Abstract Title: AdvanTIG-105: Phase 1 dose-escalation study of anti-TIGIT monoclonal antibody ociperlimab (BGB-A1217) in combination with tislelizumab in patients with advanced solid tumors

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Background: T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) is a co-inhibitory, immune checkpoint receptor. Ociperlimab (OCI; BGB-A1217), a novel humanized monoclonal antibody, binds to TIGIT with high specificity and affinity. OCI showed competent binding with C1q and all Fcγ receptors and induced antibody-dependent cellular cytotoxicity. Preclinical studies demonstrated OCI plus tislelizumab (TIS; anti-PD-1 antibody) produced synergistic immune cell activation and enhanced antitumor activity.

Methods: AdvanTIG-105, a Phase 1, open label, multicenter, dose-escalation study (NCT04047862), assessed safety and preliminary antitumor activity of OCI+TIS for advanced, unresectable or metastatic solid tumors for which standard therapy was ineffective/unavailable. Eligible patients had an Eastern Cooperative Oncology Group performance score ≤1 and no prior therapy targeting TIGIT. Patients received OCI intravenously (IV) on D1 of Cycle 1 and TIS 200 mg IV on D8; dose-limiting toxicities (DLTs) were monitored until D28. If tolerated, OCI and TIS were administered sequentially on D29 and every 3 weeks (Q3W) thereafter. Patients received escalating doses of OCI (50-900 mg) plus TIS 200 mg. The study objective was determination of the recommended phase 2 dose (RP2D) of OCI+TIS. Study endpoints included assessment of adverse events (AEs), pharmacokinetics, and antitumor activity.

Results: As of October 12, 2020, 24 patients with advanced solid tumors received OCI+TIS. Median number of prior treatment regimens was two; 9/24 patients (37.5%) received prior

immunotherapy. Median follow-up was 17 weeks. No DLTs were observed. Twenty patients had ≥1 treatment-emergent AE (TEAE; mostly Grade ≤2); fatigue (n=6) and diarrhea (n=4) were most common. Two Grade 3 immune-related AEs were reported (colitis, low cortisol). No Grade ≥4 TEAEs or TEAE-associated deaths were reported. Overall, one patient achieved partial response (OCI 450 mg) and nine had stable disease. The longest duration of stable disease was 36 weeks (OCI 150 mg; n=1). After administration, OCI serum concentration decreased in a biphasic manner. Exposure to OCI increased proportionally with dose, and TIGIT receptor occupancy was sustained at ≥50 mg doses.

Conclusions: OCI plus TIS was well tolerated across all doses in patients with advanced solid tumors. The RP2D was OCI 900 mg plus TIS 200 mg Q3W.