ACTR-39. PAMIPARIB IN COMBINATION WITH RADIATION THERAPY (RT) AND/OR TEMOZOLOMIDE (TMZ) IN PATIENTS WITH NEWLY DIAGNOSED OR RECURRENT/REFRACTORY (R/R) GLIOBLASTOMA (GBM); PHASE 1B/2 STUDY UPDATE

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Abstract

Pamiparib, an investigational, selective PARP1/2 inhibitor that has demonstrated potent PARP trapping and ability to cross the blood-brain barrier, showed synergistic cytotoxicity with TMZ preclinically. We report updated safety and antitumor effects from a phase 1b/2 study of pamiparib + RT and/or TMZ in patients with newly diagnosed or R/R GBM (SNO 2018, ACTR-30). The dose-escalation/expansion study has 3 arms: *Arm A*, pamiparib (2, 4, or 6 weeks) + RT in newly diagnosed GBM patients with unmethylated *MGMT* promoter (unmethylated-GBM); *Arm B,* pamiparib (6 weeks) + RT and increasing TMZ dosed in weeks 1 and 5 of RT in newly diagnosed, unmethylated-GBM patients; and *Arm C*, pamiparib + increasing TMZ doses in methylated/unmethylated R/R-GBM patients. *Arm A* and *B* patients receive maintenance treatment post-RT rest period at the *Arm* C expansion dose/schedule. As of 10 April 2019, accrual was completed for *Arms A* and *C* dose-escalation (*A*: n=20; *C*: n=17) and continues in the dose expansion (*A*: n=28/40; *C*: n=28/30); accrual was completed in dose escalation for *B* (n=9). Recommended phase 2 doses were established for *Arms A* (pamiparib 60 mg BID×6 weeks + 6–7 weeks RT) and *C* (pamiparib 60 mg BID d1–28 + TMZ 60 mg d1–7/28-d cycle). One dose-limiting toxicity (grade 3 febrile neutropenia) was reported in Arm B. Treatment-related adverse events (≥10%) were (overall/grade 3 [no grade 4/5]): Arm A, nausea (23%/2%); B, decreased WBC count (11%/11%); C (none). Of patients with tumor assessment post-RT: Arm A (n=17), 1 had cPR, 1 uPR, and 9 SD (disease control rate, 64.7% [95% CI, 38.3–85.8]); C (n=26), 1 had cPR (sustained 12 cycles), 1 uPR, and 5 SD (objective response rate, 7.7% [95% CI, 0.9–25.1]). Pamiparib 60 mg BID + RT/TMZ was generally well tolerated in patients with newly diagnosed or R/R GBM. Clinical trial ID: NCT03150862