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.

doi:10.1016/j.ygyno.2019.03.229

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.

doi:10.1016/j.ygyno.2019.03.230

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