**Abstract ID:** 11557

**Title:** Fuzuloparib maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer: A multicenter, randomized, double-blind, placebo-controlled, phase III trial

**Presenting Author:** Ning Li, MD

**Objectives:** Fuzuloparib (formerly fluzoparib), a poly (ADP-ribose) polymerase inhibitor, has shown promising antitumor activity and acceptable safety for the treatment of relapsed ovarian cancer patients harboring the BRCA 1/2 mutation after 2-4 lines of platinum-based chemotherapy in previous phase 2 trial. This study aimed to assess the efficacy and safety of fuzuloparib versus placebo as maintenance treatment for patients with platinum-sensitive, recurrent ovarian cancer.

**Methods:** This is a multicenter, double-blind, randomized, placebo-controlled, phase 3 trial conducted at 36 sites in China. Eligible patients had platinum-sensitive, relapsed, high-grade serious ovarian, fallopian tube, primary peritoneal or endometrioid ovarian carcinoma (≥ grade 2), had received at least 2 prior platinum-based regimens and had achieved complete or partial response to their last platinum-based regimen. Patients were randomly assigned in a 2:1 ratio to fuzuloparib (150 mg, twice daily) or matching placebo using an interactive web response system. Randomization was stratified by BRCA 1/2 mutation (presence or absence), progression-free interval after penultimate platinum-based regimen (6-12 months or >12 months) and best response to most recent regimen (complete or partial response). The co-primary endpoints were progression-free survival (PFS) assessed by blinded independent central review (BICR) in the overall population and in the BRCA 1/2 mutation population. Here, we reported the results of the prespecified interim analysis from this ongoing study, which was planned for formal statistical testing on PFS per BICR in the overall population.

**Results:** Between Apr. 30, 2019 and Jan. 10, 2020, 252 patients were randomly assigned to the fuzuloparib (n = 167) or placebo (n = 85). BRCA1/2 mutations were confirmed in 100 (39.7%) patients. Sixty-one (24.2%) patients had received more than two lines of previous platinum-based regimen, and 127 (50.4%) patients had the complete response to the most recent regimen. As of Jul 1, 2020, the median PFS per BICR assessment in the overall population was significantly improved with fuzuloparib (hazard ratio [HR], 0.25; 95% CI, 0.17-0.36; one-sided $P < 0.0001$; Figure 1). The HR derived from prespecified subgroup analyses showed a consistent trend of benefit in patients with BRCA 1/2 mutation (HR, 0.14, 95% CI, 0.07-0.28) or without it (HR, 0.46; 95% CI, 0.29-0.74). The most common grade ≥3 adverse events reported in the fuzuloparib group were anemia (25.1%), decreased platelet count (16.8%), decreased neutrophil count (12.6%) and decreased white blood cell count (10.8%), which were manageable with treatment interruption or dose modifications, with only one (0.6%) patient discontinuing treatment due to neutropenia.

**Conclusions:** Fuzuloparib as maintenance therapy achieved a statistically significant and clinically meaningful improvement in PFS for patients with platinum-sensitive, relapsed ovarian cancer compared with placebo, regardless of BRCA 1/2 mutation, and had a manageable safety profile.

**Abstract ID:** 11570

**Title:** Randomized phase II trial of weekly ixabepilone with or without biweekly bevacizumab for platinum-resistant or refractory ovarian/fallopian tube/primary peritoneal cancer

**Presenting Author:** Dana Roque, MD

**Objectives:** Ixabepilone is a microtubule-stabilizing agent that may retain activity in paclitaxel-treated patients. The goal of this multi-center randomized phase II study was to assess the activity and safety of ixabepilone with bevacizumab compared to ixabepilone alone in patients with platinum-resistant/refractory ovarian, fallopian tube, or primary peritoneal cancer. An exploratory objective was to examine the role of prior treatment with bevacizumab and tumor expression of class III ß-tubulin (TUBB3) by immunohistochemistry as a predictive biomarker.

**Methods:** Participants were randomly assigned to receive ixabepilone 20 mg/m2 days 1, 8, 15 with (IXA+BEV) or without (IXA) bevacizumab 10 mg/kg days 1, 15 every 28 days. Patients were stratified by receipt of prior BEV. The primary endpoint was progression-free survival (PFS). Overall survival (OS), safety, and response rates served as secondary endpoints.

**Results:** A total of 78 patients were randomized from March 2017-July 2020. Among 76 evaluable patients who received IXA+BEV (n = 39) compared to IXA (n = 37), the objective response rate was 33% (n = 13) versus 8% (n = 3) (P = 0.004), with clinical benefit durable at 6 months in 37% (n = 14) and 3% (n = 1) (P< 0.001). The addition of BEV significantly improved both PFS (median 5.5 vs 2.2 months, HR = 0.33, 95% CI 0.19-0.55, P < 0.001) [Fig. 1a] and OS (median 10.0 vs 6.0 months, HR = 0.52, 95% CI 0.31-0.87, P = 0.006) [Fig. 1b]. Both regimens were well-tolerated. TUBB3 expression did not predict response in either arm. Subgroup analyses revealed minimal effect of prior BEV on response to IXA+BEV [Fig. 1c/d].

**Conclusions:** IXA+BEV is a well-tolerated, effective combination for treatment of platinum/taxane-resistant ovarian cancer that extends both PFS/OS relative to IXA monotherapy. Prior receipt of BEV should not preclude use of IXA+BEV. TUBB3 is not a predictive biomarker for response to IXA+BEV.

**Abstract ID:** 11583

**Title:** Cisplatin and paclitaxel are associated with improved progression-free survival compared to cisplatin alone during interval debulking surgery with hyperthermic intraperitoneal chemotherapy in women with advanced epithelial ovarian cancer.

**Presenting Author:** Laura Chambers,

**Objectives:** To investigate progression-free survival (PFS) and peri-operative outcomes in women with EOC undergoing interval debulking surgery (IDS) with hyperthermic intraperitoneal chemotherapy (HIPEC) with paclitaxel/cisplatin (PC) vs single-agent cisplatin (C).

**Methods:** This study was an Institutional Review Board approved, a single-institution cohort study of women with stage III or IV high-grade EOC treated from 1/1/2017-3/1/2020, followed in a prospective HIPEC registry with at least six months of follow-up. HIPEC regimen was administered at primary surgeon's discretion: C alone (80-100mg/m2 for 90 minutes) or P (135-175mg/m2 for 90 minutes) with C (80-100mg/m2 for 45 minutes) in a perfusate of normal saline at 41-43C degrees for 90 minutes, as previously described.3 PFS was defined as months from HIPEC date to recurrence. A Log-rank test was performed for PFS between PC vs. C. A p-value of $< 0.05$ was considered statistically significant.

**Results:** In total, 54 eligible patients underwent IDS with HIPEC following 3-4 cycles of NACT with carboplatin and paclitaxel were identified from a prospectively maintained HIPEC registry. Patients underwent HIPEC with C (51.9%, n = 28) or PC (n = 26; 48.1%). All patients underwent optimal cytoreduction to less than 1cm of residual disease. There were no differences in patient demographics, including age (67.4 vs 63.3 years, p = 0.10), race (p = 0.99), medical co-morbidities (p > 0.05), and pre-operative American Society of Anesthesiologists (ASA) score (III or IV - 64.3% vs 80.8%, p = 0.18) for those who received C vs. PC. Additionally, the majority of patients had stage III disease (77.8% vs 76.9%, p = 0.87) and serous histology (100.0% vs 92.3%, p = 0.23). There were no differences in operative time (6.0 hours vs 5.3 hours, p = 0.11) or surgical procedures performed, including small bowel (3.6% vs 3.8%, p = 0.99) and large bowel resection (17.9% vs 23.1%, p = 0.63). Notably, no differences in the Accordion postoperative adverse events were appreciated (None – 42.9% vs 42.3%; Mild – 25.0% vs 38.5%; Moderate – 21.4% vs 7.7%; Severe – 7.1% vs 11.5%; Death – 3.6% vs 0.0%; p = 0.46). Additionally, there was no difference in need for blood transfusion (50.0% vs 57.7%, p = 0.57), intra-operative vasopressor use (75.0% vs 92.3%, p = 0.14) or ICU admission (7.1% vs 26.9%, p = 0.07) The median PFS for the entire cohort was 15.7 months. However, when stratified by treatment regimen, PFS was 10.9 vs 22.2 months for C vs PC, respectively (HR 0.38, 95% CI 0.18, 0.81, p = 0.009) (Figure)

**Conclusions:** In this analysis of a prospective HIPEC registry, we demonstrate that PC is associated with a significantly improved PFS compared to C, without increased postoperative morbidity in patients with optimally cytoreduced stage III/IV EOC undergoing IDS with HIPEC. While further study is ongoing regarding overall survival benefit, consideration should be given for incorporation of P with C at the time of IDS with HIPEC.

**Abstract ID:** 11559

**Title:** Risk based triage for complex surgery in ovarian cancer: Ready for prime time

**Presenting Author:** Deepa Maheswari Narasimhulu, MBBS

**Objectives:** We developed a triage algorithm (Figure) that identifies patients who are at highest risk of severe morbidity/mortality (M/M) after cytoreductive surgery for advanced ovarian cancer (OC). We previously validated our algorithm in a separate internal validation cohort as well as a low complexity national dataset (National Surgical Quality Improvement Program database). We wanted to test the validity of the algorithm in an international high complexity surgical setting.

**Methods:** We included patients who underwent cytoreductive surgery in the primary (PDS) or interval (IDS) setting for stage IIIC/IV OC at a single institution between 10/2011 and 11/2019. This cohort included SCORPION trial patients until 5/2016 and non-trial patients thereafter. The data was prospectively obtained. Surgical complexity was classified as low, intermediate and high using the Aletti Score as previously described. Using the algorithm we retrospectively classified patients as 'high risk' or 'triage appropriate' and compared outcomes (30-day Accordion grade 3+ complications, 90-day mortality) between the two groups using the chi-square test or Fisher's exact test.

**Results:** We included 625 patients; the mean age was 58.7 years, 73.6% were stage IIIC, 63.0% underwent PDS and 21.0% (131/625) were classified as high risk. Surgical complexity was intermediate or high in 82.6% of patients (95.7% of PDS patients and 60.2% of IDS patients) and mean operative time was 377 (SD, 140) minutes. We observed that high risk patients i) had a 3-fold higher rate of 90-day mortality (6.1% vs 2.0%, p = 0.03), ii) were more likely to experience 90-day mortality following an Accordion grade 3+ complication (25.9% vs. 10.0%, p = 0.05), and iii) had comparable rates of Accordion grade 3+ complications (20.6% vs 16.2%) when compared to triage appropriate patients. Rates of complete cytoreduction were 72.5% and 80.5% (p = 0.05) for high risk and triage appropriate patients, respectively.

**Conclusions:** Use of our evidence-based triage algorithm identifies patients at very high risk of surgical M/M after high complexity debulking surgery. These patients are not ideal candidates for surgery when a high complexity operation is anticipated. Given the validation of the algorithm in varied settings, risk-based decision making should be standard of care when considering cytoreductive surgery for patients with advanced OC.

**Abstract ID:** 11566

**Title:** Racial determinants of treatment delays in gynecologic malignancies

**Presenting Author:** Tanvi Joshi, MD

**Objectives:** Gynecologic malignancies affect racial minorities disproportionately. It is well-documented that black women have worse clinical outcomes than white women and present at later stages. While likely multifactorial, treatment delays may contribute to these disparities. The primary objective of this study was to investigate whether time from initial diagnosis to treatment initiation varied among racial groups. The secondary objective was to determine whether these observed differences affected overall survival.

**Methods:** Female patients over the age of 18 with a histological diagnosis of gynecologic malignancies, including stage III-IV ovarian cancer and stage I-IV endometrial, cervical, vulvar and vaginal cancers were identified from the National Cancer Database from 2004 - 2017. Time from initial diagnosis to initiation of treatment by race was assessed using multivariate analysis. Kaplan Meier curves were constructed for calculation of overall survival and hazards ratios were estimated from Cox proportional-hazard models.

**Results:** A total of 652,565 patients were included in this study: 99,678 with ovarian carcinoma, 406,044 with endometrial, 106,113 with cervical, and 40,730 with vulvar or vaginal carcinomas. A significant delay from diagnosis to initial treatment was observed in Hispanic (6.14 days, $p<0.01$) and Black patients (3.92 days, $p < 0.01$) relative to White patients across all gynecologic malignancies. When stratified by cancer subtype, Hispanic and Black women encountered a similar delay from diagnosis to treatment relative to their White counterparts (ovarian cancer: 2.86 days, $p < 0.01$ and 2.21 days, $p < 0.01$; endometrial cancer: 5.59 days, $p < 0.01$ and 4.20 days, $p < 0.01$; cervical cancer 8.61 days, $p < 0.01$ and 4.16 days, $p < 0.01$, respectively). In vulvar and vaginal cancers, Hispanic women alone were noted to experience an average of an 11.81-day delay ($p < 0.01$). After adjusting for cancer type, stage and other covariates, Black patients had a 25% higher risk of overall death relative to white patients. This increased risk of death was not observed amongst the Hispanic patient cohort.

**Conclusions:** In a population based study, Black and Hispanic women experience significant delays in initiation of treatment relative to White women with gynecologic malignancies. Of concern, after accounting for socioeconomic status, stage and other covariates, Black women experienced an increased overall mortality across all gynecologic malignancies. Our study supports the notion that treatment delays may contribute to worse overall survival among racial minorities, suggesting the critical importance of reducing these delays.