Abstract ID: 10962

Title: Laparoscopic predictability of minimally invasive interval debulking in advanced ovarian cancer: The MIID-SOC trial

Presenting Author: Anthony Costales, MD

Objectives: We sought to create a laparoscopic-based model to predict the ability to perform a minimally invasive (MIS) cytoreductive surgery in advanced epithelial ovarian cancer patients who have received neoadjuvant chemotherapy (NACT).

Methods: A total of 50 women with at least a partial response by RECIST 1.1 criteria to NACT were enrolled in a multi-institutional prospective pilot study (MIID-SOC trial- NCT03378128). Each patient underwent laparoscopic evaluation of 43 abdominopelvic sites followed by primary surgeon dictated surgical approach, either continue laparoscopically (MIS) or laparotomically. However, if the procedure was to continued MIS, the placement of a hand-assist port for manual palpation was mandated as to emulate a laparotomic approach and all 43 sites were re-evaluated. A total of 2 patients could not be evaluated by laparoscopy because of dense adhesions, 2 patients did not undergo cytoreductive surgery as the laparoscopy deemed the patient unresectable, and 1 patient withdrew consent prior to surgery. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated for each site to predict resectability via the MIS approach. Based on statistical probability of each factor predicting cytoreductive approach, 10 abdominopelvic sites were selected for inclusion in the final model. Each parameter was assigned a numeric value based on the strength of statistical association and a total predictive index score (PIV) was assigned for each patient. Receiver operating characteristic curve analysis (ROC-AUC) was used to assess the ability of the model to predict the MIS surgical approach. Statistical significance was evaluated using Fisher's exact test.

Results: A total of 28 patients (61%) underwent MIS cytoreductive surgery. All patients had an optimal cytoreductive surgery (< 1 cm residual disease) regardless of approach. The presence of disease on the following abdominopelvic sites were most strongly associated with predicting an MIS surgical approach: gastrosplenic ligament, rectum, left mesocolon, transverse colon, right colon, cecum, appendix, liver capsule, intrahepatic fossa/gallbladder, ileum/jejunum. Using the PIV, a ROC was generated with an AUC = 0.699. In the final model, a PIV < 2 identified patients able to undergo an optimal MIS cytoreductive surgery with an accuracy of 68.9%. The specificity, or ability to identify patients who would be able to undergo an optimal MIS interval cytoreductive surgery was 70.6%.

Conclusions: In this model, a PIV of < 2 was able to identify patients who were likely to undergo an optimal MIS interval cytoreductive surgery. This predictive index model may help to guide future inclusion criteria in randomized studies evaluating the MIS approach in advanced epithelial ovarian cancer.

Abstract ID: 11284

Title: A multi-institutional study of minimally invasive surgery compared to laparotomy for interval debulking after neoadjuvant chemotherapy in women with advanced ovarian cancer

Presenting Author: Alice Barr, MD

Objectives: Neoadjuvant chemotherapy (NAC) is becoming more ubiquitous for treatment of advanced epithelial ovarian cancer (EOC), and mode of interval debulking surgery (IDS) has not been adequately evaluated. A minimally invasive surgical (MIS) approach offers several advantages to an open approach (O-IDS), especially in the current COVID-19 pandemic, but data regarding outcomes are limited. We sought to compare the surgical and oncologic outcomes of MIS and O-IDS in patients (pts) with advanced EOC.

Methods: All consecutive patients with stages III to IV EOC who underwent NAC followed by IDS from 2008-2018 at 3 tertiary care centers were included in this retrospective cohort study. Demographic, clinical, and pathologic factors were abstracted from electronic medical records. Progression-free survival (PFS) and overall survival (OS) were analyzed on a Kaplan-Meier estimator using the log-rank method, and Cox proportional hazards regression models were used for univariate and multivariate survival analyses.

Results: A total of 415 pts underwent IDS through MIS (n = 122; robotic = 78, laparoscopic = 44), or O-IDS (n = 293). There were no statistically significant differences between age at diagnosis (O-IDS 63.2, MIS 65.3; p = 0.1), stage (p = 0.3), and grade (p = 0.06). There were also no differences between CA-125 levels measured at diagnosis (O-IDS 3145 U/mL, MIS 2247 U/mL; p = 0.2) or after completion of NACT (O-IDS 251.7 U/mL, MIS 179.1 U/mL; p = 0.4) between the 2 groups. MIS was completed without conversion in 84 of 122 patients (68.8%), with most conversions occurring in the robotic group. Patients undergoing MIS had significantly fewer complex surgeries, with 81% of the cases categorized as low complexity when scored using the Aletti SCS, compared to 64% of open surgeries ($p < 0.001$). Patients undergoing open surgeries had significantly higher estimated blood loss (EBL; 326.2cc vs 181.5cc; $p < 0.001$) and intraoperative transfusion rate (25% vs 4%; $p < 0.001$). These patients also had a longer hospital length of stay (5.9 days vs 2.2 days; $p < 0.001$) as well as 30-day postoperative complication rate (43% vs 20%, $p < 0.001$). There were no observed differences between the 2 groups in terms of operative time (191.1 minutes vs 196.3 minutes; p=0.5) and 30-day hospital readmission rates (10% vs 6%; p = 0.2). With regard to surgical cytoreduction, patients undergoing MIS had significantly higher rates of both R0 (66% vs 46%; $p< 0.001$) and optimal, or R0/R1 (93% vs 84%; p=0.02) debulking rates. Patients undergoing open surgery trended towards having a higher rate of recurrence at 24 months after diagnosis, but this difference did not reach significance (70% vs 60%; p = 0.06). Finally, there were no differences in the 2 groups in terms of PFS or OS (Figure 2). Median PFS was 15.1 months for O-IDS and 18.2 months for MIS (p=0.051). Median OS was 36.7 months for O-IDS and 40.9 months for MIS (p=0.5).

Conclusions: MIS is a feasible and potentially effective mode of IDS after NAC in patients with advanced EOC. Surgical outcomes appear to be advantageous in MIS compared with O-IDS, and oncologic outcomes appear to be no different. Further investigation of robotic MIS compared with laparoscopic MIS for IDS is warranted.

Abstract ID: 10443

Title: If looks could kill: Morphologic subtypes of high-grade serous ovarian cancer

Presenting Author: Katelyn Handley, MD

Objectives: Despite similar histologic appearance amongst high-grade serous ovarian cancers (HGSOC), anecdotally there are differences in gross appearance. However, no systematic framework to classify morphologic differences exists. Therefore, we aimed to determine whether high-grade serous ovarian cancers (HGSOC) can be reliably divided into distinct gross morphologic subtypes and to assess clinical outcomes and molecular features of these subtypes.

Methods: A retrospective review was performed of video-recordings from patients who underwent laparoscopic assessment of disease burden prior to primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT). Video recordings were reviewed by at least 2 physicians. A total of 4 sites (diaphragm, omentum, peritoneum, and pelvis) were assessed and classified as type I (deep, infiltrative disease with distortion of surrounding tissue) or type II (superficial, exophytic disease bordered by normal tissue). Tumor tissues from 16 of these chemotherapy-naïve patients were analyzed by multi-platform omics (RNA sequencing, proteomics). Clinical outcomes were assessed utilizing a prospectively collected database and compared by morphology using t-test or Fisher's exact test.

Results: Of the 99 evaluable patients, 60 exhibited uniform morphology at all involved metastatic sites (65% type I and 35% type II), and 81 exhibited a predominating morphology (58% type I and 42% type II). A total of 164 images were reviewed by a third physician with 83.5% inter-rater concordance (κ=0.6446). Patients with uniform type 1 (n=34)tumor morphology were more likely to exhibit an excellent response to NACT (defined as radiologic or CA-125 complete response) than those with type II (n=16) tumor morphology (47% vs 18%, p=0.13). Patients with type II predominant tumor morphology had a significantly higher estimated blood loss at the time of interval debulking surgery (p=0.008) as well as longer operative time (p=0.03) compared with type I tumor morphology. Patients with complete type II morphology were more likely to have a modified Fagotti score of <8 (p = 0.026), and thus were more likely to be triaged to PDS. On histopathologic review of 7 type I cases and 4 type II cases, no obvious histo-pathological pattern dominated either type. We identified distinct molecular differences between the 2 types, including increased TGF-β expression in type I and increased MYC expression in type II. Type I tumors seem to have abundant stroma and are immunologically active, whereas type II tumors seem to be dominated by cancer cells, have little stroma, and are immunologically cold.

Conclusions: There are at least two distinct gross morphological patterns of HGSOC with unique molecular differences and responses to chemotherapy. These findings could have major clinical implications for tailored therapeutic strategies.

Abstract ID: 11016

Title: Higher surgical volume is associated with better outcomes for frail patients undergoing surgery for ovarian cancer

Presenting Author: Morcos Nakhla, MS

Objectives: Frailty is a syndrome of decreased physiologic reserve and decreased resilience to stress that has been associated with adverse outcomes following many operative procedures. We aimed to evaluate these findings among patients undergoing surgery for ovarian cancer (OC) using a nationwide database.

Methods: Inpatient hospitalizations were identified for patients undergoing surgery for OC using the 2005-2017 National Inpatient Sample database. International Classification of Diseases-9th and -10th Revision (ICD-9 and ICD-10) codes were used in conjunction with the Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining diagnosis indicator to designate frailty. Multivariate regression models were used to assess the association of frailty with postoperative outcomes and resource utilization.

Results: Of an estimated 198,820 patients, 6.1% (12,085) were considered frail. Frail patients were older (66 vs. 60 years; $p < 0.001$) and had a greater burden of comorbidities as measured by the Elixhauser comorbidity index (4.3 vs 2.9; $p < 0.001$). The proportion of frail patients undergoing surgery increased significantly throughout the study period ($p < 0.001$) while the overall rate of in-hospital mortality decreased over time ($p < 0.001$). Adjusting for patient and hospital characteristics, frailty was associated with an increased likelihood of mortality (Adjusted Odds Ratio (AOR): 2.5 (CI 1.8 to 3.6)), non-home discharge (AOR:3.4 (CI 2.9 to 4.0)) and complications (AOR:1.6 (CI 1.4 to 1.8)), including respiratory (AOR:1.8 (CI 1.6 to 2.0)) and infectious (AOR:1.9 (CI 1.6 to 2.3)) complications. When evaluating surgical volume in tertiles, frail patients were less likely to be treated at the highest volume institutions (31% vs 36%; $p = 0.012$). Increased surgical volume was associated with decreased mortality among frail patients compared to non-frail counterparts (Figure). Frailty was also associated with a 4-day longer length of stay per hospitalization ($\beta = 4.3$ days; $p < 0.001$) as well as a $12,139 increase in hospitalization costs ($\beta =$ $12,139; $p < 0.001$).

Conclusions: While frailty is associated with worse outcomes in surgical patients with OC, these outcomes have improved significantly over the study period despite a simultaneous increase in frail patients. Although frail patients are less likely to be treated at institutions with higher surgical volume compared to their non-frail counterparts, those frail patients who do undergo surgery at these centers have decreased inpatient mortality rate. Efforts to mitigate the impact of frailty among OC patients should be further explored.

Abstract ID: 10463

Title: Frailty repels the knife: The impact of frailty index on surgical intervention and outcomes

Presenting Author: Katelyn Handley, MD

Objectives: We aimed to assess the impact of frailty in ovarian cancer patients on surgical procedures and outcomes.

Methods: A retrospective review of a prospectively collected database from April 2013 to September 2017 was performed. Patients with advanced disease were triaged by laparoscopy to determine primary resectability. The modified frailty index score (mFI) was calculated based on the sum of 10 items: chronic obstructive pulmonary disease or recent pneumonia, congestive heart failure, myocardial infarction, coronary artery disease, diabetes, hypertension, peripheral vascular disease, cerebrovascular disease (CVA), CVA with neurologic deficit, and Eastern Cooperative Oncology Group (ECOG) status 3 or 4, with each item receiving a score of 1 if present. Patients with an mFI ≥ 2 were classified as high frailty. Clinical outcomes were assessed and compared by mFI using t-test or Fisher's exact test. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results: A total of 591 patients met inclusion criteria. A total of 57% of patients had an mFI of 0, 29% mFI of 1, and 14% mFI ≥ 2. There was no difference in stage by mFI ($p = 0.984$). Patients with high frailty were less likely to be offered a laparoscopic surgery to determine primary resectability than those with an mFI of 1 or 0 (27.63% vs 42.77% vs 48.58%, respectively, $p = 0.004$). If laparoscopy was performed, the modified Fagotti score was more likely to be ≥ 8 in patients with a higher frailty score (58%, 48%, and 34% for a score of ≥ 2, 1, and 0, respectively, $p = 0.038$), leading to only 17% of the high frailty cohort proceeding with primary debulking surgery, compared to 26% and 34% in patients with mFI = 1 and mFI = 0 ($p = 0.015$). Furthermore, patients with a higher frailty score were less likely to undergo any tumor reductive surgery (TRS), whether primary or interval (59% vs 74% vs 85% for a score of ≥2, 1, and 0, respectively, $p < 0.001$). Death was a more frequent reason for lack of TRS in patients with a higher frailty score (52% vs 24% vs 22% in patients with a frailty score ≥ 2, 1, and 0, respectively, $p = 0.011$). Patients with high frailty were more likely to undergo splenectomy (20% vs 3% vs 6% for a frailty score of ≥ 2, 1, and 0, respectively, $p = 0.001$) and small bowel resection (SBR) (14% vs 8% vs 3% for a frailty score ≥ 2, 1, and 0, respectively, $p = 0.006$). Intraoperative complications were more frequent in patients with higher mFI (43% vs 37% vs 26% for a score of ≥ 2, 1, and 0, respectively). Postoperative complications were similarly correlated with higher mFI, more specifically, increased intraoperative hematologic complications and increased postoperative respiratory, gastrointestinal, and wound complications. The median postoperative length of stay was 4 days regardless of frailty score. On multivariate analysis, high frailty was associated with a worse PFS ($p = 0.009$) and tended towards worse OS ($p = 0.079$).

Conclusions: Frailty is associated with bulkier disease, decreased surgical intervention, and worse clinical outcomes.

Abstract ID: 10453

Title: Long-term follow-up of anal cytology and HPV genotyping among women with lower genital tract neoplasia

Presenting Author: Ashley Valenzuela, DO

Objectives: Determine the risk of abnormal anal cytology among women with a history of cervical, vulvar or vaginal high-grade dysplasia or cancer (high-risk cohort) 5 years following initial anal dysplasia screening. Determine the persistence, progression, or regression of anal dysplasia or cancer in this high-risk group over a 5 year period.

Methods: This is a 5-year follow up of an IRB approved prospective cohort study that compared the rate of abnormal anal cytology between a high-risk cohort and control group. The high-risk cohort was identified as women with a history of cervical, vulvar or vaginal high-grade dysplasia or cancer. The charts of the patients in the high-risk cohort were reviewed to determine the prevalence of anal dysplasia or cancer as well as the rate of persistence, progression, or regression based on screening results in the primary study.

Results: The 190 patients in the high-risk cohort were reviewed 5 years after initial data collection. In our prior study, 22% of the control cohort (women without a history of cervical, vulvar, or vaginal dysplasia or cancer) had abnormal anal cytology compared to 41% of the high-risk cohort. High-risk HPV was detected in the anal canal of 1.2% of the control group compared to 20.8% of the high-risk group. No anal dysplasia was detected in the control group while 13.4% in the high-risk group had anal intraepithelial neoplasia (AIN), including eight women (4.3%) with AIN 2+ or anal cancer.A total of 5 years after initial anal Pap smear, only 17 women (9%) of the high-risk cohort had repeat anal Pap smear performed. Of these, all 17 patients had abnormal anal cytology at initial anal Pap smear. A total of 3 patients had multiple repeat anal Pap smears in the follow up period. A total of 9 of these women (53%) had persistence of anal dysplasia after 5 years. One patient (6%) had progression from AIN 1 to AIN 3 over the 5 year period. Seven patients (41%) had regression of AIN to normal cytology.

Conclusions: While women with a history of HPV-related genital neoplasias are at risk for anal dysplasia and cancers, the role of screening in this population remains unclear. Anal cytology screening among HIV-positive individuals has become more common, but the appropriate frequency of screening remains unknown. While follow up was rare in this cohort, the data from this long-term follow up reveals that women with lower genital tract dysplasia or carcinoma are at increased risk for anal dysplasia or carcinoma. Routine anal Pap screening should be considered in this high-risk population. Future studies aim to contact these women to collect repeat anal cytology for a better understanding on the long-term risk of anal dysplasia with lower gynecologic tract dysplasia or malignancies.

Abstract ID: 10663

Title: COVID-19 outcomes of patients with gynecologic cancer in New York City: An updated analysis

Presenting Author: Olivia Lara, MD, MS

Objectives: Despite a growing body of literature, characterization of COVID-19 infection in patients with gynecologic cancer remains limited. Here we present an update of COVID-19 outcomes in New York City (NYC) from the initial surge of severe acute respiratory syndrome coronavirus 2 (coronavirus disease 2019 [COVID-19]). We sought to determine the hospitalization and mortality rates and their associated factors, specifically recent chemotherapy and immunotherapy use.

Methods: Data were abstracted from gynecologic oncology patients with COVID-19 infection among 8 New York City (NYC) area hospital systems. Multivariable logistic regression was utilized to analyze COVID-19 related hospitalization and mortality.

Results: Of 193 patients with gynecologic cancer and COVID-19, the median age at diagnosis was 65.0 years (interquartile range, 53.0-73.0 years). A total of 106 of the 193 patients (54.9%) required hospitalization; among the hospitalized patients 13 (12.3%) required invasive mechanical ventilation and 39 (36.8%) required ICU admission. No patients requiring mechanical ventilation survived. A total of 34 of 193 (17.6%) patients died of COVID-19 complications. On multivariable analysis, hospitalization was associated with an age greater than or equal to 65 years (odds ratio [OR] 2.12, 95% confidence interval [CI] 1.11, 4.07), Black race (OR 2.53, CI 1.24, 5.32), performance status greater than or equal to 2 (OR 3.67, CI 1.25, 13.55) and greater than or equal to 3 comorbidities (OR 2.00, CI 1.05, 3.84). Only former or current history of smoking (OR 2.75, CI 1.21, 6.22) was associated with death due to COVID-19 on multivariable analysis. A total of 13 of 34 (38.23%) patients who died of COVID-19 complications received cytotoxic chemotherapy, while 4 of 34 (11.76%) patients received immunotherapy. However, recent cytotoxic chemotherapy use was not predictive of COVID-19 hospitalization or mortality on multivariable analysis.

Conclusions: The case fatality rate among gynecologic oncology patients with COVID-19 infection is 17.6%. Cancer-directed therapy, including immunotherapy use, is not associated with an increased risk of mortality related to COVID-19 infection in this larger cohort.

Abstract ID: 10947

Title: Widening cancer care disparities in the adoption of telemedicine during COVID 19: Who is left behind?

Presenting Author: Michael Richardson, MD

Objectives: To determine the racial disparities in oncology visits of racial minorities before and after COVID-19.

Methods: Data were obtained from the electronic health records, a multi-specialty healthcare system serving a racially/ethnically diverse patient population in northern California. The study cohort included patients who had at least one oncology visit from January 2019 to August 2020. We examined the trends in the volume of oncology office visits and adoption of video visits during the ongoing COVID-19 pandemic period. Chi-square test and multivariate logistic regression were performed to examine variability in use of video visits by specific patient characteristics (sex, age, race/ethnicity and language barrier).

Results: Of 63,903 cancer patients (median age: 66; 68% female), Whites, Blacks, Hispanics, Asians and others composed of 64.8%, 3.5%, 9.2%, 11.7% and 10.8% of our study cohort. Over the 20 month study period, the drop in in-person visits began in March and peaked in April 2020. Compared to the year 2019, the office visits decreased by -16.6%, -55.9%, and -50.9% in March, April, and May of 2020. Although there was a trend towards increased office visits in June (-21.9% compared to 2019), this again decreased to -35% in July 2020. The proportion of visits conducted by video began at 16.6% in the first week after California's shelter-in-place order in March, peaked at a high rate of 43.4% in April, and remained at a rate of 33.8% in August. We focused on variability by specific patient subgroups when telemedicine was offered and used prevalently during early pandemic in April. Based on age, the younger cohorts, 18-50 and 51-64 year olds, were more likely to utilize video visit at 50.6%, and 50.6% compared to only 38.0% and 36.7% of the older groups (65-75 and 76+ years old, $p < 0.001$). In fact, the largest discrepancy, 21% difference between the younger vs older groups, was observed towards the end of April. With respect to race, Asians had the highest use of video visits (51.4%) compared to Hispanic (34.5%) and Black patients (40.3%) in April ($p < 0.001$). Although the gap narrowed over the next 4 months with only a 4% difference by August, these cancelled visits were not recovered in the minority groups. Finally, 44.6% of those who did not require an interpreter utilized video visits as compared to only 19.8% who did require an interpreter ($p < 0.001$). Age and race/ethnicity remain strong predictors of video visit use after adjusting the main and interaction effects of patient characteristics, with Asians 51-64 year old having the highest rate (58%) and Hispanics 76+ year old the lowest rate (30%).

Conclusions: Overall office visits have decreased significantly during the COVID-19 pandemic. Older patients, Black patients, Hispanic patients, and patients who required interpreting services were less likely to be treated through video visits. Future studies are needed to better understand the barriers to telemedicine care.

Abstract ID: 11002

Title: Cancer never stops: SARS-CoV-2 pandemic and the effect on research within GOG partners

Presenting Author: Brian Slomovitz, MD

Objectives: The SARS-CoV-2 pandemic forced a shift in conducting clinical research. Ensuring the safety of all stakeholders (patients, research personnel, family members), maintaining financial viability, and overcoming operational restrictions (limited access to sites, workforce restrictions, reduced data collection) are barriers to continuing clnical research. GOG Partners, the GOG Foundation industry-sponsored clinical trials group, has been proactive to implement the following: - Immediate compliance with CDC, FDA, and NIH guidelines with regard to clinical trial management. - Systems that allowed for remote monitoring and other remote activities (telemedicine patient visits, remote data collection, shipping of drug to patients, virtual study start-up). - Enhance enrollment opportunites away from university-based sites towards community-based practices. - Increased frequency of our operations meetings with industry. The objective of this report is to describe how the pandemic affected accrual to GOG Partners' trials.

Methods: Accrual data for GOG Partners trials over the past 4 years (2017- July 2020) were collected. 'Pandemic' months were considered March thru July 2020. Information collected included accrual numbers, institution type (university versus non-university), and region of country. Descriptive statistics were analyzed.

Results: Over the past 4 years, the median monthly accrual to GOG Partners trials was 43 patients (range: 14-95). Between March and July 2020, the median accrual was 59 patients (range: 43-72). For the same 5-month period over the past 3 years (March to July 2017, 2018, 2019) the median accrual was 36 (14-95). Accrual in March 2020 was 69 patients. Accrual decreased to 43 patients in April 2020 and 47 patients in May 2020 with respective z-scores of -0.25 and -0.01. June and July 2020 showed increased accrual with 59 and 72 patients respectively. The median number of participating sites per month over the past 4 years was 32 (9-66). There was an immediate decline in the number of sites participating from April to May 2020 of 36%. The number of sites participating in June and July were 38 and 52, respectively. During the pandemic, the accrual in the New England, Mid-Atlantic, Pacific and South Atlantic regions varied from their baselines. These variations followed the trends in COVID-19 spread. Non-university institutions accrued at a near-average rate throughout the months of April and May. During that same period, universities observed a decline in accrual of 48%.

Conclusions: Accrual to GOG Partners' trials increased 37% over the median monthly accrual since the pandemic began. During the pandemic, total monthly accrual fell below or reached the median during only 1 month. Regional diversity of sites participating in GOG Partners' studies helped in preventing a more dramatic drop in participation. While overall accrual has historically shown to be relatively balanced between institution types, non-university institutions were less negatively impacted.

Abstract ID: 11163

Title: Preoperative wait times in high-grade endometrial cancer: Do surgical delays impact patient survival?

Presenting Author: Andra Nica, MD, MSc, FRCSC

Objectives: Practice guidelines advocating for the regionalization of endometrial cancer surgery to gynecologic oncologists practicing in designated gynecologic oncology centres were released by Cancer Care Ontario in June 2013. We sought to determine the impact this policy had on contemporary surgical wait times. Moreover, a discussion about the impact of delays in treatment has never been more timely than in the context of the current COVID19 pandemic, which has burdened health care systems around the world. Our primary objective was to establish whether longer wait time to surgery is a predictor of survival in patients with high grade endometrial cancer.

Methods: This was a retrospective cohort study, which included patients diagnosed with non-endometrioid high-grade endometrial cancer (serous, carcinosarcoma, clear cell, and undifferentiated) between 2003 and 2017. A total of 2 regionalization periods were defined, before and after January 2014 to allow 6 months for knowledge translation after guideline publication. Patients were identified in population-based administrative provincial data sources. Multivariable Cox proportional hazards regression with a spline function was used to model the relationship between wait time and overall survival, as measured from time of surgery.

Results: We identified 3518 patients with high grade endometrial cancer. Median wait time between diagnosis and surgery for the entire cohort did not significantly change with regionalization of care (50 vs 52 days, p = 0.14). Patients who had surgery with a gynecologic oncologist had a median surgical wait time from diagnosis to hysterectomy of 55 days compared to 59 days pre-regionalization (p = 0.0002), and from first gynecologic oncology consultation to hysterectomy of 29 days compared to 32 days pre-regionalization (p = 0.0006). Survival was worst for patients who had surgery within 14 days of diagnosis (HR death 2.7, 95%CI 1.61-4.51 for 1-7 days and HR death 1.96, 95%CI 1.5-2.57 for 8-14 days), indicating disease severity. Decreased survival occurred with surgical wait times of more than 45 days from the patient's first gynecologic-oncology appointment (HR death 1.19, 95%CI 1.04-1.36 for 46-60 days and HR death 1.42, 95%CI 1.11-1.82).

Conclusions: Regionalization of surgery for high grade endometrial cancer has not had a negative impact on surgical wait times. Impact on survival is seen with patients who have surgery more than 45 days after surgical consultation.

Abstract ID: 11139

Title: Long-term safety and secondary efficacy endpoints in the ENGOT-OV16/NOVA phase III trial of niraparib in recurrent ovarian cancer

Presenting Author: Ursula Matulonis, MD

Objectives: In the ENGOT-OV16/NOVA study, maintenance therapy with niraparib significantly prolonged progression-free survival (PFS) in patients (pts) with platinum-sensitive recurrent ovarian cancer (PSROC) regardless of germline BRCA mutation (gBRCAm) or homologous recombination deficiency (HRd) biomarker status. This analysis updates long-term safety and available data on secondary efficacy outcomes.

Methods: In this randomized, double-blind, placebo-controlled, phase III trial, pts with PSROC were enrolled into 1 of 2 independent cohorts by gBRCAm status (gBRCAm or non-gBRCAm). Stratification factors were PFS after the penultimate platinum therapy (6 to <12 months vs >=12 months), best response to the last platinum-based therapy (complete or partial), and prior bevacizumab (Y/N). Pts were randomized 2:1 to niraparib 300 mg QD or placebo. The primary endpoint was PFS as assessed by blinded independent central review. Progression-free survival 2 (PFS2) and overall survival (OS) were exploratory secondary endpoints.

Results: A total of 553 pts were randomized in the NOVA study. Median follow-up was 66 months at the time of the current analysis.Hematologic treatment-emergent adverse effects (TEAEs) primarily occurred in the first year of niraparib treatment: incidence of grade ≥3 thrombocytopenia decreased from 33.8% to 2.8%, anemia decreased from 25.6% to 0.7%, and neutropenia decreased from 19.3% to 2.1% from year 1 to year 2–3, respectively. A total of 13 (3.5%; 9 gBRCAm, 4 non-gBRCAm) pts who received niraparib developed MDS/AML vs 3 (1.7%) placebo pts. Survival status could not be obtained for ~15% of pts. Data on post-progression therapy, including PARP inhibitors, were not available for 25% of the study pts. Based on data cut-off on October 2020, 127 and 238 deaths occurred in the gBRCAm and non-gBRCAm cohorts, respectively. For pts with available data, placebo pts received subsequent PARP inhibitor therapy (crossover) after disease progression: 46% (30/65) in the gBRCAm cohort and 13% (15/116) in the non-gBRCAm cohort. Hazard ratios for PFS2 were 0.67 (95% CI: 0.48, 0.95) in the gBRCAm cohort and 0.81 (95% CI: 0.62, 1.05) in the non-gBRCAm cohort. Restricted mean survival time analyses for OS up to 72 months were 43.2 months in placebo vs 45.9 months in niraparib (Δ of 2.7m, 95% CI: -4.1, 9.5) in the gBRCAm cohort and 39.1 months in placebo vs 38.5 months in niraparib (Δ of -0.6m, 95% CI: -6.0, 4.7) in the non-gBRCAm cohort.

Conclusions: These final data support the safe long-term use of niraparib for maintenance treatment in pts with PSROC. PFS2 analysis indicates that the benefit of niraparib maintenance therapy extends beyond first progression. No difference in survival was observed. The NOVA study was not powered for OS, and analysis is confounded by a high rate of crossover and missing data thus limiting its interpretation.Sponsor: GlaxoSmithKlineClinical Trial Registration: NCT01847274

Abstract ID: 10520

Title: Maintenance olaparib for patients with newly diagnosed, advanced ovarian cancer and a BRCA mutation: 5-year follow-up from SOLO1

Presenting Author: William Bradley, MD

Objectives: Newly diagnosed advanced ovarian cancer patients (pts) are at high risk of relapse and 5-year survival is 30–50%. Delay of recurrence, prolonged survival and, for some pts, increased chance of cure are goals of treatment in this setting. In SOLO1 (NCT01844986; GOG-3004) pts with advanced ovarian cancer and a BRCA1 and/or BRCA2 mutation (BRCAm) who were in response after first-line platinum-based chemotherapy derived significant progression-free survival (PFS) benefit from maintenance olaparib vs placebo (median 41 months follow-up; median not reached vs 13.8 months; hazard ratio 0.30; P < 0.001; Moore et al. NEJM 2018). We report analyses after 5-years of follow-up (data cut-off [DCO]: March 5, 2020), performed to assess the long-term efficacy and tolerability of maintenance olaparib for newly diagnosed advanced ovarian cancer.

Methods: Pts received maintenance olaparib (tablets; 300 mg bid) or placebo for up to 2 years or until progression. PFS and recurrence-free survival (RFS) were investigator-assessed by modified RECIST v1.1. An exploratory subgroup analysis of PFS in higher-risk (stage IV disease, stage III disease with residual disease following primary debulking surgery, inoperable stage III disease, or stage III disease and had undergone interval surgery) and lower-risk (stage III disease without residual disease following primary debulking surgery) pts was carried out. For pts in complete response at baseline, RFS was defined post hoc as time from randomization to disease recurrence (new lesions by imaging) or death.

Results: A total of 260 pts were randomized to olaparib; 131 to placebo (median treatment duration 24.6 vs 13.9 months, respectively). After a median of 4.8 and 5.0 years of follow-up, median PFS was 56 vs 14 months in the olaparib and placebo arms, respectively (Table). In the higher-risk subgroup 42% of olaparib-arm vs 17% of placebo-arm pts were free from progression at 5 years; in the lower-risk subgroup 56% vs 25% of pts, respectively, were progression free at this time point. Among pts in complete response at baseline, risk of disease recurrence or death was reduced by 63%. The safety profile of olaparib was consistent with previous observations. No new cases of myelodysplastic syndrome or acute myeloid leukaemia were reported (previous DCO: olaparib, 3/260 [1%]; placebo, 0/130), and incidence of new primary malignancies remained balanced between arms (olaparib, 7/260 [3%]; placebo, 5/130 [4%]).

Conclusions: For pts with a BRCAm and newly diagnosed advanced ovarian cancer, the benefit derived from 2 years of maintenance olaparib was sustained beyond the end of treatment, and after 5 years, almost half of pts were progression free vs 20% with placebo. This benefit was consistent across higher- and lower-risk pts. Over 50% of pts in complete response after first-line platinum-based chemotherapy remained free from relapse 5 years after randomization. A total of 5 years of follow-up is the longest for any PARP inhibitor in this setting and no new safety signals were observed.

Abstract ID: 10543

Title: Homologous recombination repair mutation gene panels (excluding BRCA) are not predictive of maintenance olaparib plus bevacizumab efficacy in the first-line PAOLA-1/ENGOT-ov25 trial

Presenting Author: Eric Pujade-Lauraine, MD, PhD

Objectives: In the Phase III PAOLA-1/ENGOT-ov25 (NCT02477644) trial, the addition of the PARP inhibitor olaparib to bevacizumab maintenance therapy led to a significant progression-free survival (PFS) benefit in patients with newly diagnosed advanced ovarian cancer (hazard ratio [HR] 0.59; 95% confidence interval [CI] 0.49-0.72), particularly in patients who were homologous recombination deficiency (HRD) positive, both including patients with BRCA1 and/or BRCA2 mutations (BRCAm; HR 0.33; 95% CI 0.25-0.45) and patients without a BRCAm (HR 0.43; 95% CI 0.28-0.66; Ray-Coquard et al. NEJM 2019). We explored the role of mutations in genes involved in homologous recombination repair (HRRm) excluding BRCAm as a predictive biomarker in patients with newly diagnosed advanced ovarian cancer who received olaparib + bevacizumab maintenance therapy in PAOLA-1.

Methods: Patients with newly diagnosed advanced high-grade serous or endometrioid ovarian cancer were randomized (2:1) to olaparib + bevacizumab maintenance or placebo + bevacizumab maintenance following response to platinum-based chemotherapy + bevacizumab. In an exploratory analysis, PFS was assessed in patients harboring a tumor mutation in a wide range of HRR gene panels (excluding tumor BRCAm [tBRCAm]): a panel with 13 pre-defined genes involved in HRR, an expanded panel with five additional genes involved in HRR, a restricted panel using five selected genes with the highest median genomic instability scores, and three published panels (Table). Tumors were analyzed using the Myriad myChoice HRD plus assay.

Results: Of the 806 patients randomized in PAOLA-1, 235/806 (29.2%) had a tBRCAm. The percentage of patients harboring deleterious mutations involved in HRR excluding tBRCAm ranged from 3.7% to 9.8% depending on the HRR gene panel (Table). For each gene panel, the number of patients with an HRRm in each treatment arm and HRD status are shown in the Table. PFS using different gene panels for HRRm is summarized in the Table; using the 13-gene panel, in patients with an HRRm excluding tBRCAm (n=54), the HR for PFS was 0.95 (95% CI 0.49-1.94). Expansion of this panel to include five other genes (n=72) demonstrated an HR (95% CI) for PFS of 1.01 (0.55-1.95). Consistent results were seen in patients with HRRm excluding tBRCAm using the three other published HRR gene panels (Table).

Conclusions: Acknowledging limitations of small subgroup sizes, HRRm (excluding tBRCAm) was not predictive of PFS benefit with maintenance olaparib in combination with bevacizumab, compared with bevacizumab alone, in PAOLA-1, regardless of the gene panel used. Mutation analysis using HRRm gene panels did not have utility beyond tBRCAm for selecting patients who may benefit from maintenance olaparib plus bevacizumab in PAOLA-1 and should not be considered a substitute for HRD determined by BRCA and/or genomic instability testing.

Abstract ID: 10440

Title: Pembrolizumab treatment of advanced cervical cancer: Updated results from the phase II KEYNOTE-158 study

Presenting Author: Hyun Chung, MD

Objectives: Pembrolizumab (pembro) showed durable antitumor activity and manageable safety in patients (pts) with advanced cervical cancer in an earlier interim analysis of KEYNOTE-158 (NCT02628067). Based on those results, the US FDA granted accelerated approval of pembro for pts with advanced, PD-L1-positive cervical cancer that progressed on or after chemotherapy. We present an updated analysis of pts included in the cervical cancer cohort of KEYNOTE-158 based on 17 months of additional follow-up.

Methods: KEYNOTE-158 is a phase 2 basket study investigating the antitumor activity of pembro across several cancer types. Key eligibility criteria for the cervical cancer cohort included histologically or cytologically confirmed disease, progression on or intolerance to >=1 line of standard therapy, an ECOG PS of 0 or 1, and provision of a tumor sample for biomarker analysis. Pts received pembro 200 mg once every 3 weeks for 2 years or until progression, intolerable toxicity, or physician or patient decision. Tumor imaging was performed every 9 weeks for the first 12 months, and every 12 weeks thereafter. PD-L1 positivity, defined as a combined positive score (CPS) >=1, was evaluated retrospectively by immunohistochemistry. The primary endpoint was the objective response rate (ORR) assessed per RECIST v1.1 by independent central radiology review. Secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety.

Results: A total of 98 pts were treated. Median age was 46 (range, 24 to 75) years, 65.3% had ECOG PS 1, and 94.9% had stage M1 disease. A total of 83.7% of enrolled pts had PD-L1–positive tumors. As of the June 27, 2019 data cutoff, the median follow-up duration, defined as first dose of study medication to data cutoff, was 36.9 (range, 34.3 to 41.0) months. In the updated analysis, 2 partial responses (PR) converted to complete responses (CR) and 2 additional PR occurred for a total of 5 CR and 9 PR; ORR was 14.3% (95% CI, 8.0% to 22.8%). A total of16 pts had stable disease (SD), and the disease control rate (CR+PR+SD) was 30.6%. All 14 responses were in pts with PD-L1–positive tumors, resulting in an ORR of 17.1% (95% CI, 9.7% to 27.0%) in the PD-L1–positive cohort (N=82) and 0.0% (95% CI, 0.0% to 21.8%) in the PD-L1−negative cohort. A total of 7 of 14 responses were ongoing after ≥24 months of follow-up. Median DOR had not been reached (range, 3.7+ to 35.2+). Median (95% CI) PFS and OS were 2.1 (2.1 to 2.2) months and 9.3 (7.6 to 11.7) months, respectively. Treatment-related adverse events (AEs) occurred in 65.3% of pts, and the most common were hypothyroidism (11.2%), fatigue (11.2%), and decreased appetite (9.2%). 12.2% of pts had treatment-related grade 3-4 AEs; there were no grade 5 AEs.

Conclusions: With 17 months of additional follow-up, pembro continues to show durable antitumor activity and manageable safety in pts with advanced cervical cancer, similar to the previous report.

Abstract ID: 10455

Title: A surgical window trial evaluating medroxyprogesterone acetate with or without entinostat in endometrial cancer and validation of biomarkers of cellular response: An NRG Oncology study

Presenting Author: Linda Duska, MD, MPH

Objectives: This surgical window of opportunity (window) study assessed the short-term effect of medroxyprogesterone acetate (MPA) alone vs MPA plus histone deacetylase (HDAC) inhibitor entinostat regulation of progesterone receptor (PR) in women with newly diagnosed endometrioid endometrial adenocarcinoma (EC).

Methods: A multi-site, randomized, open-label surgical window study treated women intramuscularly on day 1 with 400 mg MPA. Entinostat given 5 mg by mouth (PO) on days 1, 8 and 15 was randomly assigned with equal probability. Surgery followed on day 21-24. Pre- and post-treatment slides were assessed for PR H-scores, Ki-67 levels and histologic response.

Results: A total of 50 patients were accrued in 4 months; 22 and 20 participants had PR evaluable pre- and post-treatment slides in the MPA and MPA/Entinostat arms respectively. The median post treatment PR H-scores were significantly lower than pretreatment H-scores in both arms but did not differ significantly (MPA: 247 vs27, MPA/Entinostat: 260 vs23 respectively) p = 0.87. Decreased Ki-67 was shown in 90% treated with MPA/Entinostat compared to 68% treated with MPA alone (p = 0.13). Median PR H-score decreases were larger when Ki-67 was decreased (208) vsnot decreased (45). The decrease in PR pre- vspost-treatment was associated with a loss of Ki-67 nuclear staining, consistent with reduced cellular proliferation (p < 0.008).

Conclusions: This surgical window trial rapidly accrued in a multi-site setting and evaluated PR as its primary endpoint and Ki67 as secondary. Despite no immediate effect of entinostat on PR in this short term study, lessons learned can inform future window and treatment trials.

Abstract ID: 10882

Title: Genomic profiling of advanced cervical cancer to predict response to PD-1 inhibitor combination therapy: A secondary analysis of the CLAP trial

Presenting Author: Chunyan Lan, Dr.

Objectives: The CLAP trial (NCT03816553) is a multicenter, single-arm, phase II study in patients with metastatic, recurrent, or persistent cervical cancer who were treated with PD-1 inhibitor camrelizumab plus a VEGFR2 inhibitor apatinib. In this study, we performed genomic profiling analysis to identify potential predictive biomarkers for this combination therapy.

Methods: Genomic profiling was performed on 32 patients with available biopsy or surgical samples by targeted next-generation sequencing of 425 cancer-related genes. Somatic alterations and tumor mutational burden (TMB) were assessed for their predictive value on objective response rate (ORR), progression-free survival (PFS) and overall survival (OS). The Cancer Genome Atlas (TCGA) public dataset was used for validation.

Results: The ORR of the current cohort was 65.6%, which was consistent with the whole CLAP population. The median PFS and OS were not reached. Frequencies of genetic alterations (PIK3CA, 43.8%; STK11, 25%; FBXW7, 15.6%; PTEN, 15.6%; TP53, 15.6%) were similar to previous reports of cervical cancer. Mutations in PI3K pathway genes were found in 68.75% (22/32) of the patients. PIK3CA mutations (57.1% vs. 18.2%, P = 0.03) were significantly enriched in squamous cell carcinoma (SCC), whereas all mutations of TP53, ARID1B, DICER1, ERBB3, NF1, and TEK were detected in adenocarcinoma. Mutations in PIK3CA, PTEN, and ERBB3 were significantly associated with survival (univariate, P ≤ 0.05). PIK3CA mutations (PFS hazard ratio [HR], 0.33; P=0.05; OS HR, 0.23; P = 0.04) and PTEN mutations (PFS HR, 3.71e-09; P = 0.05; OS HR, 3.64e-09; P = 0.08) were significantly associated with improved clinical outcome. In contrast, ERBB3 mutations (PFS HR, 34.9; P < 0.001; OS HR, 19.8; P < 0.001) correlated with poor survival. Mutations in the PI3K pathway genes showed improved predictive power compared with PIK3CA or PTEN mutations alone (PFS HR 0.33, P = 0.03; OS HR 0.25, P = 0.02). The predictive effects of these mutations on PFS, but not on OS, were validated using the TCGA dataset. Furthermore, TMB-high (TMB ≥ 5 mut/Mb) were associated with prolonged PFS (HR 0.26, P < 0.01) and OS (HR 0.31, P = 0.05). Consistent with the CLAP trial, patients in this study with positive PD-L1 expression showed better outcome (PFS HR 0.36, P = 0.08; OS HR 0.31, P = 0.05). TMB combined with PD-L1 expression further stratified clinical benefit for patients, with ORR of 81.3% in TMB-high/PD-L1-positive and 25% in TMB-low/PD-L1-negative subgroup (P < 0.05). Multivariate analysis showed that ERBB3 mutation (PFS P = 0.01; OS P < 0.001), positive PD-L1 expression (PFS P = 0.01; OS P = 0.05), and high TMB (PFS P = 0.01; OS P = 0.05) remained significantly associated with survival.

Conclusions: In this study, we uncovered PIK3CA, PTEN, ERBB3, PI3K pathway genes mutations and TMB as novel predictive biomarkers in cervical cancer patients treated with PD-1 inhibitor combination therapy, which might be of great clinical relevance in patient stratification.

Abstract ID: 10636

Title: Immune markers of response to pembrolizumab and guadecitabine in platinum resistant ovarian cancer utilizing multiplex immunohistochemistry (mIHC)

Presenting Author: Matthew Cowan, DO

Objectives: Treatment options for platinum-resistant ovarian cancer (PROC) are limited by poor response (poor response) rates and short progression-free survival. Immune checkpoint inhibitors induce modest response rates (8-11%) in phase II trials for PROC, although responders can have prolonged disease control. An immunoreactive subtype of ovarian cancer (OC) was proposed from TCGA genomic analysis and susceptibility to immune checkpoint blockade seems to correlate with specific populations of tumor infiltrating lymphocytes (TILs). This study sought to identify potential markers of response to immunotherapy by using multiplex immunohistochemical staining (mIHC) to phenotype TILs in ovarian tumors obtained before and after treatment with guadecitabine and pembrolizumab in a phase II clinical trial (NCT02901899).

Methods: OC core needle biopsies were obtained at baseline and after 2 cycles of treatment from patients with PROC enrolled in a phase 2 trial testing the combination of guadecitabine and pembrolizumab. The Opal Multiplex IHC kit (Akoya Biosciences) was used to identify the TIL markers CD3, CD8, CD20, CD68 and FoxP3, and the epithelial marker pan-cytokeratin. A total of 12 paired (pre- and post-treatment) specimens from responders (PR or stable disease > 4 months, n = 6, R) vs. non-responders (progression <4 months, n = 6, NR) were stained and scanned by using the Vectra digital laser microscope and analyzed with the inForm software. The following lymphocytes were phenotyped and analyzed for spatial relationships to each other and to epithelial tumor nests: T cells, cytotoxic T cells, B cells, macrophages, and T regulatory cells (Tregs) in relationship to response to treatment. Additionally, archival tissue from 36 patients enrolled in this trial was stained with the monoclonal antibody 22C3 to assess PD-L1 expression.

Results: In this study, 48 pts were enrolled, 43 were treated, and 33 were evaluable for response. Overall, there were 3 PRs (RR=9.9%) and 16 pts had stable disease (SD) [48%]. The clinical benefit rate (PR + SD > 3 months) was 27%. Analysis of TILs in the tumor microenvironment identified an increased total and stromal numbers of CD8 cells in baseline biopsies in R vs. NR ($p = 0.05$). Likewise the total and stroma-infiltrating numbers of CD8 cells post-treatment were higher in R vs. NR ($p = 0.05$). The total, tumor, and stromal numbers of B cells at baseline and after treatment were increased in R vs. NR ($p < 0.05$). The numbers of total, stromal, and tumor infiltrating macrophages post-treatment samples were increased in R vs. NR ($p < 0.05$). There were no differences in numbers of Tregs between R and NR at baseline of after treatment. Of the 36 archival specimens, 16 (45.7%) showed PD-L1 tumor modified H score/modified percent score staining greater than 0; 20 specimens (59%) had present staining at the tumor/stroma interface.

Conclusions: Immunophenoyping using mIHC identified treatment induced changes in immune cell subpopulations predictive of response to immunotherapy in PROC.

Abstract ID: 10503

Title: ORZORA: Maintenance olaparib in patients with platinum-sensitive relapsed ovarian cancer: Outcomes by somatic and germline BRCA and other homologous recombination repair gene mutation status

Presenting Author: Sandro Pignata, MD, PhD

Objectives: The Phase III SOLO2 trial (NCT01874353) showed the significant benefit of maintenance olaparib for patients (pts) with platinum-sensitive relapsed ovarian cancer (PSROC) and a BRCA mutation (BRCAm), compared with placebo (median progression-free survival [PFS] 19.1 vs 5.5 months [m], respectively); however, no pts had a confirmed somatic (s) BRCAm and data prospectively evaluating efficacy of olaparib in this pt group were limited. ORZORA (NCT02476968), an open-label, single-arm, multicenter trial, was conducted to assess efficacy and safety of maintenance olaparib in PSROC pts with a BRCAm (s or germline [g]) who were in response to their most recent platinum-based chemotherapy after >=2 lines of treatment.

Methods: Pts underwent prospective central screening for tumor BRCAm status (myChoice CDx, Myriad Genetic Laboratories, Inc.), then s or g BRCAm status was determined by central g testing (BRACAnalysis CDx, Myriad Genetic Laboratories, Inc.). Pts received maintenance olaparib (400 mg bid; capsules) until disease progression. Co-primary endpoints were investigator-assessed PFS (RECIST v1.1) in BRCAm and s cohorts, conducted at 60% maturity. Secondary endpoints included time to second progression or death (PFS2), health-related quality of life (HRQoL; FACT-O trial outcome index) and tolerability. An additional exploratory cohort comprised pts with predefined homologous recombination repair gene mutations (HRRm) excluding BRCAm (FoundationOne CDx, Foundation Medicine, Inc.).

Results: A total of 181 pts were enrolled in ORZORA (BRCAm n = 145 [s n = 55; g n = 87; n = 3 s vs g status unknown]; HRRm n = 33; unassigned n = 3). Pt characteristics were similar between s and g cohorts: ≥3 prior lines of chemotherapy (38% vs 48%, respectively); partial response to prior platinum (45% vs 49%); tumor BRCA1-mutated (65% vs 64%). At the data cut-off (April 17, 2020), median follow-up for PFS was 22.3 months. Median PFS was similar in the BRCAm, s and g cohorts, and exploratory HRRm cohort (Figure). Median PFS2 for BRCAm pts was 30.9 m (95% confidence interval [CI] 24.7–40.0; s 24.7 [21.8–36.1]; g 32.5 [25.3–not calculable]). HRQoL was comparable in BRCAm and s cohorts (best overall change from baseline: improved 22 vs 21%; no change 69 vs 68%; worsened 11 vs 12%, respectively). Most common adverse events (AE; n = 177 treated pts) were nausea (54% pts), fatigue (43%), anemia (42%) and vomiting (28%). A total of 25% and 35% pts experienced serious and grade ≥3 (anemia 16% pts) AEs, respectively. 5% had an AE leading to treatment discontinuation. A total of 2 new primary malignancies, two acute myeloid leukemia and no myelodysplastic syndrome cases occurred.

Conclusions: PFS in pts with PSROC who received maintenance olaparib was similar irrespective of s or g BRCAm status. Activity of maintenance olaparib was also shown in pts with a non-BRCA HRRm. PFS, HRQoL and tolerability were consistent with previous olaparib studies in this population. Results highlight that PSROC pts beyond those with a gBRCAm can benefit from maintenance olaparib.

Abstract ID: 11259

Title: A clinical calculator to personalize chemotherapy in early stage clear cell ovarian cancer

Presenting Author: Anthony Bui, MD, MSCR

Objectives: To determine the utility of a clinical calculator to predict the benefits of chemotherapy and outcomes in women with early stage clear cell ovarian cancer.

Methods: Data from 2006-2015 was abstracted from the National Cancer Database. All patients had stage I clear cell carcinoma. Using a Cox regression model based on demographic, surgico-pathologic and laboratory characteristics, a clinical score was developed. Propensity score weighting was used to reduce bias between patients who did and did not receive chemotherapy.

Results: Of 1,528 patients with stage I clear cell ovarian cancer, 1309 (85.7%) did receive and 219 (14.3%) did not receive chemotherapy. Patients who underwent chemotherapy had a 5-year overall survival (OS) of 85.6% vs. 84.0% in those without treatment ($p = 0.30$). On univariate analysis, significant prognostic factors included older age (HR=1.021, 95% CI 1.002-1.021, $p = 0.03$), malignant ascites (HR 1.608, 95% CI 1.054-2.453, $p = 0.03$), and higher stage (1B or C) (HR 1.758, 95% CI 1.207-2.560, $p = 0.003$). To better define those who may have an increased benefit from chemotherapy, we designed a clinical calculator capable of dividing patients into low (n = 306), moderate (n = 916), and high-risk (n = 306) groups with associated 5-year overall survival of 90.3%, 86.8% and 76.1%, respectively ($p < 0.0001$). Using the calculator, chemotherapy was associated with decreased hazard of death in the high-risk patients, (HR = 0.483, 95% CI 0.258-0.905, $p = 0.02$), but did not benefit the moderate (HR= 1.551, 95% CI 0.752-3.199, $p = 0.57$) or low-risk patients (HR = 0.751, 95% CI 0.281-2.006 $p = 0.24$).

Conclusions: Our results suggest a clinical calculator can help direct chemotherapy decision making for women with early stage clear cell ovarian cancer.

Abstract ID: 10347

Title: Innovation in germline and somatic tumor testing pathways for ovarian cancer patients

Presenting Author: Ashley Haggerty, MD, MSCE

Objectives: New approvals for upfront maintenance therapy with parp inhibitors in ovarian cancer now indicate a need for germline genetic testing and potentially somatic testing including homologous repair deficiency (HRD) within several months of diagnosis. However, national rates of germline testing are approximately 30%1 despite being recommended for all patients. Current practice now indicates that it is even more important to obtain results quicker and more efficiently at the time of a new diagnosis of ovarian cancer. We sought to apply novel healthcare innovation techniques to this problem space to improve rates of germline and somatic tumor testing in ovarian cancer patients.

Methods: A total of 4 pilots ranging from “low to high touch” were performed in an experimental rapid cycle model, each lasting approximately 2-3 weeks. In Pilot 1, providers were “nudged” via email, text or electronic medical record (EMR) alert as per their preference that an upcoming patient was missing either genetic testing or tumor testing (HRD or somatic testing). In Pilot 2, choice architecture was used to pend orders for genetics consultation into the upcoming patient encounter in the EMR. In Pilot 3, a “Concierge Approach” was applied to capture patients in real time who were approached in person at the clinic appointment and offered immediate genetic counseling/testing. In Pilot 4, a text messaging platform was used to schedule patients for a counseling/testing appointment. Descriptive statistics were performed.

Results: Results: Pilot 1: 30 “nudges” were placed but only 50% of encounters documented discussion or ordering of genetic testing. Pilot 2: 75% of pended orders were signed, with 7/12 (58.3%) of patients scheduling a genetic counseling appointment. Pilot 3: 4/6 (66.7%) of patients completed a genetic counseling appointment when offered in real time at the visit and 3/4 (75%) completed testing. Pilot 4: If patients consented to texting for scheduling (50%), the majority of patients were scheduled for counseling or obtained outside testing results (n = 8/9, 88.9%). Attendance rates at appointments scheduled via text were 100% (n = 5/5). Potential trends in racial disparities were identified within the n = 59 patients missing germline or somatic testing, with an increased proportion of Black patients (27.1%) and Asian/Other (13.6%) missing testing, higher than the baseline practice demographics.

Conclusions: Behavioral economics can be utilized to improve rates of genetic and somatic testing for ovarian cancer patients. Patients typically complete genetic counseling/testing if an appointment is offered in real time. A 'warm hand-off' is needed for outreach via text for awareness and engagement, however once enrolled, patients participated via text for scheduling and discussion of prior results at high percentages. A 'concierge approach' is highly successful but not scalable for all but could be used to 'rescue' missed patients. Potential racial disparities need further exploration to ensure solutions are equitable and applicable to all patients. The growth of precision medicine could benefit from automation and choice architecture utilizing the EMR. This would allow for surfacing of missing clinical data by removing the mental burden of the work required to complete genetic and somatic testing.'

Abstract ID: 11189

Title: Priority assessment for women with recurrent ovarian cancer: A pilot study

Presenting Author: Stephanie Blank, MD

Objectives: There is no one best treatment option for women with recurrent ovarian cancer and the treatment plan is usually determined via shared decision-making. The primary objective of this study was to prospectively assess the feasibility of implementing a patient-centered Priorities Assessment Tool (PAT) in gynecologic-oncology clinics.

Methods: Inclusion criteria included diagnoses of recurrent ovarian cancer and English language proficiency. Exclusion criteria included cognitive impairment and non-engagement in treatment decision-making. Clinic schedules were reviewed in advance and eligible patients were contacted prior to their gynecologic-oncology appointment about the study. The study team approached interested subjects immediately prior to their visit to complete demographic information, the FACT FOSI-18 and the PAT instrument. Following the visit, patients and providers completed PAT evaluation forms. Feasibility was defined as the proportion of patients who completed all 3 study forms prior to meeting with their physician. A secondary objective was the identification of factors from the demographic form and FACT FOSI-18 associated with priority assessments from the PAT. Institutional review board (IRB) approval was obtained.

Results: Between October 2018 and December 2019, 115 women with recurrent ovarian cancer were considered for enrollment. Of these, 63 enrolled, 13 declined, and 39 were ineligible due to being non-English speaking. Reasons for declining included lack of time or interest. A total of 97% (60) of patients completed all three forms prior to their doctor's visit. The median age range was 61-70 years old, 48% (30) were of race or ethnicity other than non-Hispanic white, and 47% (29) had graduated college. A total of 18% (11) had no evidence of disease, and 78% (47) were receiving treatment. Prioritization included "having enough energy to do the things that are important to me" (66%, 41), caring for others (32%, 20), and hobbies (21%, 13). FACT FOSI-18 (Functional Assessment of Cancer Therapy Symptom Index) top concerns are shown in Figure 1. 79% (49), which indicated wanting to be involved in treatment decisions, 39% (24) needed help understanding their disease, and 76% (47) understood their goals of care. When FACT FOSI-18 scores were correlated with PAT responses, quality of life was inversely associated with wanting to be involved in treatment decision-making (Pearson Correlation -.273, $p = 0.031$). In evaluating the tool after their visits, 98% (60) said the PAT was easy to use and 61% (38) reported that it helped to communicate goals and priorities with the medical team.

Conclusions: Implementation of the PAT was feasible with 97% of enrolled patients completing all study forms prior to their appointment. The PAT allowed participants to share their treatment-related priorities and highlights that the majority of women with ovarian cancer want to engage in shared-decision making with their providers, especially those with diminished quality of life. This finding demonstrates the increasing importance of patient-physician communication over the cancer continuum.

Abstract ID: 10643

Title: Using health information technology to improve collection of family cancer history: Prospective randomized trial of web-based tool in a gynecologic oncology outpatient clinic

Presenting Author: Melissa Frey, MD

Objectives: In the US there are approximately 4 million individuals with a genetic cancer predisposition syndrome, however, the majority are not aware and cannot benefit from genetically-targeted cancer prevention. Family cancer history (FCH) can identify high risk patients and triage them to genetic assessment, however there is wide variability in accuracy, breadth and strategies for FCH collection. We aim to evaluate whether a web-based tool (WBT) can result in improved quality of FCH versus standard FCH collection via face-to-face interview.

Methods: All patients scheduled for a gynecologic oncology new patient visit between 9/2019-9/2020 were offered enrollment in an institutional review board-approved prospective trial. Patients were randomized to one of three arms: 1) standard of care FCH collection during the interview, 2) WBT administered at home prior to the visit, 3) WBT administered in the office prior to the visit. The primary endpoint was evaluation of FCH quality based on established quality measures. Chi-square test was used to compare FCH quality between intervention arms and ANOVA test for the number of relatives/generations in the pedigree. A Bonferroni correction was used to account for multiple comparison testing.

Results: A total of 100 patients were enrolled. The mean age was 56.2 years (SD 15.2). The WBT was completed successfully by 67% (22) of patients randomized to home administration vs 94% (31) randomized to office administration ($P = 0.01$). Patients cited the following reasons for failure to complete the WBT at home: difficulty with technology, concern about privacy and forgetting about the WBT invitation. In the intention-to-treat analysis, office WBT collection resulted in significantly higher quality FCH vs the control and home arms (Table 1). The WBT resulted in significantly greater mean number of relatives included in the pedigree (Arm 1 - 3.9 [SD 3.0], Arm 2 - 32.4 [SD 16.8], Arm 3 - 29.0 [SD 18.3], $P < 0.001$) and significantly greater number of included generations (2.2 [SD 0.9], 3.9 [SD 0.4], 3.7 [SD 0.6], $P < 0.001$). Patient age, race, ethnicity, and personal/family cancer history were not associated with FCH quality. When excluding patients who could not access the WBT at home, there were no differences in FCH quality when WBT was completed at home vs in the office. A total of 39 patients utilizing the WBT (74%) completed a satisfaction survey following the office visit; 38 (97%) reported that the WBT was easy to understand and 30 (77%) reported being satisfied with the tool.

Conclusions: FCH collection is an exciting application of information technology in the current healthcare setting with a growing emphasis on cancer genetics, disease prevention and thoughtful use of WBTs. In our cohort of gynecologic-oncology patients, a WBT resulted in significantly higher quality and more comprehensive family cancer pedigrees. With the COVID-19 pandemic inspired drive to minimize in-office time, future studies must assess strategies to improve patient engagement with WBT at home prior to the visit.

Abstract ID: 10568

Title: Comparative analysis of quality of life for three different adjuvant treatment modality in early stage cervical cancer: An analysis from STARS study

Presenting Author: He Huang, MD

Objectives: This analysis aimed to compare the quality of life (QoL) of patients with different adjuvant treatment modalities in STARS study for cervical cancer.

Methods: QoL assessment was done at the baseline and then longitudinally after completing of radiation or chemotherapy assigned in STARS study. In the study, post-operative FIGO stage IB to IIA cervical cancer patients with adverse pathological factors were randomized in 1:1:1 to receive adjuvant radiation alone, concurrent chemoradiation weekly cisplatin or sequential chemoradiation (with cisplatin plus paclitaxel in 21-day cycle, given 2 cycles before and 2 cycles after radiotherapy respectively). QoL was assessed with EORTC QLQ-C30 questionnaires at baseline (1 week after the surgery), during the treatment period (in the 5th week receiving pelvic irradiation), 12 months and 24 months after the completion of treatment. Analysis of variance by one-way repeated measures analyses of variance (ANOVA) was used to compare differences in QoL measures among treatment groups.

Results: Totally, 816, 633, 360 and 254 patients had completed QoL assessment at baseline, during treatment period, 12 month and 24 month after the completion of treatment. At baseline, a lowest global health status (GH) and functional dimensions including physical, emotional, role, cognitive and social functioning, and lowest scores of symptom and single item scales were presented among the 3 groups with balance ($p > 0.05$). During treatment period, GH and other functional dimension scores were elevated, with symptom item scores declined in RT group. While in CCRT or SCRT group, an elevated scores of symptom scales including of nausea and vomiting (30.93 ± 25.5 vs 20.8 ± 25.0 in SCRT group, 31.0 ± 28.1 vs 16.5 ± 24.3 in CCRT group), and appetite loss (39.6 ± 30.9 vs 34.8 ± 32.1 in CCRT group) was noted when comparing with that in baseline. The score of item concerning financial difficult declined in CCRT and SCRT group, which was similar as RT group. The scores of GH, functional dimensions and other symptom scales were not different compared with baseline in these two groups. During treatment period, a highest score of global health, functional dimensions including physical, role, cognitive, social functioning, and lowest scores of symptom including fatigue, nausea and vomit, insomnia, appetite loss, constipation and diarrhea was presented in the RT group than the other two groups (GH score 66.5 ± 16.4 in RT group, 60.7 ± 17.9 in CCRT group and 61.9 ± 17.5 in SCRT group, $p = 0.001$). No differences between CCRT and SCRT group regarding GH, functional dimensions and symptom scores. In 12 and 24 months after the completion of treatments, further improved GH, functional dimension scores and declined symptom scores were observed in the whole population, with no significant differences among the 3 treatment groups.

Conclusions: In CCRT and SCRT group, adding chemotherapy in adjuvant treatment had negative effects on GH, physical, cognitive, social and role function, as well as symptoms related to QoL during the treatment period compared with RT. While the symptoms resolved, functioning and general QoL improved after 12 months of treatment, indicating a transient impact on QoL of patients receiving adjuvant treatment.

Abstract ID: 11285

Title: Factors associated with completion of intracavitary brachytherapy: Do socio-demographic factors play a role?

Presenting Author: Angel Tabuyo, MD

Objectives: Despite new developments in the treatment of cervical cancer, intracavitary brachytherapy (ICBRT) continues to be part of the standard of care treatment for locally advanced cervical cancer. The objective of our study was to evaluate clinical and socio-demographic factors associated with not receiving indicated ICBRT and its impact on overall survival (OS) in women with locally advanced cervical cancer.

Methods: Patients diagnosed with cervical cancer between 1993 - 2017 receiving care at 2 large academic centers were included in this retrospective case control study. Demographic and clinical data were retrospectively abstracted. Data analysis was done using Mann-Whitney U test, Fischer's Exact test, logistic regression. Kaplan-Meier curves were constructed for OS and the log rank test was utilized to detect differences in OS.

Results: Of 274 patients with cervical cancer, 130 were candidates to receive ICBRT. Mean age was 50.19 (± 12.6). The majority of patients included were underrepresented minorities including 60.8% White-Hispanic patients and 30.8% Black. Spanish was identified as the primary language for 48.5% of women. The average median household income based on zip code was $45,387 (± $17,135) for the cohort. A total of 50.5% of subjects were foreign born with only 11.5% identified as USA born. Squamous cell carcinoma was the most common histologic type in the group at 86.2%. Majority of subjects included in cohort (53.8%) were Stage IIB at time of diagnosis. ECOG performance status was 0 in 72% of the subjects included.On univariate analysis, older patients (55.52 ± 11.7years, p = 0.012) (OR 0.957 [0.924, 990], p = 0.012), those with ECOG PS <2 (OR 0.153 [0.034, 0.686], p = 0.014), and those with Medicare (OR 0.096 [0.014, 0.675], p = 0.019) were less likely to complete ICBRT. Spanish speakers were more likely to complete ICBRT compared to those who spoke Haitian Creole (OR 7.8 [1.810, 34.106], p = 0.006) (reference English Speaker). When compared to Black patients, White patients more likely to complete ICBRT with OR 4.196 [1.753, 10.041], p = 0.0010. Factors such as treatment center, mean household income, bulky diseases (lesion >4cm), country of birth, BMI, and histologic type were not associated with completion of ICBRT (all p > 0.05). On multivariate analysis, Black race OR 0.216 CI (0.091-0.579) and Medicare status OR 0.039 CI (0.14-2.085) continued to be significantly associated with lack of receipt of brachytherapy.A total of 29 (22.3%) subjects did not complete the indicated ICBRT as part of their treatment. Among the reasons for not receiving ICBRT included distorted anatomy (17%), poor response to EBRT (28%), patient refusal or noncompliance (17%), ICBRT not available at the institution (7%), and inability to achieve desired dose (10%). Women who did not receive ICBRT were more likely to die of disease with a HR of 2.85 [1.071, 7.617], p = 0.046, even when external beam boost was performed. On Cox proportional-hazard analysis, receipt of ICBRT continued to be associated with OS. Receipt of intensity-modulated radiation therapy (IMRT) boost instead of ICBRT did not improve survival.

Conclusions: While ICBRT remains the standard of care for locally advanced cervical cancer, 22.3% of subjects (93% minority patients) did not receive it for various reasons. Sociodemographic and clinical factors are both associated with receipt of brachytherapy. Regardless of the reasons for not receiving,

and even when external beam boost is given in an effort to compensate for lack of receipt of brachytherapy, patients who do not receive ICBRT have a lower OS.

Abstract ID: 10654

Title: Patients with early-stage cervical cancer have an increased risk of preterm birth in a population-based cohort study

Presenting Author: Roni Nitecki, MD, MPH

Objectives: Cancer therapy can impact not only fertility but also the course of a subsequent pregnancy. Over 40% of women with cervical cancer will be diagnosed prior to age 45 and many will have not completed childbearing. Those with early-stage disease are eligible for fertility-sparing surgery (FSS), which is increasingly utilized. We sought to evaluate obstetric outcomes among cervical cancer patients in a population-based cohort.

Methods: This is a population based retrospective study of women age 18-45 years with a history of (FIGO 2009) stage IA1-IB1 cervical cancer reported to the California Cancer Registry (CCR) for the years 2000-2012. CCR data were linked to the 2000-2015 California Office of Statewide Health Planning and Development (OSPHD) birth and discharge datasets to establish a linked database with both oncologic characteristics and obstetric outcomes. Exposure status was defined as cervical cancer patients who conceived at least 3 months after fertility-sparing surgery (FSS) and delivered after 23 weeks gestational age (GA). The primary outcome was preterm birth, and only the first pregnancy following cancer diagnosis was considered. Secondary outcomes included growth restriction, fetal demise, neonatal morbidity (any of the following: need for respiratory support within 72 hours of life, hypoxic-ischemic encephalopathy, seizure, sepsis/pneumonia, meconium aspiration syndrome, birth trauma, and intracranial or subgaleal hemorrhage), and severe maternal morbidity (SMM) as defined by the CDC. Propensity score was used to match similar women in 2 groups in a 1:2 ratio (when possible) of cases to controls: group 1: women who conceived at least 1 year prior to their cervical cancer diagnosis; group 2: healthy controls. Wald statistics and logistic regression were used to evaluate outcomes.

Results: Of the 4087 patients who were 18-45 years at time of cervical cancer diagnosis, 40.9% (n = 1671) had a recorded pregnancy. Of those, 113 conceived following FSS and were primarily non-Hispanic White (52.2%) followed by Hispanic (31.9%) with a median age of 32 years (29-36). The majority had squamous cell carcinoma histology (62.8%), and of those with known type of surgery (97.3%), 90.9% had a LEEP or conization and 9.1% had a trachelectomy. Prematurity rates prior to 32 and 37 weeks were 5.3% and 26.5% respectively, and the live birth rate was 99.1%. Propensity score matching yielded 213 group 1 controls and 226 group 2 controls. Cervical cancer was associated with higher odds of preterm birth before 32 weeks compared to healthy controls (OR 4.17 95% CI 1.023-16.99), but not compared to control group 1, and higher odds of preterm birth before 37 weeks compared to both control groups (OR 2.39, 95% CI 1.34-4.25; OR 3.94, 95% CI 2.10-7.38, control 1, 2 respectively). There were no differences between the groups in rates of: growth restriction (5th or 10th percentile), fetal demise, and delivery via cesarean section. Neonatal morbidity was more common among the cervical cancer cohort compared to both control groups (OR 2.69, 95% CI 1.29-5.64; OR 2.3, 95% CI 1.15-4.72, control 1,2 respectively).

Conclusions: In a population-based cohort, patients who conceived at least 3 months following surgery for early-stage cervical cancer had a high live birth rate, but higher odds of preterm delivery and consequent neonatal morbidity compared to matched controls who had a pregnancy prior to their diagnosis as well as healthy controls.

Abstract ID: 10969

Title: Too much skin in the game? A paradigm shift in our understanding of vulvar and vaginal melanomas as distinct tumor types compared with cutaneous melanomas

Presenting Author: Annelise Wilhite, MD

Objectives: Due to the rarity of vulvar/vaginal melanoma (VVM), current therapeutic strategies mimics that of cutaneous melanoma (CM) without scientific rationale. Currently, immuno-oncology (IO) is a front-line treatment option for advanced melanoma, however data are limited for IO outcomes in advanced VVM. Considering 5-year survival for vulvar (58%) and vaginal (27%) melanoma is significantly inferior to cutaneous melanoma (81%), this calls into question the assumed similarity of these malignancies. As such, our goal is to compare molecular profiles of VVM with CM and explore the significance of IO agents on survival.

Methods: Samples were analyzed using next-generation sequencing (NextSeq, 592 Genes and WES, NovaSEQ), IHC and WTS (NovaSeq) (Caris Life Sciences, Phoenix, AZ). PD-L1 expression was tested by IHC using 28-8 (Agilent) and SP-142 (Spring Biosciences) (positive cut-off <u>></u> 1%). MSI was tested by FA, IHC and NGS. TMB was measured by totaling somatic mutations per tumor (TMB-high cut-off <u>></u> 10 mutations per MB). Immune cell fraction was calculated by QuantiSeq (Finotello 2019, Genome Medicine). Survival was extracted from insurance claims data and calculated from time of IO treatment to last contact using Kaplan-Meier survival curves. Statistical significance was determined using chi-square and Wilcoxon rank sum test and adjusted for multiple comparisons.

Results: Molecular analysis was performed on 171 VVM and 5255 CM between 1998 and 2020. Median age for VVM and CM was 65 and 63, respectively. A total of 114 (66.7%) VVM and 3538 (67.3%) CM were metastatic at time of diagnosis. Immunogenicity of VVM was significantly lower than CM, demonstrated by an absence of high tumor mutation burden (0% vs 48%) and a decrease in PD-L1 expression (34.1% vs 45.2%) (Fig 1A). Adaptive immune gene expression was lower in VVM compared to CM (Fig 1B). By QuantiSeq, the cell fractions for type I macrophages and C8+ T-cells were significantly lower in VVM compared to CM (Fig 1C). Median survival was shorter for VVM than for CM (19 vs 37 months, p=.058; Fig 1D). VVM also demonstrated significantly (p<.01) less frequent BRAF mutations (8.4% vs 35.8%), more frequent KIT mutations (13.2% vs 2.8%), KIT amplifications (14.7% vs 1.5%), ATRX mutations (28.4% vs 3.8%), and SF3B1 mutations (27.8% vs 1.6%). NRAS mutations were similar (14.6% vs 19.5%). Alteration in pathways involving DNA damage (16.4% vs 5.2%) and mRNA splicing (28.9% vs 2.8%) were more common in VVM, while alterations in cell cycle (7.2% vs 18.8%) and chromatin remodeling (6.3% vs 21.4%) were less common (Fig 1E).

Conclusions: VVM represents a distinct molecular profile from CM with a less favorable immune phenotype demonstrated by absence of TMB-high, lower rates of PD-L1 positivity, and lower adaptive immune gene expression and cell fractions of effector T-cells and immune promoting macrophages. Compared with CM, patients with VVM were found to have significantly worse survival when treated with IO therapy. Though IO has been a mainstay of treatment in recent years, these findings suggest that new therapeutic strategies are needed.