Phase 1b/2 SEASTAR Trial: Safety, Pharmacokinetics, and Preliminary Efficacy of the Poly(ADP-ribose) Polymerase (PARP) Inhibitor Rucaparib and Anogeniupharb in Patients With Advanced Solid Tumors

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INTRODUCTION

-Rucaparib is an oral, potent, and selective inhibitor of poly(ADP-ribose) polymerase (PARP) 1, PARP2, and PARP15.

-Lucitanib is an oral tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor receptor 1–3 (VEGFR1–3), platelet-derived growth factor receptors alpha and beta (PDGFR α/β), and Fibroblast growth factor receptors 1–3 (FGFR1–3).

-Rucaparib and lucitanib are being evaluated in combination in a phase 1b/2 SEASTAR (Study Evaluating Anogeniupharb and Rucaparib in Tumors, Advanced, Safety, and Tolerability) trial.

-Objective: To determine the maximum tolerated dose (MTD) and to establish the recommended phase 2 dose (RP2D) for this combination in patients with advanced solid tumors.

METHODS

-For phase 1b, patients with advanced solid tumors who had prior lines of therapy in the locally advanced, metastatic, or recurrent setting were enrolled. Patients with BRCA1- or BRCA2-related cancers must have received prior PARP inhibitor therapy. A 2:1 (n=8) design was used, with starting doses of rucaparib 300 mg twice daily and lucitanib 4 mg once daily in cohort 1.

-Phase 1b/2 patients were randomized in 1:1 (n=54) to cohorts 1–3: rucaparib 300 mg BID + lucitanib 4 mg QD; rucaparib 400 mg BID + lucitanib 4 mg QD; rucaparib 400 mg BID + lucitanib 6 mg QD.

RESULTS

-As of April 16, 2015, 18 patients were treated with rucaparib + lucitanib and included in the analyses (Table 1).

-Among patients with measurable disease, 1 patient in cohort 1 with measurable disease had an unconfirmed partial response.

-Median (range) time on treatment was 58.0 (20.0–395.0) days, with 3 patients ongoing as of the data cutoff date.

-Efficacy: Among patients with measurable disease, 1 patient in cohort 1 with an unconfirmed PR, and 1 patient each in cohorts 1, 2, and 4 with stable disease 116 weeks.

-Safety: Median (range) time on treatment was 48.0 (10–385.0) days, with 3 patients ongoing as of the data cutoff date. A CRITIC grade 3/4 pyrexia was seen in cohort 1, 4 other G3/4 events have been reported. Across all cohorts, the most common any-grade TEAEs were nausea, anemia, decreased appetite, and lymphopenia (Table 2).

-Not evaluable: 1 patient had an unconfirmed partial response.

-Pharmacokinetics: The combination of a poly(ADP-ribose) polymerase (PARP) inhibitor and an angiogenesis inhibitor is feasible and may merit further evaluation.

REFERENCES


