451PD **Updated results of the PARP1/2 inhibitor pamiparib in combination with low-dose (ld) temozolomide (TMZ) in patients (pts) with locally advanced or metastatic solid tumours**

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Background: DNA damage caused by TMZ can sensitize tumors to PARP inhibitors. Pamiparib is an investigational PARP1/2 inhibitor that has shown PARP trapping activity, brain penetration, and synergistic cytotoxicity with ld TMZ in nonclinical studies.

Methods: This ongoing study consists of a dose-escalation phase (3 + 3 design) and a dose-expansion phase enrolling pts with gastric or small cell lung cancer (GC and SCLC). During dose escalation, pamiparib was administered at 60 mg PO BID on days 1–28 and ld TMZ was given at escalating doses PO QD on days 1–7, 1–14, or 1–28 of 28-day cycles. During dose expansion, pts are being treated at the recommended phase 2 dose (RP2D); eligibility criteria include metastatic GC and extensive stage SCLC pts treated with ≤2 prior lines of chemotherapy. Tumor assessments are performed every 8 weeks. Primary and secondary endpoints include safety/tolerability and antitumor activity (RECIST v1.1)/PK, respectively; biomarker assessment (eg, BRCA) is exploratory. We present updated results that include the RP2D and data from expansion cohort pts.

Results: As of 1 March 2019, 66 pts were enrolled in 8 dose escalation cohorts and 24 pts were enrolled at the RP2D pamiparib 60 mg PO BID days 1–28 and TMZ 60 mg PO QD days 1–7 (N = 90). Median age was 65 years (range, 30–85) and median prior lines of therapy was 3 (range, 1–10). The most common adverse events (AEs) related to study drugs across all doses were nausea (46%; 0% grade (G)3/4), anemia (43%; 24% G3/4), fatigue (41%; 1% G3/4), neutropenia (26%; 21% G3/4), and thrombocytopenia (27%; 14% G3/4). There were no fatal AEs. Pamiparib + TMZ plasma exposure was similar to that of each single agent. Among 63 dose escalation pts with measurable disease evaluated for efficacy, 9 achieved partial response (PR; 14%; 95% CI, 7–25) across ld TMZ doses and indications (6 confirmed PR). Responses were seen in pts regardless of known BRCA status. Disease control rate was 53% and median duration of response was 5.5 months (range, 1.9–7.3).

Conclusions: Pamiparib combined with ld TMZ continues to demonstrate promising antitumor activity and remains generally well tolerated in pts with advanced solid tumors.

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