Preliminary safety and efficacy data of BGB-A333, an anti-PD-L1 monoclonal antibody, alone and in combination with tislelizumab in patients with advanced solid tumors

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Background: Programmed cell death protein-1 (PD-1) and its ligand, programmed death-ligand 1 (PD-L1), play critical roles in the immune modulation of tumor progression. Although both pathways have overlapping elements, each has a distinct mechanism of action. Nonclinical studies have demonstrated that potential synergistic antitumor effects can result from blocking both PD-1 and PD-L1. BGB-A333 is an investigational humanized IgG1 monoclonal antibody against PD-L1 that has antitumor activity in xenograft models. Tislelizumab, a clinical-stage anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, has demonstrated clinical activity in patients with advanced solid tumors. Here we report preliminary results from the phase 1 component of an open-label phase 1/2 study (NCT03379259) of BGB-A333 alone and in combination with tislelizumab in patients with advanced solid tumors.

Methods: Phase 1 of this study consisted of two parts. In *Part A,* patients received single-agent BGB-A333 IV Q3W at increasing doses; in *Part B* patients received BGB-A333 1350 mg IV Q3W + tislelizumab 200 mg IV Q3W. Eligible patients had unresectable advanced or metastatic cancer and an ECOG performance status of ≤1. Safety/tolerability profile (primary endpoint) was examined by monitoring adverse events (AEs); secondary endpoints included antitumor activity, assessed by RECIST v1.1, and the pharmacokinetic (PK) parameters of each antibody.

Results: As of Oct 30, 2019, 15 patients were enrolled in *Part A* (450 mg, n=3; 900 mg, n=3; 1350 mg, n=6; 1800 mg, n=3) and 12 in *Part B*. Across both parts, patients were female (n=17/29; 63%); squamous cell carcinoma of either skin or head and neck (n=5) and ovarian cancer (n=4) were the most common tumor types. Thirteen patients (48%) had ≥2 lines of prior systemic therapy. The most common treatment-related AEs (TRAEs) were fatigue (N=5; *Part A*, n=3; *Part B*, n=2) and nausea (N=4; n=2 in *A* and *B*); the only grade ≥3 TRAE occurring in ≥1 patient was grade 3 maculo-papular rash (N=2; n=1 in *A* and *B*). One patient in *Part B* experienced a fatal AE (acute kidney injury) considered possibly related to study treatment. Of the 15 patients receiving BGB-A333 monotherapy in *Part A,* three (20%) achieved a confirmed complete response and two (13.3%) achieved a partial response (PR). Two of the 12 (16.7%) patients receiving combination therapy in *Part B* achieved a PR. The PK of BGB-A333 was comparable to a typical IgG1 antibody, and was similar as a single-agent or in combination with tislelizumab. The PK of tislelizumab was comparable with historical data.

Conclusions: BGB-A333, alone or in combination with tislelizumab, was generally well tolerated and demonstrated antitumor activity in patients with advanced solid tumors. Based on these data, expansion cohorts have been initiated.