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

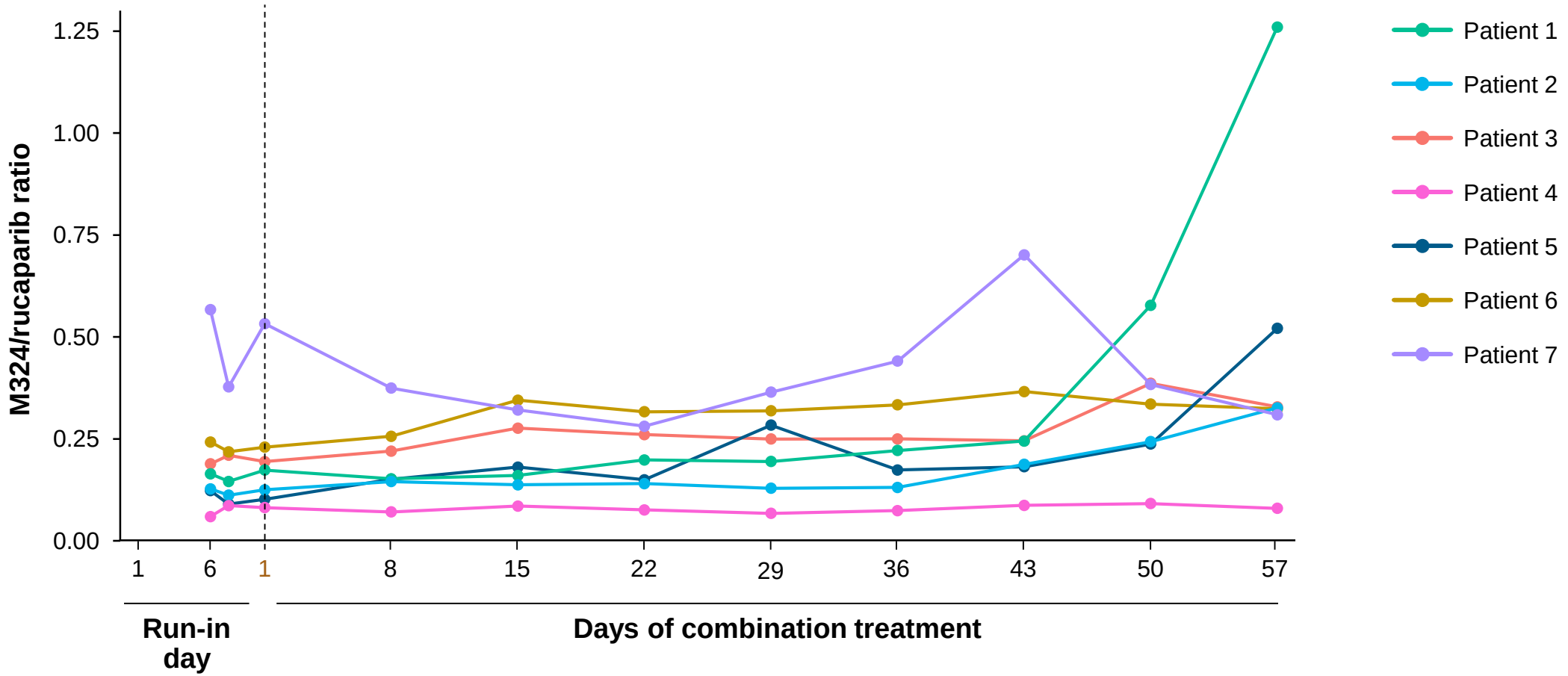
To be considered DLT evaluable, patient must have received ≥70% of the scheduled doses of both rucaparib and enzalutamide and completed 2 cycles of combination treatment or have had a DLT in either cycle 1 or cycle 2.

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.

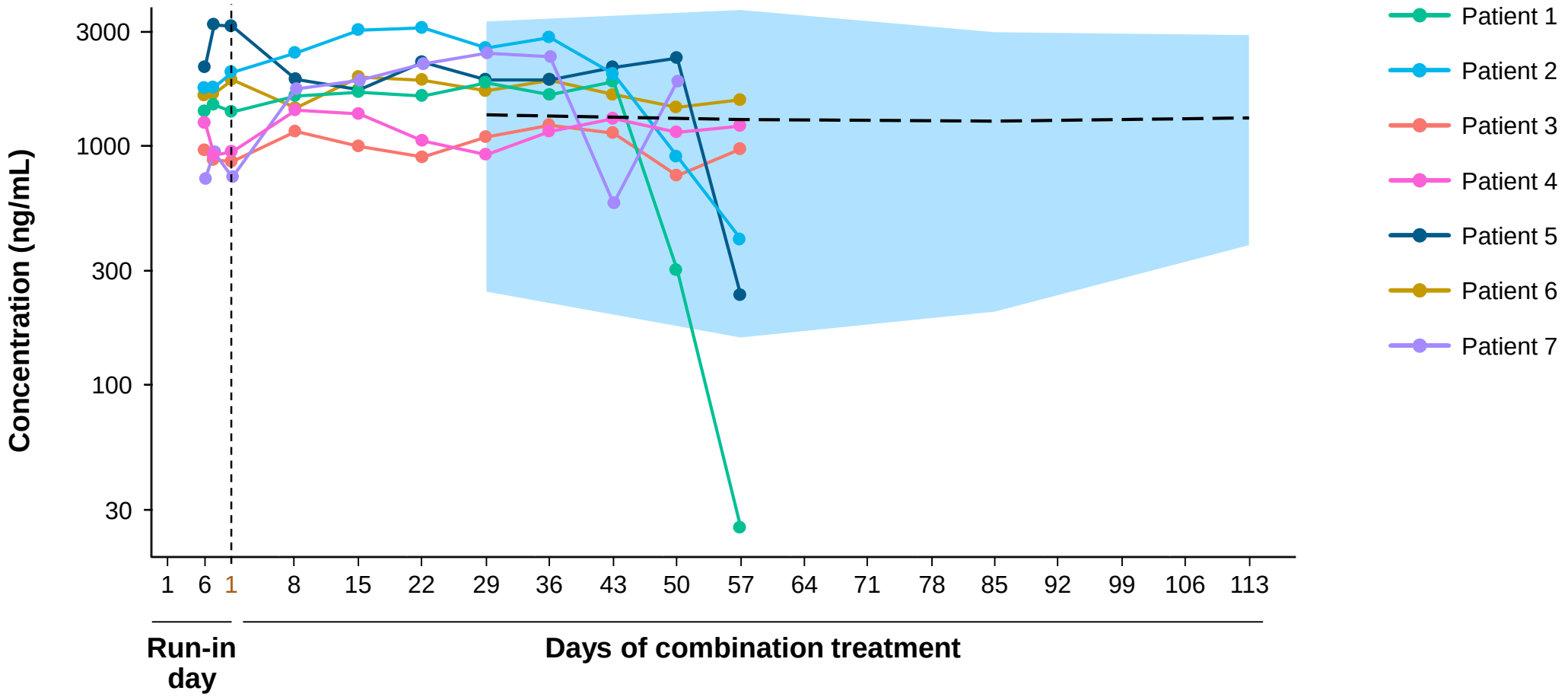
Supplementary Figure 1. Effect of Enzalutamide on M324/Rucaparib Ratio in Patients From the RAMP Study



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

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

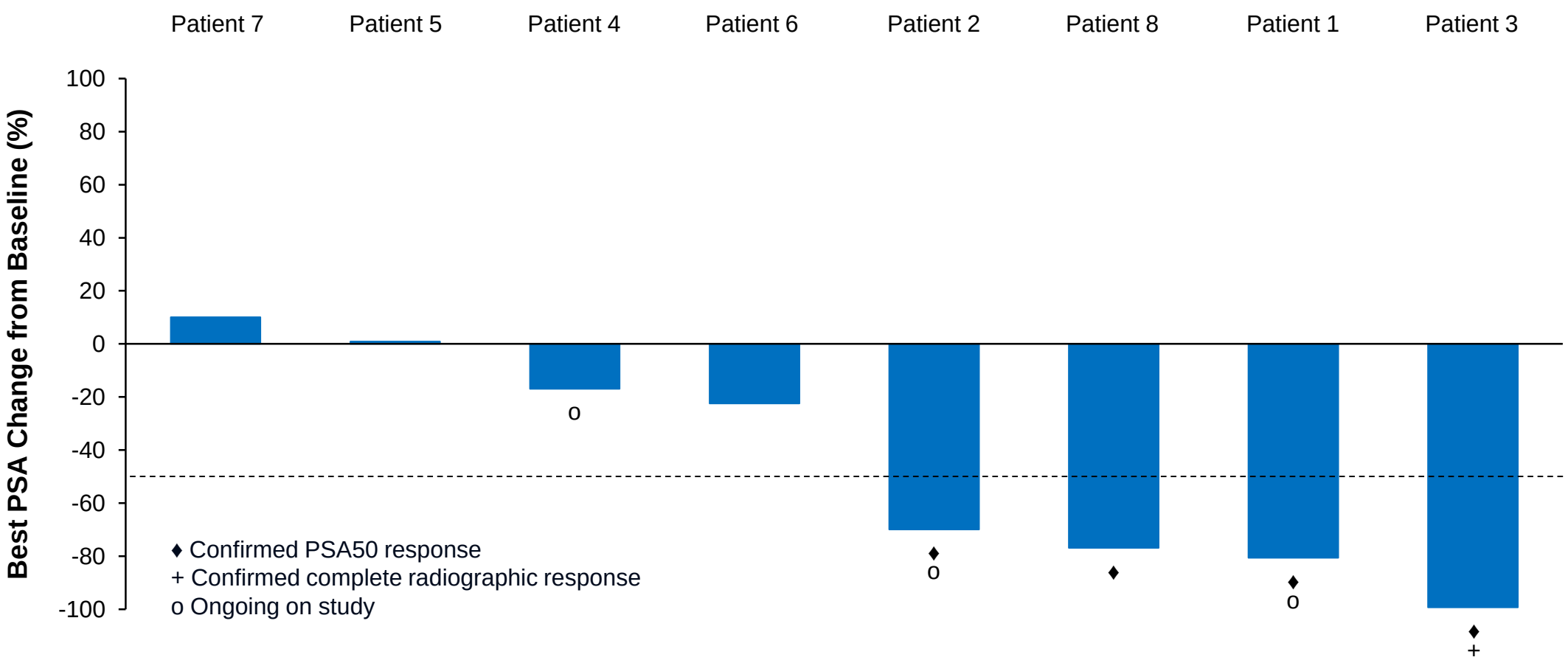
Supplementary Figure 2. Rucaparib Concentration Over Time



Horizontal dashed black line and regions shaded blue represent median and 90% confidence interval, respectively, for TRITON2 PK data[1] 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.

1. Chowdhury et al. *Ann Oncol*. 2020;31(4 suppl):S533-4.

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.