BGB-A333, an Anti-PD-L1 Monoclonal Antibody, in Combination With Tislelizumab in Patients With Urothelial Carcinoma

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Background Preclinical studies have shown potential synergism from blocking both programmed cell death protein-1 (PD-1) and programmed death-ligand 1 (PD-L1). BGB-A333 is an investigational humanized monoclonal antibody against PD-L1 that has antitumor activity in xenograft models. Tislelizumab, a clinical-stage anti-PD-1 antibody, showed clinical activity in patients (pts) with advanced solid tumors. We report results from the expansion cohort (phase 2B) of an open-label phase 1/2 study (NCT03379259) of BGB-A333 plus tislelizumab in pts with previously treated advanced urothelial carcinoma (UC).

Methods Patients received BGB-A333 1350 mg IV Q3W + tislelizumab 200 mg IV Q3W. Eligible pts had locally advanced or metastatic UC without prior PD-(L)1 therapy, could not tolerate or progressed during/after treatment with platinum-based chemotherapy, and had an ECOG performance status of ≤1. The primary endpoint was investigator-assessed objective response rate (ORR) per RECIST v1.1. Key secondary endpoints included duration of response (DoR) per RECIST v1.1, progression-free survival (PFS) estimated with Kaplan-Meier analysis, and the safety/tolerability profile evaluated by monitoring adverse events (AEs).

Results As of 10 March 2020, 12 pts (median age, 69.5 yr; 92% male) with UC were enrolled; median study follow-up, 8.3 mo. Most pts (n=10, 83%) had 1 prior systemic therapy. Median duration of treatment for both BGB-A333 and tislelizumab was 5.5 mo (range: 1.2, 9.9). Confirmed ORR was 42% (95% CI: 15.2, 72.3); 3 pts had complete responses, 2 had partial responses, 4 had stable disease (SD; 2 had SD >6 mo), 2 had progressive disease, and 1 was not evaluable (due to missing postbaseline assessment). Median DoR was not reached; median PFS was 6.1 mo (95% CI: 1.9, not estimable). Across

the entire study (n=39), treatment-related AEs (TRAEs) occurred in 19 pts. Of the 24 pts receiving combination treatment, four pts (including one with UC) had grade ≥3 TRAEs. One pt with UC had an immune-related AE (myositis); no pts with UC had a fatal TRAE.

Conclusion BGB-A333 in combination with tislelizumab was well tolerated and demonstrated antitumor activity in pts with advanced UC.