Title: Analysis of Response to Poly (ADP-Ribose) Polymerase Inhibitors for Maintenance Treatment of Ovarian Cancer in Patients with Homologous Recombination Deficiency

Background: Clinical trials have evaluated the efficacy of poly (ADP-ribose) polymerase inhibitors (PARPi) in patients with homologous recombinant deficiency (HRD) mutations; however, there is a paucity of literature comparing the response when the mutations are germline or somatic.[1-3]

Objective: This study aimed to determine if germline, somatic, or absence of HRD mutations impacted duration of response to PARPi used for maintenance treatment of ovarian cancer.

Methods: A single center, retrospective chart review was conducted for patients that received a PARPi from May 1, 2017 to September 1, 2020. Data regarding PARPi line-of-therapy, specific HRD mutation, duration of response, and disease relapse were recorded. Patients had previously undergone next-generation sequencing to determine homologous recombination repair status. The primary objective of time to next treatment (TTNT) was defined as the time from PARPi initiation to Day 1 of subsequent chemotherapy and was compared between three patient cohorts: presence of a germline HRD mutation, a somatic HRD mutation, or absence of an HRD mutation. The secondary objective was response to subsequent therapy after progression on PARPi maintenance treatment.

Results: Of 139 charts reviewed, 75 patients met criteria for eligibility. Germline and somatic HRD mutations were identified in 14 and 24 patients, respectively. The remaining 37 patients lacked an HRD mutation. The estimated restricted mean TTNT was 21 months for patients with germline mutations versus 13.5 months for patients with no HRD mutations (HR 0.25; 95% CI 0.08 to 0.87). Similarly, the estimated restricted mean TTNT was 19.7 months for patients with somatic mutations versus 13.5 months for patients with no HRD mutations (HR 0.36; 95% CI 0.13 to 0.96). Statistical significance was unchanged when controlling for PARPi line-of-therapy. For patients who experienced disease relapse after PARPi maintenance therapy and had been re-staged (n=21), 38% had a partial response/stable disease and 62% had disease progression to subsequent chemotherapy. When evaluating the effect of HRD mutation status on response to subsequent chemotherapy, there was no significant difference identified between germline mutations versus no HRD mutations (OR 0.5; 95% CI 0.02 to 14.5), or somatic mutations versus no HRD mutations (OR 1; 95% CI 0.08 to 24.6).

Conclusions: Patients with germline or somatic HRD mutations receiving PARP inhibitors for maintenance treatment of ovarian cancer experienced a significantly longer TTNT compared to patients without HRD mutations, regardless of line-of-therapy. HRD mutational status did not appear to impact response to subsequent chemotherapy after PARPi maintenance therapy.

References:

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