A Phase 3, Double-Blind, Randomized Study of Pamiparib Versus Placebo as Maintenance Therapy in Patients With Inoperable, Locally Advanced, or Metastatic Gastric Cancer (GC) that Responded to Platinum-Based First-Line Chemotherapy.

Fortunato Ciardiello, Yung-Jue Bang, Johanna C. Bendell, Andres Cervantes, Rainer Karl Brachmann, Yuting Zhang, Mitch Raponi, Heinrich Farin, Lin Shen; Medical Oncology, University of Campania "Luigi Vanvitelli", Napoli, Italy; Medical Oncology, Seoul National University Hospital, Seoul, Korea, Republic of (South); GI Oncology Research, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; Medical Oncology, Instituto de Investigación Sanitaria INCLIVA, Valencia, Spain; Clinical Development, BeiGene USA, Inc., San Mateo, CA; Department of GI Oncology, Peking University Cancer Hospital and Institute, Beijing, China

Background: Gastric cancer is the fifth most common cancer, and is the third leading cause of cancer deaths worldwide. In patients with locally advanced or metastatic GC, fluoropyrimidine- and platinum-based combination chemotherapy is first-line standard of care. Despite refinement in chemotherapy regimens, outcomes are poor and survival after first-line treatment remains low. A subset of GCs exhibit platinum sensitivity and genomic instability that is characteristic of homologous recombination deficiency (HRD). Poly (ADP-ribose) polymerase proteins 1 and 2 (PARP1/2) are involved in DNA damage repair, and their inhibition is cytotoxic for cells with HRD. Pamiparib is a selective PARP1/2 inhibitor that crosses the blood-brain barrier, has shown potent DNA–PARP trapping, and has demonstrated antitumor activity in preclinical models. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib was generally well tolerated and showed preliminary antitumor activity; 60 mg oral twice daily (BID) was established as the recommended dose. **Methods:** This ongoing, global, double-blind, placebo- controlled, randomized, multicenter phase 3 study (NCT03427814) is designed to compare the efficacy, safety, and tolerability of pamiparib vs placebo as maintenance therapy in ~540 patients with advanced GC who have responded to first-line, platinum- based chemotherapy. Patients who are ≤8 weeks after their last dose of first-line platinum based chemotherapy will be randomized 1:1 to receive either pamiparib 60 mg BID or placebo in 28-day cycles. Patient randomization will be stratified by genomic loss of heterozygosity status (ie, high vs low), region, and ECOG status. Radiologic assessments will be centrally evaluated per RECIST every 8 weeks after first dose. The primary endpoint is progression-free survival; key secondary endpoints include safety/tolerability, overall survival, objective response rates, time and duration of response, and time to second subsequent treatment. Correlative biomarker analyses in tumor tissues and blood will be performed.