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.

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Poster #21

Clinical outcomes of patients with pole mutated endometrioid endometrial cancer

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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.

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Poster #22

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

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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, $p = 0.97$).