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

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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 gastric cancer, fluoropyrimidine- and platinum-based combination chemotherapy is first-line standard of care. Despite refinement in chemotherapy regimens, outcomes are poor and median survival after first-line treatment remains low. A subset of gastric cancers 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 (previously known as BGB-290) 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. These studies also established 60 mg orally twice daily as the recommended pivotal dose.

Methods: This double-blind, placebo-controlled, randomized, multicenter phase 3 study (NCT03427814) conducted in Asia, Australia, Europe, and North America is designed to compare the efficacy, safety, and tolerability of pamiparib with placebo as maintenance therapy in ~540 patients with advanced gastric cancer who have responded to first-line, platinum-based chemotherapy. Patients who are ≤8 weeks after their last platinum dose of first-line chemotherapy will be randomized 1:1 to receive either pamiparib 60 mg twice daily or placebo. Patient randomization will be stratified by genomic loss of heterozygosity status (ie, high versus 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, and duration of response.