**Presentation:** Comparison of PARP Inhibitor Maintenance Therapy Duration Between Germline vs Somatic BRCA Mutated Ovarian Cancer

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**Background:**

Defects in BRCA1/2, tumor suppressor genes involved in the process of homologous recombination repair, result in the development of certain ovarian cancers. 1,2 Poly (ADP-ribose) polymerase inhibitors (PARPi), target these defects by further preventing DNA repair, leading to synthetic lethality.3 Molecular analysis has demonstrated a high rate of loss of heterozygosity (LOH) in patients with germline BRCA1/2 mutations (gBRCA) and/or those with BRCA associated cancers. Conversely, LOH is rare in those with somatic BRCA1/2 mutations (sBRCA), suggesting these mutations do not drive tumorigenesis as strongly.4 The National Comprehensive Cancer Network (NCCN) guidelines recommend using PARPi in patients with either gBRCA or sBRCA mutation status for ovarian cancer maintenance therapy.5 However, the efficacy of PARPi inhibitor maintenance therapy based on germline versus somatic mutation status has not been formally evaluated.

**Objective(s):**

To compare the duration of PARP inhibitor maintenance therapy in ovarian cancer patients with gBRCA versus sBRCA mutations.

**Methods:**

This was a single center, retrospective analysis that included adult patients diagnosed with ovarian cancer receiving PARPi maintenance therapy at the University of North Carolina Medical Center between December 2018 and April 2021. The primary outcome was the duration of PARPi maintenance therapy. Secondary outcomes included the rate of dose interruptions, reductions, and discontinuation due to adverse events, and the rate of LOH testing.

**Results:**

Twenty-one patients met eligibility criteria, with four patients receiving more than one PARPi during the study period. Fourteen (67%) patients had a BRCA1 mutation of which eleven were germline and three were somatic. The remaining seven (33%) patients had a BRCA2 mutation of which six were germline and one was somatic. Median duration of PARPi 18.5 months (gBRCA) and 20.1 months (sBRCA) (P=0.46). Most patients experienced dose interruptions (60% gBRCA; 60% sBRCA) and/or reductions (60% gBRCA; 80% sBRCA) due to adverse events during the study period. Discontinuation of PARPi due to toxicity was 30% in those with gBRCA compared to 20% of those with sBRCA. Of the twenty-one patients included in the study, none had LOH results.

**Conclusions:**

Among ovarian cancer patients receiving maintenance PARPi therapy, there was not a significant difference in the duration of PARPi therapy between gBRCA and sBRCA mutated patients. Larger patient populations and more data regarding correlation of LOH to responses is needed to determine the best biomarker to predict duration of response to PARPi maintenance.

**References:**

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