Dose Escalation of Pamiparib in Chinese Patients With High-Grade Non-Mucinous Ovarian Cancer (HGOC) or Advanced Triple-Negative Breast Cancer (TNBC)

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Background Pamiparib is an investigational PARP1/2 inhibitor that has demonstrated PARP-DNA complex trapping and robust antitumor activity in nonclinical models. In a first-in-human study (NCT02361723), pamiparib was generally well tolerated and showed preliminary antitumor activity, notably in patients (pts) with HGOC. The RP2D was established as 60 mg PO BID.

Methods In the Phase 1 dose-escalation (DE) portion of this study (NCT03333915), Chinese pts with TNBC or advanced HGOC, including fallopian and primary peritoneal cancer, were enrolled. The DE cohorts were designed to confirm RP2D. Germline *BRCA1/2* mutation status was retrospectively evaluated by central testing. Primary endpoint was incidence and severity of AEs (CTCAE v4.03); antitumor activity was assessed per RECIST v1.1 (all pts) and CA-125 response criteria (HGOC pts).

Results As of 14 Mar 2019, 9 HGOC and 6 TNBC pts were enrolled. Seven pts were $gBRCA^{mut}$ (HGOC: n=5; TNBC: n=2); all HGOC pts were platinum-resistant/refractory. Pamiparib BID dose levels of 20 (n=4), 40 (n=4), and 60 mg (n=7) were evaluated. At data cutoff, 1 HGOC pt was still on treatment. The most commonly reported treatment-related AEs (TRAEs) were asthenia and nausea (n=12 each). Decreased hemoglobin (n=3) was the only Grade 3 TRAE reported in more than 2 pts. No $\geqslant$ Grade 4 AEs were reported. Serious AEs (abdominal infection, ileus, and pleural effusion, n=1 each) were considered not related to pamiparib. No DLTs were reported; 60 mg PO BID was confirmed as RP2D. Across the 13 RECIST-evaluable pts, 2 HGOC pts achieved a confirmed PR ($gBRCA^{mut}$=1) and 6 achieved SD ($gBRCA^{mut}$=4). Median treatment duration for the 8 HGOC pts was 182 days (range: 43, 795). Two of the 8 CA-125-evaluable pts had a confirmed CR or PR (n=1 each). Best response was PD in the 5 RECIST-evaluable TNBC pts ($gBRCA^{mut}$=1); all these 5 pts experienced PD previously during platinum-based chemotherapy.

Conclusions Pamiparib at 20, 40, and 60 mg PO BID was generally well tolerated in Chinese pts with advanced HGOC or TNBC. The previously established RP2D of 60 mg BID was confirmed. Antitumor activity in pts with HGOC was observed, notably in pts who were resistant/refractory to platinum.