Phase 1/2 Study Investigating Safety, Tolerability, Pharmacokinetics, and Preliminary Antitumor Activity of Anti-PD-L1 Monoclonal Antibody BGB-A333 Alone and in Combination With Anti-PD-1 Monoclonal Antibody Tislelizumab in Patients With Advanced Solid Tumors

Background: Programmed cell death-1 (PD-1) and its ligand, programmed death-ligand 1 (PD-L1), play critical roles in the immune modulation of tumor progression. Tislelizumab is a humanized IgG4 monoclonal antibody against PD-1. A first-in-human, phase 1A/1B study (NCT02407990) demonstrated that single-agent tislelizumab was generally well tolerated and showed evidence of antitumor activity in patients with advanced solid tumors at the recommended phase 2 dose (RP2D) of 200 mg administered every 3 weeks (Q3W). BGB-A333 is a humanized IgG1 monoclonal antibody against PD-L1 which increased functional activities of human T cells in in vitro studies, and showed antitumor activity in various cancer xenograft models. BGB-A333 blocks the interaction between PD-L1 and CD80 (B7-1), which in turn release the inhibitory signals to T-cells, enhances T-cell expansion, and prevents T-cell energy induction. Therefore, combination of anti-PD-1 and anti-PD-L1 can potentially elicit stronger antitumor immunity through blockade of multiple complementary immune-suppressive signals in tumor microenvironments.

Trial design: This open-label study (NCT03379259) consists of two phases, each phase consisting of two parts. Phase 1 is designed to investigate the safety and tolerability of BGB-A333 RP2D alone and in combination with tislelizumab. Phase 1A (BGB-A333 dose escalation) will follow a 3+3 design to establish the RP2D of BGB-A333. Phase 1B (combination dose confirmation) explores safety and tolerability of IV BGB-A333 (determined from dose escalation) in combination with IV tislelizumab (200 mg Q3W). Phase 2 is designed to evaluate the antitumor activity of BGB-A333 alone and in combination with tislelizumab. Phase 2A (BGB-A333 dose expansion) will enroll patients into two cohorts: non-small cell lung cancer and urothelial carcinoma. Phase 2B (combination dose expansion) will enroll patients with specific tumor types, which will be chosen based on data from phase 2A and other studies. The primary endpoint of the phase 2 study is overall response rate.