**Risk Assessment of Myelosuppression with PARP Inhibitors in Prostate Cancer: Insights from FAERS.**

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**Background:** DNA damage repair defects are prevalent in 15% of Prostate cancer. FDA has approved four PARP inhibitors to be used for metastatic castration resistant prostate cancer (mCRPC). Based on the approvals, currently Olaparib, Niraparib, Rucaparib and Talazoparib have been approved alone or in combination with an Androgen receptor pathway inhibitor (ARPI). All these agents have myelosuppressive (MS) events. We aimed to assess the pharmacovigilance (PV), reporting rate, and reaction outcomes of different approved PARP inhibitors in the mCRPC setting reported to the United States Food and Drug Administration Adverse Event Reporting System (FAERS).

**Methods:** We analyzed MS events in 2,137 patients on PARP inhibitors. MS event reports were submitted to FAERS between 2004-2023 and analyzed using the AERS*Mine* framework. MS incidences were analyzed within different PARP inhibitors utilized for prostate cancer. Our primary composite endpoint was the PV of MS caused by olaparib, rucaparib, niraparib and talazoparib for the treatment of mCRPC. PARP inhibitors were analyzed as mutually exclusive cohorts. Standard PV metrics were used to determine MS association with PARP inhibitors and two-way ANOVA testing was used to evaluate for statistical significance across the treatment groups.

**Results:** 2,137 prostate cancer patients on PARP inhibitors were identified. MS events (n = 677)– olaparib (227/831, 27.32%), rucaparib (n = 171/495, 34.55%), niraparib (63/111, 56.76%), and talazoparib (34/47, 72.34%). MS events were further categorized into five classes – anemia (n = 311, 45.94%), leukopenia (n = 123, 18.17%), thrombocytopenia (n = 107, 15.81%), pancytopenia (n = 102, 15.07%), and myelodysplastic syndrome (MDS) or Acute Myeloid Leukemia (AML, 34, 5.02%). Anemia rates across the four cohorts were identical (table 1). Leukopenia rates were highest in talazoparib cohort (27.66%). Thrombocytopenia rates were highest in niraparib cohort (24.32%). For pancytopenia, rates were highest in talazoparib 10.64%. MDS/AML rates were Talazoparib (2.13%), Olaparib (1.8%). The relative rates of MS events were significantly different across the PARP inhibitors ($p < 0.05$, Table 1).

**Conclusions:** This is the first study specific to prostate cancer analyzing the relative rates of MS events across different PARP inhibitors. Talazoparib exhibited the highest incidence of myelosuppression. This underscores the careful patient selection and vigilant monitoring needed in PARP inhibitors. Prompt recognition of myelosuppression is needed to optimize the safety and efficacy of PARP inhibitor therapies in prostate cancer.

Table 1:

| | **Olaparib, n = 831 (%)** | **Rucaparib, n = 495 (%)** | **Niraparib, n = 111 (%)** | **Talazoparib, n = 47 (%)** |
|---|---|---|---|---|
| **ANEMIA (311)** | 14.56 | 13.94 | 14.41 | 14.89 |
| **LEUKOPENIA (123)** | 3.01 | 8.08 | 13.51 | 27.66 |
| **THROMBOCYTOPENIA (107)** | 3.25 | 4.04 | 24.32 | 17.02 |
| **PANCYTOPENIA (102)** | 4.69 | 8.48 | 4.50 | 10.64 |
| **MDS/AML (34)** | 1.81 | 0.00 | 0.00 | 2.13 |