Preliminary Results from Patients with Urothelial Carcinoma (UC) in a Phase 1A/1B Study of BGB-A317, an Anti-PD-1 Monoclonal Antibody.

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Abstract Text:

Background: Monoclonal antibodies (mAb) against programmed cell death-1 (PD-1) have demonstrated antitumor activity across multiple malignancies. BGB-A317 is a humanized IgG4 mAb with high affinity and binding specificity for PD-1. Previous reports from an ongoing Phase 1A/1B study (NCT02407990) in patients with advanced solid tumors suggested that BGB-A317 was generally well tolerated and had antitumor activity in multiple tumor types. Here, we present the preliminary results from a subset of patients with UC enrolled in this study. **Methods:** Patients with UC received intravenous BGB-A317 at doses of 2, 5, 10 mg/kg Q2W or Q3W and 200 mg Q3W. Tumor cell (TC) and immune cell (IC) PD-L1 expression was retrospectively assessed with the VENTANA PD-L1 (SP263) assay. Safety and tolerability was assessed by monitoring adverse events (AEs) and antitumor effects were assessed by RECIST v1.1 criteria. **Results:** As of 8 June 2017, 15 patients with UC (median age, 72 yr [range: 39–79]) received BGB-A317 during phases 1A (n = 8) and 1B (n = 7). All patients were Caucasian and 13 patients were male; the median number of prior systemic anticancer therapies was 1 (range: 0–4). Median duration of treatment was 115 d (range: 27–476); 6 patients remain on treatment. The most common treatment-related AEs (TRAEs) were fatigue (n = 5) and rash (n = 3); grade ≥3 TRAEs included fatigue (n = 1), and hyperglycemia and type 1 diabetes mellitus (T1DM; n = 1). Serious TRAEs occurred in 2 patients (infusion-related reaction [n = 1]; hyperglycemia and T1DM [n = 1]). All patients were evaluable for response assessment. Confirmed complete and partial responses occurred in 1 and 3 patients, respectively, for a response rate of 27%; the disease control rate (CR+PR+SD) was 53%. Nine samples were available for PD-L1 evaluation. Responses were observed in 3 of 6 patients with PD-L1^{+} tumors (defined as ≥25% TC or IC expressing PD-L1 by IHC) while 1 in 3 patients with PD-L1^{-} tumors responded. **Conclusions:** BGB-A317 was generally well tolerated in patients with UC and objective responses were observed in both PD-L1^{+} and PD-L1^{-} diseases. BGB-A317 is currently being investigated in China as monotherapy for patients with PD-L1^{+} UC (CTR20170071).