PARALLEL 303: Phase 2 randomized study of pamiparib vs placebo as maintenance therapy in patients (pts) with inoperable locally advanced or metastatic gastric cancer that responded to platinum-based first-line (1L) chemotherapy.

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Background:

A subset of gastric cancers exhibits platinum sensitivity and genomic instability that is characteristic of homologous recombination deficiency (HRD). Cells with HRD are sensitive to poly (ADP-ribose) polymerase (PARP) inhibition. PARP inhibitor maintenance therapy following platinum-based chemotherapy has been a successful treatment strategy in pts with ovarian cancer. Pamiparib is an orally administered selective PARP protein 1 and 2 (PARP1/2) inhibitor that has shown potent DNA-PARP trapping activity and crosses the blood brain barrier in preclinical studies. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib showed an acceptable safety profile and promising antitumor activity. PARALLEL 303 compared the efficacy and safety of pamiparib vs placebo as maintenance therapy in pts with inoperable locally advanced or metastatic gastric cancer that responded to platinum-based 1L chemotherapy.

Methods:

The primary endpoint of this double-blind, randomized, global Phase 2 study (NCT03427814) was progression-free survival (PFS) as determined by the investigator per RECIST Version 1.1. Key secondary endpoints included time to subsequent treatment, objective response rate, duration of response, time to response, overall survival (OS) and safety. At the time of this analysis, OS data were immature due to the short duration of study. Data presented here will focus on PFS and safety.

Results:

136 pts were randomized 1:1 to receive pamiparib 60 mg orally (PO) twice daily (BID) (n = 71) or placebo PO BID (n = 65) in 28-day cycles. The median PFS was longer with pamiparib vs placebo, but did not reach statistical significance (3.7 months; 95% CI, 1.94–5.26 vs 2.1 months; 95% CI, 1.87–3.75 months); hazard ratio 0.799 (95% CI, 0.534–1.193; P = 0.1428). Treatment-emergent adverse events (TEAEs) of ≥ Grade 3 were experienced by 29 pts (40.8%) in the pamiparib arm, and 20 pts (30.8%) in the placebo arm. The most common TEAEs of ≥ Grade 3 were blood and lymphatic system disorders in the pamiparib arm, and gastrointestinal disorders in the placebo arm. TEAEs leading to treatment discontinuation were: 8 pts (11.3%) in the pamiparib arm and 2 pts (3.1%) in the placebo arm. TEAEs leading to death were: 2 pts (2.8%; 1 pneumonia, 1 unexplained) in the pamiparib arm, and 2 pts (3.1%; 1 hepatic rupture, 1 sepsis) in the placebo arm.

Conclusions:

Although pamiparib did not meet statistical significance for superiority vs placebo for its primary endpoint, it was generally well tolerated with few treatment discontinuations due to TEAEs. No new safety signals were identified with pamiparib, and its safety profile was consistent with that of other PARP inhibitors.