

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. 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 robust antitumor activity in preclinical models. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib was generally well tolerated and showed promising antitumor activity. These studies also established 60 mg orally twice daily as the recommended pivotal dose.

Trial design: The purpose of this double-blind, placebo-controlled, randomized, multicenter Phase 3 study (NCT03427814) conducted in Asia, Australia, Europe, and North America is 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 in 28-day cycles.

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. Safety will be assessed on Day 1 of each cycle, and Day 15 of Cycles 1 and 2, and as needed. Blood samples will be collected at various time points to determine the pharmacokinetics of pamiparib in inoperable, locally advanced gastric cancer patients. 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.