 5/7 (71%) in the GI cohort had a smoking history ($P = 0.64$). Stage distribution in the GYN and GI cohorts was as follows: stage I–II, 11/14 (79%) and 4/7 (57%), respectively, and stage III, 3/14 (21%) and 3/7 (43%), respectively ($P = 0.35$). Grade distribution in the GYN and GI cohorts was as follows: grade 1, 8/14 (57%) and 1/7 (17%), respectively, and grade 2/3, 6/14 (43%) and 5/7 (71%), respectively ($P = 0.16$). The 3-year PFS rate was 85.1% (95% CI 52.3%–96.1%) in the GYN cohort and 53.6% (95% CI 13.2%–82.5%) in the GI cohort. The 3-year OS rates were 85.1% (95% CI 52.3%–96.1%) and 83.3% (95% CI 27.3–97.5%), respectively (Figure 1).

Conclusion: With a limited sample size, there was no difference in PFS or OS between PMOC patients who received an adjuvant GYN versus GI regimen. International collaborative research to expand the cohort and further define the association between adjuvant chemotherapy regimen and survival in PMOC is ongoing. Ongoing research to molecularly characterize PMOC will be important to define appropriate therapeutic options.

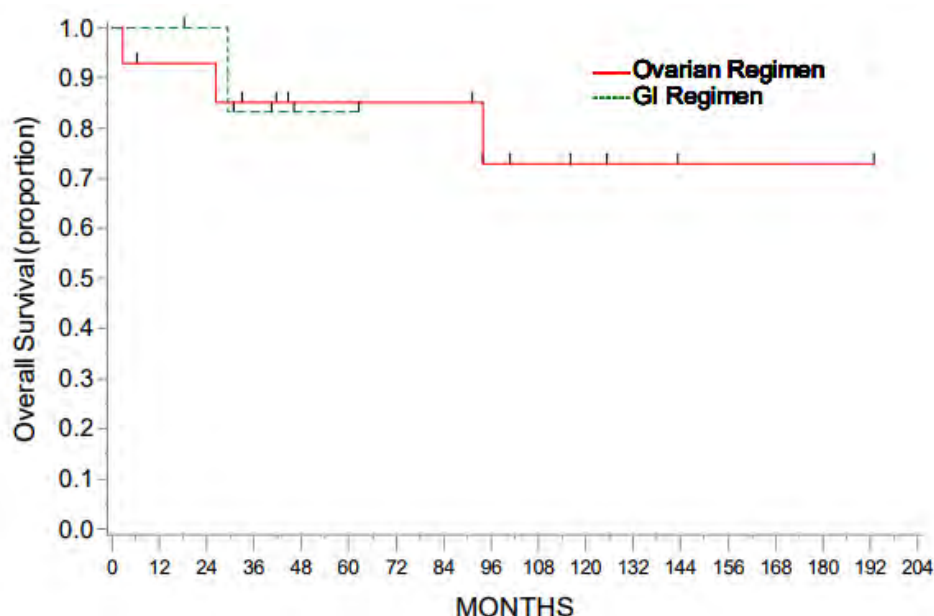


Fig. 1. OS by Adjuvant Chemo Type (landmark analysis).

525 - Poster Session

Genomic profiling of patients with advanced-stage uterine serous carcinoma: Is there difference in genomic signature when stratified by outcome?

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Objective: To assess the genomic and transcriptomic profile of patients diagnosed with stage III–IV uterine serous carcinoma (USC) stratified by outcome

Method: We included patients diagnosed with stage III–IV USC who were treated with surgery and chemotherapy +/- radiation therapy. Patients were divided into 2 cohorts based on progression-free survival (PFS): those with PFS <12 months versus those with PFS >12 months. Overall survival (OS) was calculated from date of diagnosis to last follow-up or death. All tumor samples underwent RNA sequencing, but only 28 tumor samples underwent whole exome sequencing and copy number analysis. All samples were matched to normal tissue from the same respective patients.

Results: A total of 38 patients were included in the study with 76 samples (38 tumor and 38 normal tissue). The most frequently mutated gene was *TP53* (83% of all samples with mutation). Other frequently mutated genes that were noted between 12% and 21% of the samples include *PIK3CA*, *PPP2R1A*, *ARID1A*, *ATM*, *CHD4*, *FBXW5*, *FRG2C*, and a few other genes. We also noted frequent mutation in the ZFN genes family. The median somatic mutations per sample were 55, which is lower than the reported TCGA pan-cancer level. The tumor samples were noted to have differential RNA signatures for USC compared to normal tissue. Also interestingly, patients with PFS <12 months and patients with OS <24 months have a different RNA signature pattern in tumor tissue than those with PFS > 12 months and those with OS >24 months, respectively.

Conclusion: In this pilot study, there is a differential RNA signature pattern when patients with advanced-stage USC are stratified by outcome. This can help create a genomic prognostic panel, which would need to be clinically validated in a larger sample size.

526 - Poster Session

Choriocarcinoma associated with term pregnancy

A.E. Strohl and J.R. Lurain III. Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Objective: To identify patient characteristics, determine prognostic factors, and evaluate outcomes for women with choriocarcinoma associated with term pregnancy.

Method: We reviewed the records of 78 patients with choriocarcinoma associated with term pregnancy treated at a trophoblastic disease center from 1962 to 2009. Patient and disease characteristics, treatment course, and clinical response and survival were analyzed retrospectively.

Results: The median age at diagnosis was 28 years (range 16–56 years). Median duration of disease was 5 months (range 0–144), and median human chorionic gonadotropin (hCG) was 50,000 mIU/mL (range 14–10,000,000 mIU/mL). Fifty-one patients (65.4%) had metastatic disease at time of initial diagnosis, including lung ($n = 47$) and brain ($n = 15$). Twenty-two patients (43%) presented with multiple sites of metastatic disease. Median WHO score was 7 (range 2–20). Overall response to first-line chemotherapy was 43.6% ($n = 34/78$). Twenty-five patients (64.1%) were successfully treated with salvage chemotherapy following failure of first-line chemotherapy. Thirty-nine patients (50%) underwent adjuvant surgery, with hysterectomy as the most common surgery ($n = 30$). Fourteen patients (17.9%) received whole brain radiation therapy. Overall survival for the entire cohort was 75.6%. Survival for nonmetastatic disease was 100%, while survival for metastatic disease was 60.8%. After the introduction of EMA-CO as first-line multiagent chemotherapy in 1986, overall survival improved from 40.9% to 87.5% in patients with metastatic high-risk disease.

Conclusion: Choriocarcinoma associated with term pregnancy usually presents with high-risk features. Patients with metastatic or high-risk disease should be treated with first-line multiagent chemotherapy, specifically EMA-CO, often in conjunction with surgery and/or radiation therapy, resulting in survival rates approaching 90%.

527 - Poster Session

A prospective study on the diagnostic pathway of patients with stage IIIC-IV ovarian cancer: Can laparoscopy improve CT-scan?

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Objective: To compare the efficacy of the CT scan to exploratory laparoscopy in evaluating the extent of the disease in patients with FIGO stage IIIC–IV ovarian cancer (OC). To investigate whether the addition of exploratory laparoscopy (EXL) to CT scan can reduce unnecessary laparotomies.

Method: We reviewed our prospectively collected database on 200 consecutive patients with stage IIIC–IV OC who underwent EXL prior to visceral-peritoneal debulking (VPD) in the period 2006–2014. Patients included in the study were those who had radiological diagnosis of stage IIIC–IV primary ovarian cancer later on confirmed by histology. At laparoscopy, a decision was made whether to proceed to laparotomy based on rigorous inclusion criteria aimed at a complete resection (CR). The data analysis compared the rate of patients who would undergo laparotomy based on the CT scan alone and the rate of patients undergoing laparotomy after CT scan and EXL. Also, we measured the rate of patients actually undergoing VPD after CT and EXL using laparotomy as the gold standard. In case the procedure would end with the laparoscopy, the reasons for not proceeding were recorded and the CT scan was compared to laparoscopy. These patients were not included in the analysis.

Results: Median time for the EXL was 14 minutes (SD \pm 3). No intra- or postoperative complication was related to the laparoscopic surgery. At EXL, a CR was judged feasible in 186/200 patients (93%) and not feasible in 14/200 (7%). The latter group did not undergo a laparotomy. In 176 patients out of 200 (85.5%), the EXL was followed by VPD. Ten patients had laparotomy but no VPD, contradicting the laparoscopic assessment. Thanks to EXL, 7% of patients were spared an unnecessary laparotomy. However, another 2% of patients were still submitted to an unnecessary laparotomy despite CT and EXL.

Conclusion: The prelaparotomy workup of patients with stage IIIC–IV ovarian cancer is clearly improved by EXL. While carrying only a minimal morbidity, EXL helps confirm the diagnosis, identifying the tumor extent and reducing the rate of unnecessary laparotomies.

528 - Poster Session

Comprehensive genomic profiling (CGP) of uterine adenosarcomas (uAS) suggests novel therapeutic approaches

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Objectives: uAS is a rare malignancy composed of benign epithelial and low grade sarcoma. Sarcomatous overgrowth, heterologous sarcoma, and depth of myometrial invasion are associated with more aggressive clinical course and metastatic disease. It remains unclear which, if any, adjuvant treatment improves uAS outcomes. CGP of uAS may provide additional insights into tumor biology, molecular risk factors for recurrence, and additional therapeutic strategies.

Methods: CGP of 39 FFPE uAS specimens by hybridization-capture of 406 cancer-related genes (FoundationOne and FoundationOneHeme) provided GA (short variants, indels, copy number alterations, and rearrangements). Tumor mutational burden (TMB) was assessed across a 0.8 to 1.11Mb region (TMB-low: <6 muts/Mb; TMB-intermediate: 6-19.9 muts/Mb; TMB-high: \geq 20 muts/Mb). Microsatellite instability status (MSI-High or MS-stable) was assigned by a computational algorithm examining 114 intronic loci. Clinically relevant GA (CRGA) were defined as GA associated with on-label-targeted therapies and targeted therapies in mechanism-driven clinical trials.

Results: GA were identified in 97.% (38/39) of uAS samples affecting a total of 70 genes. Inactivating GA in *TP53* was most common, present in 35.9%. 69.2% (27/39) of uAS \geq 1 CRGA: 20.5% *CDK4*, 15.4% *MDM2* amplification, 12.8% *CDKN2A* loss, 7.7% each *NRAS*, *KRAS*, & *ERBB3*, 5.1% each *PDGFRA*, *NF1* & *PIK3CA*. The median TMB was low 2.7 muts/Mb [range 0-11.7], but 4 uAS were TMB-I. All 31 uAS with MSI assessment were MSS. Gene fusions were identified in 7 cases. In 2 cases *JAZF1-BCORL1* rearrangements were identified in recurrent uAS with heterologous differentiation. In another uAS, an *NTRK1-TPR* fusion, predicted to be activating, was identified.

Conclusions: This CGP study of the largest uAS cohort to date identifies CRGA in more than 2/3 of cases, most commonly in the CDK and MEK pathways, suggesting potential targeted treatment options. *JAZF1* fusions, commonly seen in endometrial

stromal sarcomas (ESS), may suggest that some uAS have similar drivers as ESS. Activating *NTRK1* alterations may predict sensitivity to TRK inhibitors, as in a recent phase 1 study of LOXO-101. CGP of uAS may enhance diagnostic accuracy and contribute to clinical decision-making.

Special Interest Session II: Contemporary Issues in Gynecologic Oncology: An International Focus **Friday, March 23, 2018**

Course Directors: Teresa Diaz-Montes, MD, *Mercy Medical Center, Owings Mills, MD*
Daniela Gomez Pue, MD, *Clinica de Ginecologia Integral, Mexico City, Mexico*

1 - International Session

Expanding the cervical cancer screening guidelines in resource limited settings

A. Hari¹, D.E. Brabender², J.E. Temko² and A. Shen². ¹*University of California - Los Angeles, Los Angeles, CA, USA*, ²*University of California, Irvine, Irving, CA, USA*

Objective: The World Health Organization (WHO) guidelines for cervical cancer prevention in low-resource countries recommend a screen-and-treat method of Visual Inspection with Acetic Acid (VIA) and cryotherapy for women ages 30 to 50 years. Our study, performed in Tanzania, examined the clinical benefit of extending the screening to include patients ages 18 to 75 years.

Disease/Procedure/Practice Issue: A total of 841 women were screened at 2 different sites, 1 urban and 1 rural, over the course of 2 screen-and-treat campaigns in Tanzania. VIA+ women, regardless of age, were treated with cryotherapy. Women with advanced cervical cancer were referred to a tertiary medical center in Mwanza for gynecologic oncology consult.

Outcomes: Combining data from the 2 clinic sites, the VIA+ rate was 13.32% overall (112 out of 841), 14.94% for women younger than 30 years (39 out of 261), and 7.32% for women older than 50 years (6 out of 82). Of all VIA+ results, 34.82% were found in women between ages 18 to 29 years (39 out of 112). Severe dysplasia and cervical cancer was detected in 15 patients overall, 1 younger than 30 years, 3 at age 30, and 2 older than 50.

Conclusion: Although WHO guidelines do not recommend screening women younger than 30 years because of a higher rate of clearance of HPV and proximity in age of sexual debut, we found a high rate of VIA+ results in patients younger than 30 years, consistent with studies assessing VIA+ prevalence in resource-limited areas. Evidence exists supporting the sensitivity and specificity of VIA (~79% and 85%, respectively) in identifying CIN2+ lesions, which guidelines advise to treat in younger patients. Patients older than 50 years may have higher false positive rates because of atrophy after menopause, but given the low rates of pelvic exams in this population and low complication rates of cryotherapy, they should also be screened. We propose reassessing the WHO guidelines to reflect the need for screening and appropriate treatment for women aged 18–75 years, especially in resource-limited countries like Tanzania.

2 - International Session

Comparison of cervicography and human papillomavirus test as an adjunctive test to pap cytology to detect high-grade cervical neoplasia in country with high prevalence of HPV infection

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Objective: Cervical cancer is one of leading causes of cancer mortality among women worldwide, despite existing screening programs. This study aimed to compare the diagnostic capacities of cervicography and human papillomavirus (HPV) testing as an adjunctive test to Papanicolaou (Pap) cytology to detect high-grade cervical neoplasia in Korea with high prevalence of HPV infection.

Disease/Procedure/Practice Issue: Of 33,531 women who had a cervicography as a screening test for cervical cancer at private clinics and university hospitals in Korea between January 2015 and December 2016, we retrospectively analyzed the records of 4,117 women who simultaneously or subsequently underwent Pap cytology, HPV test, cervicography, and colposcopically directed biopsy. At the cervical intraepithelial neoplasia (CIN2+) disease threshold, the diagnostic capacities among screening tools were compared.

Outcomes: The prevalence of CIN2+ disease based on colposcopic biopsy was 10.8% (446 of 4,117 women), and the positive rate of high-risk HPV was 61.0% (2,511 of 4,117 women). Among three single screening methods (Pap cytology, HPV test, and cervicography), cervicography was most sensitive (89.2%) for detection of high-grade lesions, and Pap cytology was most specific (65.1%). Moreover, cervicography as an adjunctive to Pap cytology was more sensitive (97.3% vs 93.7%) and showed higher odds ratio (13.84 vs 5.86) than the HPV test.

Conclusion: Cervicography had excellent diagnostic capacities for detection of high-grade CIN. Especially, cervicography may be a practical test and useful alternative or adjunctive screening for Korean women with high prevalence of HPV. Cervicography-based screening may also provide an effective tool in low-resource settings with poor funding to afford HPV testing or lack of the health infrastructure and trained personnel to read cytology or perform colposcopy.

3 - International Session

Necessity of colposcopy according to different human papillomavirus (HPV) genotypes in women with cytology negative, but high-risk HPV positive

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Objective: Current guidelines for cervical cancer screening recommend that women who are cytology negative, but human papillomavirus (HPV) 16- or 18-type positive should be performed colposcopy. However, despite other established high-risk (HR) types (26/31/33/35/39/45/51/52/53/56/58/59/66/68/69/70/73/82) also considered oncogenic, there is no guideline for women with cytology-negative but other HR-HPV positive except 16 and 18 types. This study investigated the risk of the risk of cervical intraepithelial neoplasia grade 2 or higher (CIN2+) according to different HR-HPV types in Korean women with cytology-negative.

Disease/Procedure/Practice Issue: Of 33,531 women who had a cervical cancer screening at private clinics or university hospitals in Korea between January 2015 and December 2016, all records of women who simultaneously or subsequently underwent Pap cytology, HPV test, and colposcopically directed biopsy were retrospectively reviewed. We compared biopsy results between cases that were cytology-negative and HPV-positive for 16 or 18 types versus other HR-HPV types. To estimate the risk of CIN2+ associated with different HR-HPV types, we calculated odds ratios (ORs) and 95% CI by logistic regression.

Outcomes: Of 1,337 women with cytology-negative and HR-HPV positive included in the analysis, 160 women (12.0%) had 16 or 18 types positive and 1,177 women (88.0%) had other HR types positive. The most prevalent HR-HPV genotype was 58 (15.4%), followed by HPV52 (11.6%), HPV16 (9.9%), HPV56 (9.4%), and HPV51 (9.2%). Single and multiple HR-HPV infections were 86.6% and 12.4%, respectively. The prevalence of CIN2+ disease based on colposcopic biopsy was 3.7% (50 of 1,337). HPV16 or HPV18 was strongly associated with a diagnosis of CIN2+ compared to other HR-HPV types (OR = 8.53, 95% CI 4.77–15.28, $P < 0.001$). In 1,177 women with HPV16-negative, HPV18-negative, and other HR-HPV-positive, the risk for CIN2+ was statistically increased in women with multiple HR-HPV infections (OR = 5.40, 95% CI 2.37–12.73, $P < 0.001$), HPV35 (OR = 4.77, 95% CI 1.36–16.77, $P = 0.015$), and HPV58 (OR = 4.83, 95% CI 2.17–10.74, $P < 0.001$).

Conclusion: Our data validate the 2013 American Society of Colposcopy and Cervical Pathology guidelines for HPV16/HPV18 genotyping, which recommend referral to colposcopy of HPV16/HPV18 positive women with negative cytology. Furthermore, we also recommend colposcopy for women with multiple HR-HPVs, HPV35, and HPV58 infection.

4 - International Session

Uterine corpus invasion is a risk factor in patients with early-stage cervical carcinoma receiving radical surgery

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Objective: To explore whether pathologically verified uterine corpus invasion (UCI) is a risk factor for patients with early-stage (IB1–IIA2) cervical carcinoma receiving radical surgery.

Disease/Procedure/Practice Issue: A matched-case comparison of early-stage cervical carcinoma patients with pathologically verified UCI to patients without UCI on a 1:1 ratio was conducted. High-risk factors (lymph node metastasis, parametrial invasion, vaginal margin invasion) and intermediate risk factors (lymphovascular space invasion, LVSI, and deep stromal invasion) were completely matched between UCI and non-UCI groups. Kaplan-Meier and log rank tests were applied for univariate analysis, and Cox proportional hazard regression models were used for multivariate analysis.

Outcomes: A total of 1,320 consecutive patients with cervical carcinoma received surgery in our center from January 1, 2009, to December 31, 2014. Seventy-nine (5.98%) cases with UCI were identified. Median follow-up time was 43 months. There were 22 cases with recurrence. In the UCI group, the recurrence rate was 20.3% (16/79), and in the non-UCI group, 7.6% (6/79). On univariate analysis, SCC, neoadjuvant chemotherapy (NACT), lymph node metastasis, parametrial invasion, LVSI, deep stromal invasion, vaginal invasion, and UCI were significantly associated with disease-free survival (DFS). After multivariate analysis, UCI ($P = 0.02$, $RR = 3.832$, 95% CI 1.235–11.893) and lymph node metastasis ($P = 0.042$, $RR = 2.890$, 95% CI 1.038–8.045) were still independent risk factors for decreased DFS. See Table 1.

Conclusion: Pathologically verified uterine corpus invasion might be an independent risk factor for decreased DFS in patients with early-stage cervical carcinoma receiving radical surgery.

Table 1. Multivariate analysis for DFS.

	HR (95%CI)	<i>P</i>
SCC (ng/ml)		0.342
<3	1	
>=3	1.693 (0.571-5.019)	
NACT		0.158
yes	1	
no	0.480 (0.173-1.331)	
Node metastasis		0.014
no	1	
yes	3.566 (1.289-9.863)	
Parametrial invasion		0.802
no	1	
yes	1.136 (0.419-3.082)	
LVSI		0.324
no	1	
yes	1.735 (0.581-5.183)	
Deep stromal invasion		0.973
no	1	
yes	340110.757 (0.000-NA)	
Vaginal invasion		0.148
no	1	
yes	1.943 (0.791-4.772)	
Uterine corpus invasion		0.014
no	1	
yes	3.606 (1.301-9.998)	

5 - International Session

Enhanced recovery after surgery program in older patients undergoing gynecologic oncological surgery is feasible and safe

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Objectives: Enhanced Recovery After Surgery (ERAS) programs include multimodal approaches of perioperative patient clinical pathways designed to achieve early recovery after surgery and a decreased length of hospital stay (LOS). By quickly allowing patients to recover their environment, older patients are those who could benefit the most from ERAS programs. This study is the first to date to assess feasibility and safety of these programs in older patients undergoing gynecologic oncological surgery.

Disease/Procedure/Practice Issue: Data were prospectively collected between December 2015 and September 2017 at the Institut Paoli-Calmettes, a French comprehensive cancer center. All the included patients were referred for hysterectomy and/or pelvic or paraaortic lymphadenectomy for gynecological cancer. The primary objective was to achieve LOS in patients ≥ 70 years similar to that in younger patients without increasing the proportion of complications and readmission rates. A binary (LOS $<$ or ≥ 2 days) logistic regression was built, including age, Charlson score, BMI, ASA score, oncological indication, surgical procedures, and surgical approaches. G8 score was estimated for all the ≥ 70 -year-old patients.

Outcomes: Of a total of 284 patients, 75 were ≥ 70 years old and 254 were < 70 . Except for a disparity in oncological indications with a higher proportion of endometrial cancer in the ≥ 70 -year-old group (56% vs 27%, $P < 0.01$), there were no differences in patient characteristics and surgical procedures. Age ≥ 70 years was associated with a longer LOS (means, 3.88 vs 3.11 days, $P = 0.024$) only in univariate analysis. Considering the logistic regression, age was no longer associated with LOS. Total hysterectomy with pelvic lymphadenectomy and ASA score ≥ 3 were independently associated with longer LOS while mini-invasive techniques were associated with a shorter LOS (Table 1). Morbidities and readmissions occurred in 23% and 8%, respectively, of the total population without any difference between the two groups. In the ≥ 70 -year-old population, G8 score was not predictive of LOS, morbidities, or readmissions.

Conclusion: Although it is already widely accepted that ERAS programs improve early recovery, our study shows that ERAS programs in patients older than 70 years undergoing gynecologic oncological surgery is as safe and feasible as in younger patients.

Table 1.

	HR	[95% CI]		P-value
		min	max	
Age, y				
< 70	Reference category			
≥ 70	1.49	0.77	2.86	0.237
Charlson				
< 3	Reference category			
≥ 3	0.79	0.10	6.16	0.821
BMI				
< 30	Reference category			
≥ 30	1.14	0.58	2.25	0.696
ASA				
< 3	Reference category			
≥ 3	3.40	1.16	9.99	0.026
Oncological indications				
Cervical cancer	Reference category			

Endometrial cancer	1.14	0.52	2.48	0.743
Ovarian cancer	1.84	0.49	6.91	0.368
Uterine sarcoma	2.64	0.18	39.59	0.483
Other (Border line ovarian tumor, endometrial hyperplasia, CIN)	1.05	0.42	2.62	0.915

Surgical procedures				
Total Hysterectomy**	Reference category			
Total Hysterectomy** with pelvic lymphadenectomy	3.41	1.46	7.97	0.005
Total Hysterectomy** with pelvic and aortic lymphadenectomy	2.15	0.55	8.51	0.274
Total Hysterectomy** with pelvic and aortic lymphadenectomy and omentectomy	4.11	0.70	23.96	0.116
Isolated Lymphadenectomy:				
Pelvic lymphadenectomy	2.01	0.60	6.77	0.259
Para-aortic lymphadenectomy	0.50	0.19	1.34	0.169
Both	7.92	0.86	73.15	0.068

Surgical approaches				
Open surgery	Reference category			
Conventional laparoscopy	0.02	0.00	0.15	0.000
Robotically assisted laparoscopy	0.03	0.00	0.20	0.001

6 - International Session

Cervical cancer prevention training program in Mozambique

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Objective: More than 85% of cervical cancer cases occur in low- and middle-income countries, where there are not enough medical specialists to provide prevention, screening, and treatment services. Mozambique is a Portuguese-speaking country in sub-Saharan Africa where cervical cancer is the primary cause of cancer among women. Our goal is to train and mentor health care providers locally in Mozambique to perform colposcopy and LEEPs (loop electrosurgical excision procedure) to improve clinical capacity to prevent cervical cancer and treat preinvasive disease.

Disease/Procedure/Practice Issue: We initiated a cervical cancer prevention education program with 3 complementary components: (1) locally held, hands-on training courses using innovative teaching aids developed by Rice University that are low cost and allow course participants to simulate different cervical cancer screening and early treatment techniques including colposcopy with cervical biopsies, and LEEP; (2) discussion of patient cases and observation of clinical exams with a mentor; and (3) Project ECHO (Extension for Community Health Outcomes) telementoring using regularly held video conferences to discuss patient cases held in Portuguese. This training was provided by a collaborative team with providers from the United States and four Brazilian institutions.

Outcomes: Beginning in 2016, our team has traveled to Maputo at least twice per year to perform the hands-on colposcopy and LEEP course using the innovative models. Each course has had an average of 25 attendees who learned colposcopy/biopsy and LEEP. This was followed by direct supervision of the attendees performing colposcopy and LEEP at the local hospitals. To

supplement the courses, monthly video conferences are held between Mozambique, Brazil, and the United States using Project ECHO to review patient cases and discuss management plans.

Conclusion: Through this program we have found that locally held hands-on colposcopy and LEEP training courses and direct supervision by an international mentor, complemented with Project ECHO telementoring, is an effective way to improve cervical cancer screening and prevention efforts in low-resource settings. Formal evaluation of the course and participants' skills and knowledge is ongoing.

7 - International Session

Predictive factors of survival and recurrence in ovarian cancer patients treated surgically: Series of 139 patients

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Objective: To define predictive factors of better survival and delayed recurrence in ovarian cancer patients undergoing a cytoreductive surgery.

Disease/Procedure/Practice Issue: This study included 139 ovarian cancer patients receiving cytoreductive surgery for an initial or recurrent disease, in an adjuvant or neoadjuvant setting, between 2005 and September 2017 at Hôtel-Dieu de France University Hospital.

Outcomes: Median age at surgery was 55 years (range 16–83 years). Of all patients, 82.5% had their first surgery at our institution; 76.9% of operated patients were in stage III. Lymphadenectomy was performed in 88.5% of cases. Median number of removed lymph nodes (LN) was 57. Node involvement was noted in 57.7% of cases. Bowel resection and upper abdominal surgery were performed in 47.5% and 37.4% of cases, respectively. Survival rate was 67% (93 out of 139 patients). No recurrence was seen in 56% of cases, and the mean interval of recurrence was estimated at 22.5 months with 73.3% of recurrences occurring after 12 months from surgery. No impact on survival was detected whether the patient benefited from an upfront surgery or an interval one post-neoadjuvant chemotherapy: 42 months versus 36 months, respectively ($P = 0.36$). According to Cox regression test, we found that survival is significantly correlated to age, menopausal status, lymph node status, number of positive lymph nodes, and lymph node ratio (LNR) ($P = 0.009$, $P = 0.004$, $P = 0.001$, $P = 0.002$, and $P = 0.004$, respectively). Patients with $LNR \leq 0.03$ had a survival of 50 months versus 27 months in patients with $LNR > 0.03$. Mean survival was estimated at 51 months in patients with only 1 positive LN versus 26 months in patients with more than 1 positive LN. Recurrence was encountered more frequently in advanced stages: 55% (stage III) and 33% (stage IV) versus 6% (stage I) and 14% (stage II), $P = 0.006$, as well as in case of positive LN (52.9% vs. 32.7%; $P = 0.027$). Lymphadenectomy neither increased the postoperative complications nor the transfusion rate and was only associated with longer operative time ($P = 0.7$, $P = 0.85$, and $P = 0.000$, respectively). In case of bowel resection, fistulas were more seen in case of multiple anastomoses ($P = 0.000$).

Conclusion: $LNR \leq 0.03$ and the presence of only 1 positive LN predict a better survival in ovarian cancer patients undergoing cytoreductive surgery. Advanced stages and positive LN predict a higher risk of recurrence.

8 - International Session

Artificial intelligence solo surgery for laparoscopy: A survey for clinical expectancy

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Objective: We performed a survey to determine current limitations of the role of assistants during laparoscopic surgery, and to investigate expectancy for developing artificial intelligence solo surgery (AISS) for laparoscopy.

Disease/Procedure/Practice Issue: We made 24 questions about limitations and improvement points of the current laparoscopic system. All questions were classified into 3 categories: experience ($n = 8$), limitation ($n = 6$), and expectancy ($n = 10$). We conducted this survey of laparoscopic surgeons from July to August 2017.

Outcomes: A total of 508 surgeons participated in the survey: gynecologists ($n = 278$, 54.7%), general surgeons ($n = 173$, 34.1%), and urologists ($n = 57$, 11.2%). About 60% of responders worked at tertiary medical centers; 44.1% had more than 10 years of experience in laparoscopic surgery; and 51.3% performed laparoscopic surgery on more than 10 patients per month. Moreover, 80.5% required 2 or more assistants during laparoscopic surgery. Unintended movement of the laparoscopic

camera (84.8%) and devices (59.6%) was a more common limitation. The skill of assistants using the camera and devices was considered as important for successful laparoscopic surgery in 84.1% and 73.4% of responders, whereas 64.2% required automatic cleansing of camera lens for AISS. Replacement of more than 60% of manpower with AISS was expected in 24.8% of responders, and 83.3% intended to buy AISS in the future. In terms of gynecologic surgery, keeping the uterine elevator in the same position for a long time and the difficulty of manipulating it due to the opposite direction between camera and assistants' view were more frequent obstacles. The skill of uterine manipulation was considered as important in 60.4% of responders. About 83% of gynecologists intended to buy AISS for uterine manipulation, because they expected to improve convenience and safety most commonly.

Conclusion: Laparoscopic surgeons expect that AISS may improve the quality of laparoscopic surgery in the future.

9 - International Session

Proportion of women <30 years of age with high-grade cervical dysplasia and cervical cancer in the south of Brazil

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Objective: Cervical cancer (CC) is the fourth cancer in women globally and the second in less developed countries, responsible for about 85% of this cancer deaths. Brazilian cervical cancer screening protocols recommend screening of sexually active women between the ages of 25 and 64 years, regardless of the age of first intercourse (AFI), although we know our population has early sex exposure (mean AFI 15.2 years). To evaluate the prevalence of women ≤30 years of age among women with a confirmed diagnosis of preinvasive and invasive cervical lesions—high-grade squamous intraepithelial lesions (HSIL), adenocarcinoma in situ (AIS), and CC. In addition, we sought to describe the demographic characteristics and the treatment rendered in this young population.

Disease/Procedure/Practice Issue: This was a cross-sectional study to analyze the prevalence and characteristics of patients ≤30 years of age with confirmed diagnosis of HSIL, AIS, or CC in the Laboratory of Pathology at Irmandade Santa Casa de Misericórdia de Porto Alegre (ISCMAPA), Brazil, from January 2004 to May 2016.

Outcomes: Of the 1,039 patients, 221 (21.3%) were ≤30 years of age, corresponding to 31.4% of patients with preinvasive lesions and 8.1% with CC. Regarding the clinical characteristics of women ≤30 years, we noted early sexual initiation (mean AFI 15.5), high multiparity (47.1% had 2 or more previous pregnancies), and high current smoking prevalence (57.3%). All patients with HSIL and AIS ($n = 195$) were treated with excisional procedures, 79.8% with a single surgery: loop electrosurgical excision procedure (LEEP), cold knife cone (CKC), or hysterectomy. Among CC patients ($n = 36$), 80.6% had surgical treatment (30.5% of them were referred to radiotherapy with or without adjuvant chemotherapy), 6 had recurrence of CC, and 3 died due to CC.

Conclusion: We noted a high number of patients ≤30 years of age with HSIL, AIS, and CC. Additional investigation is necessary to determinate the best strategy for screening in this young population in Brazil.

10 - International Session

Gene expression profiles between two major histological types of cervical cancer: Squamous cell carcinoma and adenocarcinoma

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Objective: Cervical cancer is the second cause of cancer-related deaths among women in developing countries. Locally advanced disease is frequently seen, with a high rate of treatment failure. Most common histological types are squamous cell (SCC) and adenocarcinoma (AC). Concurrent chemoradiation is the standard treatment for both histologies. However, different studies suggest a worse prognosis for AC. Therefore, it is important characterize the biological behavior of the neoplasm in order to personalize treatment. The purpose of this study was to characterize a global expression profile between SCC and AC and correlate with clinical outcome after standard treatment.

Disease/Procedure/Practice Issue: A group of 32 cervical tumors of patients with locally advanced cervical cancer was included in the present study; each patient was clinically followed during the protocol after treatment. Genome-wide

expression profile by high-density expression microarray and class prediction was performed (8 AC, 24 SSC) to classify both histological types. The profiles were validated by qRT-PCR and immunohistochemistry. To determine the main biological functions altered, the dataset was subjected to WEB-based Analysis WebGestalt, and disease-free survival was analyzed by the Kaplan-Meier method.

Outcomes: Through the study of group analysis ($P < 0.05$), 2,780 genes that reveal 2 molecular groups with correspondence to histological types AC and SCC were identified. The molecular profiles statistically significant with $P < 0.0001$ were grouped with a cluster of 63 genes that allowed us to clearly separate histologies. The P2RY2, IRF6, S100A2, and CALML3 genes confirm our results by qRT-PCR and immunohistochemistry. The bioinformatic analysis showed 1,688 genes involved in the biological processes of regulation and metabolic. As cellular components, 891 genes correspond to membrane and 1,000 genes code for binding proteins. Finally, the response to standard treatment was evaluated and showed no significant differences between the 2 groups in terms of persistence or recurrence rates.

Conclusion: The results evidenced a gene expression profile that correlates with each histological type in this cohort. Molecular differences have greater involvement in cellular functions and apparently have no influence in treatment outcome. It is necessary to evaluate a greater number of cases to identify a possible group of genes associated with a worse prognosis.

11 - International Session

Cisplatin and radiation therapy in HIV-infected women with locally advanced cervical cancer in sub-Saharan Africa (SSA)

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Objective: Numerous trials have shown improved survival when cisplatin was added to radiation therapy (RT) in women with locally advanced cervical cancer (LACC). None of these trials included HIV-infected women, for whom there was concern about treatment tolerance. This is a particular concern in Sub-Saharan Africa, where comorbid conditions are common. Our primary objective was to prospectively determine the feasibility and toxicity of administering chemoradiotherapy to HIV-infected women with LACC receiving concomitant antiretroviral therapy (ART).

Disease/Procedure/Practice Issue: HIV-infected women with LACC were enrolled in this prospective trial. Planned therapy included external beam RT (EBRT) and brachytherapy with curative intent at standard doses together with weekly cisplatin, 40 mg/m², during EBRT and prescribed ART. The protocol allowed for dose delays and dose reductions of cisplatin.

Outcomes: Forty-one women with LACC, mean age (SD) 44.2 (5.6) years, were enrolled in Harare, Zimbabwe ($n = 26$), and Johannesburg, South Africa ($n = 15$); 39 initiated treatment and were evaluable. FIGO stages were as follows: IIA, 1; IIB, 29; IIIA, 1; and IIIB, 10. Median CD4 counts and HIV viral load were 427 (range 139–1204) and <20 (range <20–39,900), respectively. Thirty-seven of 39 women (95%) completed treatment per protocol, which in some cases required dose reduction or elimination. A total of 228 cycles of chemotherapy were administered, most at the full dose. Of the 36 participants who started at 40 mg/m², more than half were able to tolerate 4 or more doses. GCSF was administered at the investigator's preference to 13 women. Two women with persistent hematologic toxicity did not complete treatment as per protocol. See Table 1.

Conclusion: Concomitant chemoradiotherapy in HIV-infected women with LACC on ART is well tolerated at standard doses used in HIV-uninfected women. Dose delays and reductions were similar to those typically seen in HIV-uninfected women with LACC. Women who completed therapy continue to be followed for survival and correlative endpoints.

Table 1. Total cisplatin cycles completed for 39* patients undergoing concomitant chemo/EBRT.

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Cisplatin						
No dose modifications	39 (100)	30 (77)	31 (79)	24 (62)	17 (44)	13 (33)
Dose delayed	0	6 (15)	1 (3)	0	2 (5)	0
Dose reduced	0	2 (5)	7 (18)	12 (31)	11 (28)	14 (36)
Delayed & reduced	0	1 (3)	0	2 (5)	3 (8)	3 (8)
Drug discontinued / not administered	0	0	0	1(3)	6 (15)	9 (23)

* includes the 3 women starting at lower dose cisplatin

12 - International Session

Surgical management of ovarian tumors without the support of intraoperative pathology readings in Bhaktapur Cancer Hospital

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Objective: The objective was to evaluate the outcome of surgical management of ovarian tumors in a low-resource setting that lacks the information provided by intraoperative frozen section (IOFS) pathology.

Disease/Procedure/Practice Issue: Intraoperative assessment of an ovarian mass with IOFS offers imperative guidance for surgical management. In Bhaktapur Cancer Hospital, IOFS pathology reading is not available, subjecting women with ovarian masses to possible additional surgery and exposing them to additional perioperative risks. In a setting without IOFS technology, surgeons must rely on clinical suspicion and laboratory results when choosing the appropriate surgical procedure. We conducted a retrospective analysis of all patients who underwent surgical treatment for ovarian masses at Bhaktapur Cancer Hospital in Nepal between May 1, 2015, and October 30, 2017. The Fisher exact test was used to determine significant differences in the surgical management of patients with benign, borderline, and malignant ovarian tumors.

Outcomes: Sixty-two patients underwent surgical management of ovarian masses at Bhaktapur Cancer Hospital between May 1, 2015, and October 30, 2017. Postoperative pathology classified 43 cases as malignant, 3 as borderline, and 16 as benign. Surgical management is shown in Table 1. Statistical analysis revealed that benign and malignant ovarian masses were managed similarly. There was no significant difference between the percentage of patients with benign versus borderline/malignant masses who received staging and debulking surgeries (94% vs 80%, $P = 0.43$). Neither clinical suspicion nor clinical suspicion combined with CA-125 levels accurately determined malignant/borderline versus benign masses (93% vs 94%, $P = 1.0$; 100% vs 91%, $P = 0.56$, respectively). There was no significant difference in perioperative complications between the benign, borderline, and malignant cases ($P = 0.49$).

Conclusion: In this low-resource setting lacking IOFS pathology readings for ovarian masses, clinical suspicion and CA-125 levels were poor predictors of malignancy. Many patients with benign masses underwent extensive surgery, and multiple patients with malignant disease did not undergo full staging. IOFS technology is as an important support for surgeons treating ovarian masses and is unfortunately lacking in many low-resource settings.

Table 1.

Final pathology	Cystectomy	BSO + Hysterectomy	Omentectomy	Lymph Node Biopsy
Benign	0% ($N = 0$)	100% ($N = 16$)	88% ($N = 14$)	94% ($N = 14$)
Borderline	33% ($N = 1$)	66% ($N = 2$)	66% ($N = 2$)	33% ($N = 1$)
Malignant	12% ($N = 5$)	86% ($N = 37$)	79% ($N = 34$)	86% ($N = 37$)

13 - International Session

Ovarian neoplasia: Characteristics and diagnostic concordance between ultrasound, tumor markers and histopathology in Honduras 2015-2016

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Objective: To determine the diagnostic concordance between ultrasound, tumor markers, and histopathology for the detection of malignant ovarian tumors at San Felipe Hospital in Honduras between 2015 and 2016.

Disease/Procedure/Practice Issue: The diagnostic difficulty of ovarian cancer is due to the nonspecific symptoms of the disease as well as the lack of proven effective screening methods. The International Ovarian Tumor Analysis (IOTA) Group models help ultrasonographers predict risk of malignancy of an adnexal mass before surgery with sensitivity of 92%–93% and specificity of 81%–83%. Elevated CA-125 levels may help differentiate benign and malignant adnexal masses in postmenopausal women. Histopathology remains the gold standard for diagnosis. Because of the lack of intraoperative assessment with frozen section at San Felipe Hospital, preoperative assessment is imperative in guiding surgical management. Kappa index calculation ($Po - Pe / 1 - Pe$) was used to evaluate interobserver agreement.

Outcomes: A total of 111 patients were surgically treated for suspected ovarian malignancy at San Felipe Hospital between January 1, 2015, and December 31, 2016. Ultrasound was performed transabdominally in 58.5% ($n = 65$) and transvaginally in 21.6% ($n = 24$) of patients; 51% ($n = 57$) of patients had 1 of the 5 IOTA criteria reported. Tumor marker results were available for 68.4% ($n = 76$) of patients. Based on histopathology, 55.8% ($n = 62$) had malignant ovarian tumor, and 44.1% ($n = 42$) had benign tumor. For histopathological confirmed ovarian malignancy, 43.5% ($n = 27$) had abnormal CA-125 levels; 16.1% ($n = 10$) had normal CA-125 levels; and 35.4% ($n = 22$) had no markers available. For ultrasound and histopathological diagnosis, $k = 0.03$ (SE = 0.04, 95% CI 0.11 to -0.05), which is slight concordance; sensitivity 97%, specificity 6%, PPV 56%, NPV 60%. For ultrasound, tumor markers and histopathological diagnosis, $k = 0.60$ (SE = 0.11, 95% CI 0.37–0.82), which is moderate concordance; sensitivity 80%, specificity 81%, PPV 82%, NPV 78%.

Conclusion: Preoperative assessment is particularly important in low-resource countries, where intraoperative frozen section is not available to guide surgeons of possible malignancy. At San Felipe Hospital, the inclusion of IOTA criteria will help distinguish malignant and benign masses. Tumor markers should be considered in postmenopausal women and if resources allow.

14 - International Session

HE4 is the marker of choice in discriminating endometriosis from ovarian cancer in pelvic mass patients: Sub-analysis of a prospective multicentric study

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Objectives: Differential diagnosis of endometriosis and early ovarian cancer might be challenging, as ultrasound features might be difficult to interpret and CA-125 is usually elevated in both diseases. Adequate preoperative risk assessment is a prerequisite for an optimal surgical approach. The aim of this subanalysis was to assess the sensitivity and specificity of HE4 compared to CA-125 in discriminating between endometriosis and ovarian cancer.

Disease/Procedure/Practice Issue: Within the prospective multicentric pelvic mass study, 1,438 pelvic mass patients have been included. All patients received ultrasound according to IOTA and blood sampling for CA-125 and HE4. Surgical removal of the pelvic mass was an inclusion criteria. Both CA-125 and HE4 were determined using ROCHE Kits at Labor Berlin. Receiver operator characteristics (ROC) curve analysis was performed to evaluate the predictive accuracy of HE4 and CA-125 expression for discriminating between patients with ovarian cancer and those with endometriosis.

Outcomes: In our study 114 patients have been diagnosed with epithelial ovarian cancer, 104 patients with endometriosis. The results showed that HE4 performed better than CA-125 alone with an AUC of 0.912 (95% CI 0.872–0.953) and 0.812 (95% CI 0.753–0.871). At a predefined specificity of 75.4%, CA-125, HE4, and ROMA reached a sensitivity of 75%, 98.1%, and 99%, respectively.

Conclusion: HE4 and ROMA can better discriminate between endometriosis and ovarian cancer patients.

15 - International Session

The economics of prevention in the BRCA mutation carrier: Epithelial ovarian cancer (EOC) prevention by risk-reducing surgery (RRS) is cost effective compared to treatment upon cancer development

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Objective: To evaluate from a Canadian perspective the cost-effectiveness of prevention of EOC via risk-reducing surgery (RRS) in germline *BRCA1/2*-positive family members of index EOC cases with the *BRCA1/2* mutation, compared with treatment upon cancer development.

Disease/Procedure/Practice Issue: For high-grade EOC, cure is unlikely and there is no effective screening. Prevention of EOC by risk-reducing bilateral salpingo-oophorectomy (RRBSO) is effective and can be offered to *BRCA*-positive family members of index cases with a *BRCA* mutation. However, testing and RRS incurs upfront costs; does this therefore represent value for money at a societal as well as at an individual level in the long term? Cost-effectiveness models allow this to be assessed by weighing the benefits of an intervention against the cost.

Methods: A cost-effectiveness model using a 50-year time horizon was developed to compare germline testing for *BRCA* mutations followed by RRS with no testing and treatment only if cancer developed. All index patients were tested for *BRCA*; if positive (12.46% risk), first-degree relatives were tested (50% risk) followed by second-degree female relatives (25% risk) if the first-degree relative was positive. In the base case all positive relatives were assumed to receive RRBSO. Cancer risks and model costs are summarized in Table 1; an annual rate of 0.5%–1.5% for EOC was conservatively applied based on published literature.

Outcomes: In the base case a single year of *BRCA* testing of 2,786 incident cases identified 424 *BRCA*-positive female relatives of 390 *BRCA*-positive index cases, with RRS preventing 56 cases of EOC and 25 all-cause deaths over 50 years compared with no testing/treatment upon cancer development (Table 2). In a scenario in which 50% underwent RRBSO, 32 cases of EOC and 15 all-cause deaths were avoided. In the base case testing was cost saving (–\$1,780,780), compared with no testing, with a saving of –\$239,226 in the 50% scenario. Testing dominated no testing in both the base case and the 50% scenario (less expensive and more effective). Cost-effectiveness increased in sensitivity analysis as age for RRBSO and proportion undergoing RRBSO decreased and EOC risk increased.

Conclusion: Index case germline *BRCA* testing with subsequent RRS in as-yet-unaffected carriers prevented deaths and was cost-effective compared with no testing and treatment upon cancer development.

Table 1. Cancer risk, risk reduction following surgery, and costs included in the model.

Cancer risk		
10-year risk of ovarian cancer without surgery		
Current age	BRCA1	BRCA2
30 – 39	5%	5%
40 – 44	10%	5%
45 – 49	10%	10%
50 – 54	15%	10%
55 – 59	10%	10%
60 – 64	10%	5%
65 – 69	10%	5%
70 – 79	10%	5%
Risk reduction following surgery		
Bilateral salpingo-oophorectomy	0.16	0.12
Costs		

Cost component	Cost	Source
BRCA test	\$675	Estimate
Genetic counselling	\$300	Estimate
Bilateral salpingo-oophorectomy	\$9,080	Ontario Case Costing Initiative
Hormone replacement treatment (annual cost)	\$101	Ontario Drug Benefit Formulary
Ovarian cancer treatment, with surgery	\$40,420	Estimate based on an 'average' cost of treating ovarian cancer
Ovarian cancer treatment, without surgery	\$34,412	Estimate based on an 'average' cost of treating ovarian cancer
Ovarian cancer palliative care	\$14,687	Hollander MJ. Costs of end-of-life care: findings from the province of Saskatchewan. Healthc Q. 2009;12(3):50-8. Inflated to 2016 costs
All-cause mortality palliative care	\$14,687	Hollander MJ. Costs of end-of-life care: findings from the province of Saskatchewan. Healthc Q. 2009;12(3):50-8. Inflated to 2016 costs

Table 2. Base case model results.

Clinical results					
Arm	Family EOC cases	Family EOC avoided	Family deaths	Family deaths avoided	
No BRCA testing	103	-	293	-	
BRCA testing	47	56	268	25	
Costs - Total					
Arm	Testing and counselling	RRBSO and HRT	EOC treatment	Palliative care	
No BRCA testing	\$0	\$0	\$114,692,213	\$8,410,766	
BRCA testing	\$3,716,305	\$3,145,098	\$106,294,121	\$8,166,675	
Costs - Family members only					
Arm	Testing and counselling	RRBSO and HRT	EOC treatment	Palliative care	
No BRCA testing	\$0	\$0	\$21,427,196	\$3,194,000	
BRCA testing	\$1,718,755	\$3,145,098	\$13,029,103	\$2,949,910	
Cost-effectiveness results					
Arm	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER
No BRCA testing	\$123,102,979	9,426	-	-	-
BRCA testing	\$121,322,199	9,718	-\$1,780,780	292	Dominant

Discounting of costs and QALYs was applied at 1.5%.

Abbreviations: EOC, epithelial ovarian cancer; HRT, hormone replacement therapy; RRBSO, risk-reducing bilateral salpingo-

oophorectomy.

16 - International Session

Epidemiology of type 1 endometrial cancer: A tale from 2 cities

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Objective: Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries and the second most common in developing nations. In developed countries, risk factors for EC such as obesity and late menopause are highly prevalent. The effects of modernization contribute to EC in developing countries. Unfortunately, health inequity can result in a later diagnosis and poorer outcomes for women in developing countries. The objective of this study was to compare the epidemiological differences of type 1 endometrial cancer (T1 EC) in 2 tertiary gynecologic oncology centers: in a developed country (Australia) and an emerging nation (Malaysia).

Disease/Procedure/Practice Issue: This is a retrospective cohort study, comparing T1 EC in Hospital Sultan Ismail (HSI), Malaysia, and Flinders Medical Centre (FMC), Australia. Ethics approval was obtained from both hospitals. Medical databases in HSI and FMC were analyzed, and T1 EC cases were identified. Case notes were examined to obtain relevant data from HSI (2012–2015) and FMC (2010–2015).

Outcomes: A total of 106 cases in FMC and 70 cases in HSI were identified. The average annual number of cases managed by HSI and FMC were 23 and 18, respectively. Women in HSI were younger at diagnosis (54.4 ± 9.6 years) compared to FMC (66.2 ± 11.2 years). In HSI, 40 patients had an office endometrial biopsy with 18 inconclusive results; 31% were diagnosed with a hysteroscopy, dilatation and curettage (H D&C). In comparison, 100% of women underwent an H D&C in FMC with only 2 inconclusive results. All patients in HSI underwent definitive surgery with grade 2 EC being most common (46%). In FMC, grade 1 EC was most common (50%) with 4 patients managed conservatively. Fifty percent of cases in HSI were stage I compared to 78% in FMC. There were no stage IV cases in FMC compared to 16% of cases in HSI. All patients in FMC attended follow-up, while only 75% of women attended follow-up in HSI. Recurrence rates were also higher in HSI (32%) compared to FMC (7%). The majority of recurrence occurred in patients with stage III and IV diseases.

Conclusion: Women in HSI were more likely to have a higher grade and stage at diagnosis and disease recurrence. Contributing factors include high inconclusive rates of preoperative histology, delayed presentation to hospital, surgical factors, and lack of resources for adjuvant treatment. Follow-up rates were higher in FMC compared to HSI (100% vs 75%) due to a robust method for patient recall. Other barriers to follow-up in HSI include a lack of knowledge, access, and cost of transport to attend appointments.

17 - International Session

Surgical candidacy among women presenting at Mulago National Referral Hospital and the Uganda Cancer Institute with new diagnoses of cervical cancer

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Objective: To report the proportion of surgical candidates and to identify predictors of candidacy among women with new diagnoses of cervical cancer at government-funded tertiary care centers in Kampala, Uganda.

Disease/Procedure/Practice Issue: We recruited women with cervical cancer presenting at Mulago National Referral Hospital and/or the Uganda Cancer Institute (UCI). Interviews occurred after a gynecologist had assessed biopsy results, performed a staging examination, and recommended treatment. This was an observational study and is part of a larger study to evaluate predictors of delay in the steps leading to treatment initiation. We used univariate and multivariate analysis to investigate associations between explanatory variables and surgical candidacy.

Outcomes: Between April and November 2017, 138 patients with cervical cancer presented to Mulago and/or UCI and consented for participation. Of these, 18.2% were stage IA2, IB1, or IB2; 36.4% were stage IIB; 38.7% were stage IIIA or IIIB; and 6.82% were stage IVA or IVB. Of all participants, just 12% were recommended for radical hysterectomy. In multivariate

analysis adjusted for age, occupation, marital status, parity, and HIV serostatus, prior screening (OR = 3.78, 95% CI 1.16–12.35) and at least primary education (OR = 3.96, 95% CI 1.14–13.80) were associated with higher odds of surgical candidacy. Of those who had previously been screened (35/138), 81% underwent visual inspection with acetic acid (VIA), 16% Pap, and 3% HPV test. More than one-third (13/35) of these women had screened positive, but only less than half (6/13) had been treated. See Table 1.

Conclusion: This is the first study to report the proportion of new cervical cancer cases assessed by Ugandan gynecologists to be candidates for primary surgery. Given improved outcomes with earlier disease and the relative inaccessibility of radiation and chemotherapy, interventions should facilitate earlier diagnosis, which, in turn, should increase the proportion of surgical candidates. Women with prior screening and women with at least primary education had higher odds of surgical candidacy. In this study, just one-quarter of women with cervical cancer had ever been screened, mostly with VIA, and less than half of those with positive screens had been treated. In the future, we must increase access to screening in order improve prevention and early detection of cervical cancer.

Table 1. Characteristics of women diagnosed with cervical cancer at Mulago Hospital by surgical candidacy.

Variable	Total N	Non-surgical treatment recommended %	Surgical candidate %	Unadjusted Odds Ratio of Surgical Candidacy (95% CI)	Adjusted* Odds Ratio of Surgical Candidacy (95% CI)
Total (N, %)	N=138	N=121 (88%)	N=17 (12%)		
Age, yrs (mean, SD)	49 (13)	49 (12)	49 (16)	0.99 (0.96-1.04)	1.01 (0.95-1.07)
Education					
< primary	68	91	9	1.0	1.0
≥ primary	64	83	17	2.14 (0.74-6.19)	3.96 (1.14-13.80)
Occupation					
Industry/business	53	92	8	1.0	1.0
Farming/domestic	85	85	15	2.21 (0.68-7.18)	3.60 (0.83-15.6)
Urban versus rural					
Rural	61	87	13	1.0	**
Urban	77	88	12	0.88 (0.31-2.42)	**
Marital status					
Single/divorced /widowed	79	90	10	1.0	1.0
Married	59	85	15	1.5 (0.58-4.42)	1.56 (0.47-5.20)
Parity					
≤ 6	77	88	12	1.0	1.0
> 6	61	87	13	1.14 (0.41-3.16)	0.67 (0.15-2.97)
Family Planning					
No method	132	88	12	1.0	**
Using a method	5	80	20	1.81 (0.19-17.24)	**
Prior Screening					
No prior screening	103	91	9	1.0	1.0
History prior screening	35	77	23	3.09 (1.09-8.79)	3.78 (1.16-12.35)
HIV serostatus					
HIV -	87	85	15	1.0	1.0
HIV +	48	92	8	0.52 (0.16-1.69)	0.44 (0.11-1.87)

18 - International Session

Patients with recurrent gynecological cancers referred for pelvic exenteration but not operated on: Exclusion criteria and outcomes

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Objective: Pelvic exenterative surgery (PES) for recurrent gynecological cancers (RecGC) after radiotherapy is performed most often with curative intent. Case selection is critical and involves excluding extra-pelvic disease and evaluation of the

likelihood of achieving R0. We reviewed those patients who were referred for, but did not undergo, PES to determine the exclusion criteria and outcomes.

Disease/Procedure/Practice Issue: A prospective database of all patients referred with RecGC between 2004 and 2017 for PES was analyzed for case selection criteria and survival after the diagnosis of recurrence.

Outcomes: There were datasets on 87 of 93 patients who did not have PES, 52% of all referrals for PES. The median age at initial diagnosis was 55 years (mean 52 years, range 24–80 years). The initial cancer diagnosis was cervical ($n = 48$, 55%), endometrial ($n = 21$, 24%), vaginal ($n = 8$, 9%), vulval ($n = 4$, 4.5%), ovarian ($n = 3$, 3.75%), and other ($n = 3$, 3.75%). Exclusion criteria were as follows: (1) review of imaging indicated R0 not achievable and/or extensive disease ($n = 49$, 56.5%), (2) patient choice ($n = 17$, 20%), (3) metastatic disease ($n = 15$, 17%), (4) patients deemed unfit for surgery ($n = 5$, 5.5%), and (5) abandoned intraoperatively due to progressive disease ($n = 1$, 1%). The median age at diagnosis of recurrence was 56.5 years and at death, 59 years. The median disease-free interval after primary treatment was 31.7 months for all cancers (range 0–122 months). The median survival after recurrence was 15 months (mean 21.8 months, range 2–65 months). Only 4.5% ($n = 4$) of the patient cohort are still alive. Cervical cancer patients had a median survival after date of diagnosis of recurrence of 11 months (mean 17.8 months) compared to median survival of 34 months (mean 32.6 months) in endometrial cancer patients.

Conclusion: About half of patients with RecGC referred for PES did not undergo surgery. The main exclusion criteria were (1) locally advanced disease, R0 considered not feasible, (2) metastatic disease, and (3) patient choice. The data pose questions about possible late referral for PES in this cohort of patients. Median survival for recurrent gynecological cancer patients excluded from PES was 15 months.

19 - International Session

BRCA1/BRCA2 mutations behavior and clinical evaluation in Mexican ovarian cancer patients

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Objectives: Ovarian cancer (OC) is the leading cause of gynecologic cancer death and the fifth cause of overall women cancer death in the United States. In Mexico about 4,000 new OC cases are diagnosed per year; it represents the second gynecologic malignancy cause of death. Cancer family history (CFH) is associated with OC in 10%–15% of the cases, attributable to germinal mutations in *BRCA1/2* genes among Caucasian women. However, there is currently a lack of studies assessing the presence of *BRCA* mutations in other specific populations. The aim of this study was to investigate the prevalence of germinal *BRCA1/2* mutations on OC Mexican patients and to correlate with clinical outcomes.

Disease/Procedure/Practice Issue: A total of 107 OC patients were enrolled between October 2015 and August 2017 at the Instituto Nacional de Cancerología, Mexico. The NGS method, which interrogates all coding regions, and up to 50 bases in each intronic region was used to detect small mutations in the *BRCA1/2* genes, and MLPA of both genes. Analytical sensitivity was >99%. Mutation status was correlated with the clinical-pathologic characteristics.

Outcomes: The prevalence of *BRCA+* (positive) mutations patients is higher (31.7%) than previously published (28%) for Mexican population (Villareal-Garza C, 2015). *BRCA1/BRCA2* mutations represent 70.6% and 29.4% respectively. Founder mutation *BRCA1* Del ex9-12 was detected in 33.3% of *BRCA1+*. HGSP was the most common histology among *BRCA+* patients (82.45%). All the patients with double primary malignancy (breast/ovarian) were *BRCA+*. Patients with better OS were *BRCA+* compared with WT's (100.3 vs 70.9 months, respectively, $P = 0.598$). *BRCA+* patients have CFH associated for breast cancer, 80%, and OC, 20%. Relevant result was carriers of the founder *BRCA1* mutation have better DFS compared with others *BRCA1+* (21.5 vs 10.9 months, $P = 0.044$).

Conclusion: The results of our study show the highest prevalence of *BRCA1/BRCA2* mutations genes among Mexican OC patients so far. The founder mutation appears to have an important role in the clinical outcomes for the Mexican population. Also, we highlight the importance of testing all the OC HGSP patients with/without CFH. We are beginning to integrate genetic testing in the Mexican health system, but it is not enough in this moment, understanding its importance as a diagnostic tool with clinical and therapeutic implications.