**Poster #39**

**Genomic profiling in gynecologic cancer: Current practice patterns and implications for therapy**

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**Objectives:** Genomic profiling is increasingly used to identify therapeutic targets for patients with cancer. The approval of treatments for tumors sharing a molecular profile and agnostic to tissue of origin (i.e. PD1 inhibitors) highlights the promise of this approach. We performed targeted tumor sequencing in gynecologic cancer patients and report on the clinical and molecular features observed, as well as effects on clinical decision-making.
**Methods:** This is a retrospective review of the electronic medical record for 74 gynecologic cancer patients who underwent tumor sequencing from 2016-2017 with a hybridization-based target enrichment panel of 429 genes for analysis of mutations, copy number variants, and structural rearrangements. We describe clinical and molecular features for patients with mutations deemed clinically actionable vs. nonactionable.
**Results:** Patients undergoing testing were frequently diagnosed with stage III or IV disease (64.4%), high-grade serous histology (55.4%), and ovarian, fallopian or peritoneal origin (58.2%). Multiple recurrence was the most common indication for testing; most patients received at least two prior lines of chemotherapy (55.3%) and were tested a median of 2.2 years from initial diagnosis (IQR 0.8-5.9). Testing was also performed up front for patients with rare or aggressive histology (10.8%) or when histologic diagnosis was uncertain (8.1%). An actionable variant was detected in 50% of cases, with 54.1% of those patients subsequently receiving therapy targeted for the identified gene. Clinical characteristics between patients with actionable and nonactionable findings were similar, although patients with actionable findings were older (mean age 58.8 vs. 52.2, $p = 0.01$). Presence of an actionable finding did not affect progression-free survival ($p=0.61$) or overall survival ($p=0.39$). The most common genes with actionable pathogenic variants were PI3KCA (14.9%), BRCA1 or 2 (10.8%), and ERBB2 (8.1%).
**Conclusions:** Genomic profiling can reveal clinically actionable genetic changes in patients with gynecologic malignancies. The benefits of testing include identification of commonly mutated genes as targets for novel therapy, and detection of pathway alterations with already available targeted agents that may be currently underutilized (i.e. ERBB2 amplification). Future studies should continue to assess the clinical utility of this type of testing for patients both at time of initial diagnosis and after failing standard treatment.

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**Poster #40**

**Nivolumab use for BRCA gene mutation carriers with recurrent epithelial ovarian cancer: A case series**

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**Objectives:** A recent trial has shown the efficacy of anti-tumor activity with immune checkpoint inhibitors against tumors with DNA mismatch repair deficiencies. Our case series examines the effectiveness of the immune checkpoint inhibitor nivolumab in women with a germline BRCA gene mutation and recurrent epithelial ovarian cancer.
**Methods:** This IRB-approved retrospective case series examined 6 women (high-grade serous ovarian cancer n=5, primary peritoneal cancer n=1) with a BRCA mutation (BRCA1 n=3, BRCA2 n=3) who received salvage treatment for recurrent ovarian and primary peritoneal cancers. Adverse events and survival outcome related to nivolumab use are described.
**Results:** The median age at initiation of nivolumab treatment was 57 (range: 51-64) years. The majority had stage III-IV disease (n=4) and all received a platinum/taxane doublet as initial therapy. Prior to nivolumab initiation, all women received salvage chemotherapy: 4 women received 3 or less regimens and 2 women received >6 regimens. 4 women had platinum resistant disease and 3 women were previously on a PARP inhibitor prior to nivolumab initiation. Median follow-up time after nivolumab initiation was 10.5 months (range: 5.7-18.4) with a median of 9 cycles given (range 3-18). There were 4 women with a complete response, 2 women with progressive disease (clinical benefit rate: 66%). 1 woman has had nivolumab held secondary to developing abnormal thyroid function after 5 cycles. 1 woman has had nivolumab therapy held secondary to developing lichen planus (believed to be a grade 2 toxicity). 1 woman received nivolumab with venetoclax/decitabine in the setting of pre-existing myelo-dysplastic syndrome.
**Conclusions:** Our case series suggests that nivolumab is well tolerated and may achieve prolonged benefit in women with recurrent epithelial ovarian cancer with a BRCA mutation.

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**Poster #41**

**Therapeutic efficacy of vocimagene amiretrorepvec (Toca 511) prodrug activator gene therapy in peritoneal carcinomatosis models of ovarian cancer**

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**Objectives:** Ovarian cancer causes more deaths in the U.S. than any other malignancy of the female reproductive system. Vocimagene amiretrorepvec ('Toca 511'), a tumor-selective retroviral replicating vector (RRV) encoding yeast cytosine deaminase (CD) which converts the prodrug 5-fluorocytosine (5-FC) into the chemotherapy drug 5-fluorouracil (5-FU), is being evaluated in an international Phase III trial (NCT02414165) for recurrent glioma, and a Phase I trial (NCT02576665) evaluating systemic delivery of Toca 511 to several tumor types is now underway, so it is timely to consider applying this approach to gynecologic malignancies. Here we report on the first preclinical studies to evaluate RRV-mediated prodrug activator gene therapy for ovarian cancer.
**Methods:** In vitro RRV replication was monitored by flow cytometry, and cytotoxicity quantitated by MTS assay after 5-FC treatment of RRV-transduced ovarian cancer cells. In vivo RRV-GFP replication and spread in SKOV3-IP peritoneal carcinomatosis models was also examined by flow cytometry following intraperitoneal (IP) vector injection, and therapeutic efficacy examined following 5-FC prodrug treatment by bioluminescence imaging and Kaplan-Meier analysis.
**Results:** Efficient RRV replication and spread was observed in vitro in both established and primary ovarian cancer cell lines with >80~90% transduction achieved by Day 9-12. After RRV-CD transduction, significant reduction of cell viability was observed in a 5-FC prodrug dose-dependent manner. In vivo vector replication and spread were confirmed following IP vector delivery in SKOV3-IP peritoneal carcinomatosis models. Reduced tumor burden and

significantly increased survival was observed associated with higher tumor transduction levels after 5-FC treatment compared to controls.
**Conclusions:** These results using Toca 511/5-FC prodrug activator gene therapy in preclinical models of disseminated ovarian cancer support future efforts toward clinical translation.

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**Poster #42**
**Intraperitoneal chemotherapy is equally safe and effective in ovarian cancer patients with and without Germline BRCA1 or BRCA2 mutations**
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**Objectives:** Intraperitoneal chemotherapy (IPC) achieves higher local drug concentrations and has demonstrated superiority in some settings to intravenous delivery for the treatment of epithelial ovarian cancer (OC). Because OC in patients with BRCA1 or BRCA2 (BRCA) mutations is hypersensitive to platinum agents, BRCA status may modify the efficacy of IPC. It is unknown whether BRCA haploinsufficiency in normal cells of mutation carriers could result in increased toxicity from platinum based IPC. The objective of this study was to compare the toxicity profiles and survival of OC patients with and without germline BRCA mutations who received IPC.
**Methods:** We conducted a retrospective review of the medical records of patients who received at least one cycle of IPC for the treatment of OC at a single center between 2005 and 2015. We restricted the review to patients who either carried BRCA mutations or had negative multigene testing. We abstracted demographic, clinical and tumor characteristics and compared characteristics between groups using t-tests for continuous data and chi-square tests or Fisher's exact tests as appropriate for categorical data. We constructed Kaplan-Meier curves for survival analysis. We had 80% power to detect a 25% difference in toxicity and a 62.5% survival difference.
**Results:** We identified 142 patients, 31 of whom had a BRCA mutation and 111 without mutations. The average age at diagnosis was 53 for BRCA patients and 62 for non-carriers (p=0.003). Histology and stage distributions were similar, as were the percentages of patients undergoing bowel surgery (38.7%). Most patients (74.2% in BRCA group and 91% in wildtype group) received IPC in the front-line setting, while the remainder did so for recurrences. BRCA carriers were more likely to have received chemotherapy for a prior malignancy (12.9% v 2.7%, p=0.04). Overall, 45% of patients in the BRCA group and 51.4% in the wildtype group experienced at least one chemotherapy-related toxicity (p=0.54). There was no difference between the two groups in rates of dose adjustments (13% v 18%, p=0.51) or IPC discontinuation (0% v 10%, p=0.12) due to toxicity. In the subgroup of patients who received front-line IPC (n=124), the median overall survival was 75.4 months for the BRCA group and 77.5 months for the wildtype group (p= 0.46).
**Conclusions:** Germline BRCA mutation status does not appear to have a large impact on toxicity or survival in patients with OC treated with IPC. These findings should be replicated in larger studies.

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**Poster #43**
**Pelvic disease control in patients undergoing vaginal brachytherapy for stage II endometrial cancer**
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**Objectives:** To estimate the pelvic recurrence rate in patients with stage II endometrial cancer (EC) undergoing vaginal brachytherapy without pelvic external beam radiotherapy.
**Methods:** Data from women with pathology confirmed stage II EC were extracted from our institution's brachytherapy database from January 2006 to December 2012.
**Results:** From 2006-2012, 20 women with stage II EC underwent surgery with curative intent and adjuvant vaginal brachytherapy. Patients were followed for a median time of 87.5 months (range, 17.3-120.3 months). The median age at diagnosis was 62 (range, 49-76). The majority of specimens were of endometrioid histology (75%), with serous, clear cell, carcinosarcoma, and other representing 5%, 5%, 10%, and 5%, respectively. Lymphovascular invasion was noted in 10% of cases, with 45% Grade 1, 20% Grade 2, and 35% Grade 3. Twenty percent of patients received adjuvant chemotherapy and 90% underwent pelvic nodal dissection at the time of surgery. The 5 year-estimates for in-field vaginal, pelvic, and distant control were 85% (95% CI: 69%-100%), 90% (95% CI: 75%-100%), and 70% (95% CI: 50%-90%). The five-year overall survival (OS) estimate was 85% (95% CI: 69%-100%). We noted a trend towards reduced distant disease control in patients with non-endometrioid versus endometrioid histology with 5-year rates of 79% (95% CI: 58%-100%) versus 40% (95% CI: 0%-83%); (p=0.11). Five-year OS was significantly better in patients with distant disease control versus distant failure with 5-year rates of 100% (95% CI: 79%-100%) versus 63% (95% CI: 29%-97%); (p=0.02). No such OS association was seen for patients who experienced pelvic failure (p=0.20). Crude rates of Common Terminology Criteria for Adverse Events (CTCAE) grade 0 and 1 urinary toxicity were 85% and 15%. CTCAE grade 0 and 1 gastrointestinal (GI) toxicity were 65% and 35%. No patients developed grade 2 or greater urinary or GI toxicity by last follow-up. Vaginal stenosis/atrophy was seen in 15% of patients.
**Conclusions:** Vaginal brachytherapy is well-tolerated and associated with acceptable rates of pelvic disease progression in patients with stage II EC. Patients with stage II EC and non-endometrioid histology have a high-risk of distant recurrence and consideration of systemic therapy is warranted in this setting.

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**Poster #44**
**Topical vaginal estrogen use and risk of endometrial hyperplasia or cancer**
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**Objectives:** To estimate the yearly incidence rate of endometrial hyperplasia or cancer in women categorized by their unopposed topical vaginal estrogen (VE) prescriptions.
**Methods:** Women aged 46 years and older were identified from our institution's database from 2006-2012. ICD-9 diagnosis codes and our internal cancer registry were used to identify the first date of endometrial hyperplasia/cancer diagnosis. Pharmacy records were used to identify dispensed prescriptions for VE within 3 years prior to the reference date. The reference date used for dispensed estrogen or progesterone was defined as the index date for cases and December 31 for non-cases. Women exposed to systemic estrogen (SE) or progesterone within 2 years prior of the reference date were