**INTRODUCTION**

- Rucaparib, a poly(ADP-ribose) polymerase (PARP) inhibitor, is approved in the United States as monotherapy (BRCA1/2-mutated metastatic castration-resistant prostate cancer (mCRPC)) that has been treated with an androgen receptor (AR)-directed therapy and a taxane.
- Enzalutamide, an AR inhibitor, is approved in the United States for patients with CRPC or metastatic castration-sensitive prostate cancer.
- Synthetic lethality has been observed, independent of DNA-damage repair gene defects, when combining PARP inhibition with androgen deprivation therapy (eg, enzalutamide). 
- Enzaludamide is a strong inhibitor of cytochrome P450 (CYP) 3A, and nonclinical studies suggested that the coadministration of enzalutamide and rucaparib could potentially lead to clinical drug-drug interacions.

**Methods**

- Participants were enrolled with histologically or cytologically confirmed adenocarcinoma or poorly differentiated adenocarcinoma of the prostate after ≥2 lines of AR-directed therapy (eg, enzalutamide, abiraterone) and ≥2 lines of chemotherapy for mCRPC, prior PABP inhibitor treatment was not allowed.
- Participants received rucaparib monotherapy (600 mg twice daily (BID) during a 1-week run-in period, followed by rucaparib (600 mg BID) + enzalutamide (160 mg once daily (QD)) in continuous 28-day cycles.
- Drug-drug interactions (DDIs) were assessed during the first 2 cycles (see Supplementary Material).
- Though PA was evaluated for rucaparib and enzalutamide and their respective metabolites, data were not available as of this date.

**Results**

- Plasma PK samples were collected on days 6 and 7 during the run-in period, on days 1, 8, 15, and 22 of cycle 1 and 2, and on day 1 of cycles 3, 4, 5, and 6, all samples were collected prior to the morning doses.
- Non-parametric PK parameters were used to detect DDI damage repair gene alterations (eg, BRCA1/2) or genomic signatures associated with resistance to treatment.

**Safety**

- Median treatment duration was 119.5 days (range 44.0–260.0 days).
- No DLTs were reported among 8 evaluable patients.
- Two patients were not evaluable for DLTs due to enzaludamide dose reductions during the DDI period.
- Among the 8 patients overall, the most common any-grade treatment-emergent adverse events (TEAEs) were nausea, decreased appetite, and fatigue (Table 2).
- The most common grade 3 TEAEs were anemia and fatigue.
- Of the 8 patients, 7 (87.5%) required treatment interruption or dose reduction of rucaparib (n=2), enzaludamide (n=2), or both (n=3) due to TEAEs.