A Phase 1 Study of the Anti-PD-1 Monoclonal Antibody Tislelizumab (BGB-A317) in Combination with the PARP Inhibitor Pamiparib (BGB-290) in Advanced Solid Tumors

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Background: Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1 with no FcγR binding. Pamiparib, a potent inhibitor of PARP 1/2, is hypothesized to promote neoantigen release that may increase efficacy of tislelizumab. Recommended phase 2 doses for single-agent pamiparib (60mg PO BID) and tislelizumab (200mg IV Q3W) have been previously identified.

Methods: This study consists of dose escalation followed by expansion into various solid tumor types. Cohorts of 6–12 patients with advanced solid tumors were treated in each of 5 planned dose levels (DLs). In DLs 1–3, pamiparib doses ranged between 20–60mg BID with tislelizumab 2mg/kg Q3W. In DLs 4–5, pamiparib doses were 40 or 60mg BID; tislelizumab was given at 200mg Q3W based on pharmacokinetic data from a single agent Phase 1 study.

Results: As of 31 March 2017, 43 patients [median age 63 years (34–75)] were treated in DLs 1–5. Three patients experienced four dose-limiting toxicities: grade 2 nausea (DL4), grade 2 nausea and grade 2 vomiting (DL5), and grade 4 autoimmune hepatitis (DL5). The recommended dose for combination Phase 2 studies was identified as tislelizumab 200mg IV Q3W+pamiparib 40mg PO BID. Fatigue was the most common AE considered related to both tislelizumab and pamiparib. Immune-related AEs ofgrade ≥3 were elevated ALT/AST (n=3), autoimmune hepatitis (n=3), and hepatitis (n=1). Eleven patients achieved complete or partial response, four had confirmed PR or CR. Plasma/serum exposure of pamiparib and tislelizumab were consistent with exposures in single-agent trials.

Conclusions: The combination of tislelizumab/pamiparib was well tolerated in most patients and the activity of the combination support enrollment into disease-specific cohorts, which is ongoing. These data have previously been presented at ASCO-SITC (January 25–27, 2018) and published in the conference proceedings as abstract 48.