Rucaparib + Enzalutamide in Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC): Pharmacokinetics (PK) and Safety Data From the Phase 1b RAMP Study

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Supplementary Material
Dose-limiting Toxicity Criteria

To be considered DLT evaluable, patient must have received ≥70% of the scheduled doses of both rucaparib and enzalutamide and completed 2 cycles of combination treatment or have had a DLT in either cycle 1 or cycle 2.

DLTs were defined as follows:

- Grade ≥3 febrile neutropenia (ie, fever >38.3°C with absolute neutrophil count <1.0 × 10^9/L) of any duration or grade 4 neutropenia lasting >7 days despite granulocyte-colony-stimulating factor administration
- Grade 3 thrombocytopenia (platelets <50 × 10^9/L) with significant bleeding or grade 4 thrombocytopenia (platelets <25 × 10^9/L) ≥5 days duration
- Grade 4 anemia (ie, life-threatening consequences, urgent intervention indicated)
- Any nonhematological AE grade ≥3, except:
  - Nausea, vomiting, and diarrhea well controlled by systemic medication and lasting ≤72 hours
  - Fatigue
  - Grade 3 ALT or AST increase not accompanied by a concomitant increase in total bilirubin above the upper limit of normal. Note that any grade 4 ALT/AST increase was considered a DLT
  - Grade 3 arthralgia treated with nonsteroidal anti-inflammatory drug(s) (or equivalent) that resolves to grade ≤2 within 14 days
  - Alopecia of any grade

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLT, dose-limiting toxicity.
Supplementary Figure 1. Effect of Enzalutamide on M324/Rucaparib Ratio in Patients From the RAMP Study

The vertical dashed line indicates the start of the combination treatment, following a 1-week run-in with rucaparib monotherapy.

- The increases toward the end of the combination treatment for several patients were due to the holding of rucaparib.

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Supplementary Figure 2. Rucaparib Concentration Over Time

Horizontal dashed black line and regions shaded blue represent median and 90% confidence interval, respectively, for TRITON2 PK data on days 29, 57, 85, and 113 (n=213). The vertical dashed line indicates the start of the combination treatment, following a 1-week run-in with rucaparib monotherapy.

Supplementary Figure 3. Best Percent Change in PSA From Baseline in Patients Treated With Rucaparib and Enzalutamide

The horizontal dashed line indicates the threshold for PSA response, a 50% decrease from baseline. PSA, prostate-specific antigen; PSA50, reduction of ≥50% from baseline in PSA level.