Objectives: Bi-allelic alterations in *BRCA1* or *BRCA2* (*BRCA1/2*) are associated with genomic features of homologous recombination DNA (HRD) repair deficiency. We aimed to determine if endometrial cancers (ECs) arising in *BRCA1/2* germline mutation carriers harbor bi-allelic alterations and/or features of HR deficiency.

Methods: EC patients with *BRCA1/2* germline mutations whose tumors were subjected to a) massively parallel sequencing targeting 410 cancer-related genes under an IRB-approved protocol (n=7) and b) whole-exome sequencing (WES) by The Cancer Genome Atlas (n=3) were identified. Sequencing data were analyzed to define somatic mutations, copy number alterations, loss of heterozygosity (LOH) and microsatellite instability (MSI); in cases subjected to WES, genomic features of HRD were assessed.

Results: Of the 10 ECs included, 6 and 4 were from patients with pathogenic *BRCA1* and *BRCA2* germline mutations, respectively. The median age at EC diagnosis was 60 years (range 44-78). The ECs were of various histologic types, including endometrioid (grade II, n=1; grade III, n=5), serous/clear cell (n=2) and carcinosarcoma (n=2). Staging information was available for 8 cases, and ECs presented at all stages (stage I, n=3; stage II, n=1; stage III, n=3; stage IV, n=1). Allele-specific copy number analysis revealed that 5 (83%) and 1 (25%) ECs harbored bi-allelic *BRCA1* and *BRCA2* alterations, respectively, uniformly through LOH of the wild-type allele. All ECs analyzed, irrespective of the presence of mono- or bi-allelic *BRCA1/2* alterations, harbored somatic *TP53* mutations. Of note, one *BRCA1* and one *BRCA2* EC with mono-allelic alterations had a high mutational burden and were MSI-high by MSIsensor. The three ECs subjected to WES harbored *BRCA1* bi-allelic alterations, were of grades II and III endometrioid subtype, and displayed genomic features of HRD, including high large-scale transition scores and a dominant mutational signature 3.

Conclusions: Our findings demonstrate that a small subset of patients with ECs arising in patients with pathogenic germline *BRCA1/2* mutations harbor bi-allelic alterations, and may benefit from HR-directed treatment regimens. Another subset of *BRCA1/2*-associated ECs, however, may be sporadic and MSI-high.

doi:10.1016/j.ygyno.2019.03.125

Poster #21

Clinical outcomes of patients with pole mutated endometrioid endometrial cancer

I.U. Tunnage[b], M. Stasenko[a], C.W. Ashley[a], M. Rubinstein[a], A.J. Latham[a], J.J. Mueller[a], M.M. Leitao Jr[a], C.F. Friedman[a], V. Makker[a], R.A. Soslow[a], B. Weigelt[a], D. DeLair[a], D.M. Hyman[a], C.A. Aghajanian[a], N.R. Abu-Rustum[a], K.A. Cadoo[a]. [a]*Memorial Sloan Kettering Cancer Center, New York, NY, USA,* [b]*Georgetown/Washington Hospital Center, Washington, DC, USA*

Objectives: Data from the selected patients (pts) included in The Cancer Genome Atlas suggested that somatic *POLE*endonuclease domain (END) hotspot mutation (mut) associated endometrioid endometrial cancers (EEC) have a better prognosis. We sought to describe the outcomes of a clinical cohort of pts with this mut profile.

Methods: Pts provided consent to an IRB approved protocol of tumor-normal sequencing via a custom massive parallel sequencing platform (MSK-IMPACT) that identifies somatic genomic alterations in 468 cancer genes. We captured all EEC sequenced 2014 - 2018 with a somatic *POLE* END hot spot muts: A456P, V411L, P286R, F367V. All tumors were assessed for microsatellite instability (MSI) via MSIsensor and had immunohistochemical (IHC) staining for mismatch repair (MMR) proteins. Clinical data was abstracted and descriptive statistics were employed.

Results: 451 EEC tumors were sequenced; 22 had *POLE*- END mut (5%). Primary tumor was sequenced in 19 cases (86%) and recurrent in 3 (14%). 17 (77%) were stage 1, 3 (14%), stage III and 2 (9%) had de novo stage IV tumors. 12 had low- and 10 high-grade tumors (55, 45%, respectively). 21 pts had surgery (95%) and 1 had neoadjuvant chemotherapy then surgery (5%). 16 pts (73%) received adjuvant radiation therapy (RT) with or without chemotherapy, and 6 (27%) stage I, low-grade tumors had no adjuvant therapy.

Tumors had a median of 161 muts (range 39-527). MMR protein IHC were retained in 18 (82%). 1 tumor (5%) had loss of MLH1/PMS2, with MLH1 hypermethylation. 4 (18%) had MSH6 IHC loss, of which, 3 had dual somatic MSH6 muts potentially underpinning the phenotype, 1 had a single MSH6 and single PMS2 mut in addition to the POLE mut. None had Lynch syndrome. MSIscores were obtained: 19 were microsatellite stable (MSS), 2 MSI-high, 2 MSI-indeterminate.

There were 4 recurrences: 2 pts with initial stage I disease, 2 with stage III. All were treated with a combination of surgery, chemotherapy, and RT. After a median follow up of 21 mo, all pts was alive, 3 with evidence of disease.

Conclusions: In this clinical cohort of pts with *POLE* mutant EEC, de novo metastatic disease was noted and recurrences were seen in 4 cases. These tumors are hyper/ultra - mutated phenotype with most being MSS and MMR proficient. Further research is needed to evaluate if *POLE*EDM mutant EEC are susceptible to immunotherapy.

doi:10.1016/j.ygyno.2019.03.126

Poster #22

Postoperative survival analysis of laparotomy vs robotic interval debulking in epithelial ovarian cancer patients following neoadjuvant chemotherapy

S.E. Paraghamian, A. Staley, K. Tucker, Y. Zhang, M. Wang, L.H. Clark. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Objectives: Neoadjuvant chemotherapy (NACT) is a commonly utilized strategy for primary treatment of advanced epithelial ovarian cancer (EOC) in women with unresectable disease or poor surgical candidates. Minimally invasive surgery offers several advantages, including decreased postoperative morbidity, shorter hospitalization, and faster recovery; however, there are limited published data to demonstrate that these advantages are also balanced by non-inferior survival or improved time to adjuvant chemotherapy. Thus, we sought to assess if there is a difference in time to disease recurrence as well as time to adjuvant chemotherapy in robotic (RA) versus open (OA) interval debulking surgeries (IDS).

Methods: We performed a retrospective review of EOC patients diagnosed and treated with 3-6 cycles of NACT with platinum and taxane chemotherapy followed by IDS from January 2014 through February 2017. Demographic, clinicopathologic, and treatment data were recorded from review of records from a single tertiary care institution. Survival analysis with Kaplan-Meier estimation with Wilcoxon rank test for significance were utilized for statistical assessment.

Results: Forty-seven patients met inclusion criteria from the initial cohort of 207 patients. Thirteen (28%) underwent RA and 34 (72%) underwent OA IDS. In comparing the RA vs OA groups, there were non-significant differences in age (60 vs 64 yrs, $p = 0.23$); rate of Stage IV disease (62% vs 44%, $p = 0.29$); rate of debulking to no gross residual (46% vs 59%, $P = 0.43$); and rate of complete response on preoperative imaging (31% vs 12%, $p = 0.12$). There was no difference in time to disease recurrence in the RA vs OA groups (8.9 vs 7.9 months, $p = 0.7$). There was no difference in time to adjuvant chemotherapy between the two arms (29.7 vs 33.3 days, $p = 0.97$).

Conclusions: Preliminary data suggest safety of RA IDS compared to OA IDS with no difference in time to recurrence or in time to initiation of chemotherapy. Future research should explore whether minimally invasive surgery could be used to shorten time to re-initiation of chemotherapy which could improve oncologic outcomes.

doi:10.1016/j.ygyno.2019.03.127

Poster #23

Independent radiologic review in ovarian cancer research

C. Polen-De[a], A. Loreen[a], C.C. Billingsley[a], A.L. Jackson[b], T.J. Herzog[c]. [a]*University of Cincinnati Academic Health Center, Cincinnati, OH, USA,* [b]*University of Cincinnati, UC Health Medical Arts Building, Cincinnati, OH, USA,* [c]*University of Cincinnati, Cincinnati, OH, USA*

Objectives: Independent radiologic review (IRR) has been increasingly utilized in ovarian cancer clinical trials to minimize potential bias when evaluating for progression. Though there is potential for bias in non-blinded trials given the inherent subjective nature of progression-free survival (PFS) evaluation, an IRR has the potential to introduce new biases, and is associated with significant added study cost and logistical burden. The aim of our study is to evaluate the concordance in PFS and HR between investigator (INV) and (IRR) among key trials in ovarian cancer.

Methods: PubMed was systematically queried for randomized controlled trials involving ovarian cancer, utilizing the terms "ovarian cancer" plus "independent radiologic review", "independent central review", and "independent review committee". All landmark randomized phase II-III, registration, and GOG ovarian cancer trials in addition to their supplemental data, if available, were reviewed. Studies were excluded if patients were not randomized, if they reported IRR data only and if they did not utilize IRR in the study. Studies with a separate IRR analysis were included.

Results: Eight studies met study criteria out of 29 evaluated. Differences in PFS medians and HR's were analyzed between INV and IRR for each study and associations were calculated utilizing logistic regression analysis. The PFS between INV and IRR was found to have a mean difference of -1.76 months (INV-IRR), median -0.4 (95% CI -3.44 - -0.08). The degree of association between INV and IRR HR was high by logistic regression analysis, with $R^2 = 0.957$ (Correlation coefficient 0.97; 95% CI 0.91-0.99; P<0.0001). This illustrates in the majority of cases the INV HR and IRR HR are highly concordant. The HR ratio was determined for each study (HR IRR/HR INV) (Table 1) with a mean HR ratio of 1.03 (95% CI, 0.94-1.12, p=0.82) and an estimated HR difference illustrating a 10% average absolute difference between the evaluations.

Conclusions: Concordance was noted between both INV and IRR reported PFS and HR data in ovarian cancer. Since IRR adds significant cost, logistical burden, and potential bias while not altering the primary endpoint conclusion in any of these trials, the need for IRR is questionable and these data support use of primary investigator assessed PFS.

doi:10.1016/j.ygyno.2019.03.128

Poster #24

Clinical trial participation and measures of aggressive care at the end of life in patients with ovarian cancer

R. Nitecki[a,b,c], A. Bercow[a,b,c], A.A. Gockley[b,c], W.B. Growdon[a,c]. [a]*Massachusetts General Hospital, Boston, MA, USA,* [b]*Brigham and Women's Hospital, Boston, MA, USA,* [c]*Harvard Medical School, Boston, MA, USA*

Objectives: Many patients with advanced ovarian cancer seek investigational therapy as a therapeutic option. In non-gynecologic cancers, clinical trial participation has been associated with measures of aggressive care at the end of life. The objective of this investigation was to examine the association between participation in clinical trials and measures of aggressive care as well as hospice care at the end of life among ovarian cancer patients.

Methods: With institutional approval, we conducted a retrospective review of all women treated for ovarian cancer at our institution from 2010 through 2016. We examined several clinical variables which have been identified by the National Quality Forum as measures of aggressive end of life (EOL) care including chemotherapy in the last 14 days of life, ICU admission in the last 30 days of life, and death in the acute care setting. Data were analyzed with univariable and multivariable parametric and non-parametric testing, and survivals were calculated using the Kaplan-Meier method and cox-proportional hazard models.

Results: We identified 175 women treated for ovarian cancer that died of disease, 19% of whom were enrolled in at least 1 clinical trial. Patients who enrolled in clinical trials experienced a higher overall survival and were found to live a median of one year after a trial. Interestingly, patients who enrolled in clinical trials were more likely to have undergone primary debulking surgery (PDS, OR .42, p<0.009). A cox proportional hazard model incorporating PDS and clinical trial enrollment found both to be independently associated with improved survival estimates (HR 0.63 and HR 0.53 respectively, both $p < 0.002$). While clinical trial participants were more likely to start a new line of chemotherapy within 30 days of death ($p < 0.03$), no association with other metrics of aggressive care at the end of life including administration of chemotherapy in the last 14 days of life, ICU admissions and death in an acute care setting was observed.

Conclusions: Women with ovarian cancer who are enrolled in clinical trials appear to present with an increased overall survival. While they also have a higher rate of starting a new line of chemotherapy within 30 days of death, they do not undergo more measures of aggressive care at the end of life when compared with ovarian cancer patients who are not enrolled. Further study to understand drivers of patient selection and quality of life will be crucial to understanding how clinical trial participation interacts with outcome for women with ovarian cancer.

doi:10.1016/j.ygyno.2019.03.129

Poster #25

Age-related risk of postoperative mortality after cytoreductive surgery for advanced ovarian cancer

A. Melamed[a], M. del Carmen[a], A. Bercow[a], K.M. Bunnell[a], J.A. Rauh-Hain[b], J.D. Wright[c], L.W. Rice[d]. [a]*Massachusetts General Hospital, Boston, MA, USA,* [b]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA,* [c]*New York-Presbyterian/Columbia University Medical Center, New York, NY, USA,* [d]*University of Wisconsin School of Medicine and Public Health, Madison, WI, USA*

Objectives: Surgical cytoreduction is a critical component of primary therapy for advanced ovarian cancer. However, patients who die within 90 days of cytoreductive surgery do not benefit from the operation and may experience significant harm. We investigate the association between age and 90-day postoperative mortality after cytoreductive surgery, and how neoadjuvant chemotherapy (NACT) modulates this association.

Methods: Using the National Cancer Database, we conducted an analysis of age-related trends in 90-day postoperative mortality after cytoreductive surgery among women with stage IIIC or IV epithelial