

Poster 36: Somatic NF1 alterations as potential biomarker for response to immune checkpoint inhibition in recurrent ovarian cancer

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Topic: Ovarian

Objectives

There remains no standardized prognostic biomarker for response to immune checkpoint inhibitor (ICI) therapy in recurrent ovarian cancer.

Methods

This retrospective cohort study reviewed patients with ovarian, fallopian, peritoneal cancer of any histology who received ICI at a large referral, academic medical center. Baseline demographics, prior lines of chemotherapy and targeted therapy, type and number of ICI cycles were collected. Clinical parameters including overall response rate, duration of response, time to response and toxicities were analyzed. Tumor molecular characteristics including mismatch repair status, PD-L1 expression, tumor mutation burden, homologous recombination status were correlated with clinical response.

Results

73 patients were treated with ICI for recurrent ovarian, fallopian tube or peritoneal cancer from June 2016 to August 2022. High grade serous adenocarcinoma was the most common histology (71.2%). Most cases were platinum resistant (71.4%) at the time of ICI therapy initiation with 62.5% of all patients having had 3 or more lines of prior chemotherapy. The majority of tumors were mismatch repair proficient (90.4%) and homologous recombination proficient (74.0%). Tumor PD-L1 expression was positive in 11.0% but unknown in 58.9% of tumors. Pembrolizumab monotherapy was used in 78.0% of patients with a mean 4.8 cycles per patient (range 1-16). One patient experienced a complete response, six patients had a partial response and four patients had stable disease (ORR = 9.6%). Median duration of response was 5 months (range 1-8). PD-L1 tumor expression and BRCA germline or somatic status did not correlate with response. Four out of the six partial responders had a NF1 mutation. Two partial responders had NF1 splice site mutations, one partial responder had a NF1 loss within exons 1-55 and another partial responder had a NF1 truncation of intron 1. Toxicities occurred in 84.9% of patients with fatigue, nausea and hypothyroidism being the most common. Autoimmune adverse events of interest including pneumonitis, uveitis, vasculitis were observed. ICI was discontinued in 16 (21.9%) patients due to toxicity. 13.7% of patients received ICI treatment within 90 days of death.

Conclusions

In this cohort of heavily pretreated recurrent ovarian cancer patients, ICI treatment was administered regardless of molecular status. Somatic NF1 mutation may be a potential biomarker for response to ICI therapy in this patient population.