Safety, antitumor activity, and pharmacokinetics (PK) of pamiparib (BGB-290), a PARP1/2 inhibitor, in patients (pts) with advanced solid tumours: Updated phase I dose-escalation/expansion results

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Background: Pamiparib is an investigational PARP1/2 inhibitor that has demonstrated brain penetration and PARP–DNA complex trapping in preclinical studies. In the phase 1 dose-escalation/expansion study of pts with advanced solid tumors, pamiparib was generally well tolerated and showed preliminary antitumor activity. Here we report updated antitumor activity focused on the ovarian cancer cohort and safety data.

Methods: This is a two-stage dose-escalation/expansion study (NCT02361723). The dose-escalation study component established the pamiparib PK profile, and the recommended phase 2 dose (RP2D) of pamiparib administered orally 60 mg BID in pts with solid tumors. The dose-expansion component was conducted in pts with ovarian, breast, prostate, gastric, and small cell lung cancer.

Results: As of 1 January 2019, 97 pts (median age, 60 years; Eastern Cooperative Oncology Group performance status of 0, 1, or 2 [37%, 62%, and 1%, respectively]) were enrolled in the dose-escalation (n = 60) and dose-expansion (n = 37) components. Among the 97 enrolled pts, 48 pts (n = 30, ovarian pts) received 60 mg BID, the RP2D. Of 57 ovarian pts in the efficacy evaluable population ($\geq$1 postbaseline tumor assessment), 22 (39%) achieved a confirmed objective response (complete response, n = 4; partial response, n = 18) per RECIST v1.1 criteria. Median duration of response was 12.3 months (range, 1.3–40.8). Biomarker data will be included in future analyses. In the safety population (n = 97), drug-related adverse events (AEs) in $\geq$ 10% of pts were nausea, fatigue, anemia, diarrhea, vomiting, and decreased appetite. The most common drug-related G3 (no G4 or G5) AEs were anemia (18.6%) and neutropenia (6.2%). AEs led to treatment discontinuation in 6.2% of pts. Four pts died due to disease progression with non-drug–related AEs. Pamiparib plasma exposure generally increased with increased dose, with a median $t_{1/2}$ of ~13 hours.

Conclusions: Pamiparib continues to be generally well tolerated and demonstrates antitumor activity in this update of an ongoing, phase 1 dose-escalation/expansion study in pts with advanced solid tumors.

Clinical trial identification: NCT02361723.

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