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:

Anti-programmed death 1 (PD-1) therapy has improved clinical outcomes for patients (pts) with advanced solid tumors but unmet needs remain. T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domains (TIGIT) is a co-inhibitory, immune checkpoint receptor. Ociperlimab (OCI; BGB-A1217) is a novel, humanized, monoclonal antibody that binds to TIGIT with high affinity and specificity. OCI has demonstrated competent binding with C1q and all Fcγ receptors and induces antibody-dependent cellular cytotoxicity. Preclinical studies demonstrated dual targeting with OCI and tislelizumab (TIS), an anti-PD-1 antibody, produces synergistic immune cell activation and enhanced antitumor activity.

Methods:

AdvanTIG-105 is a Phase 1, open label, multicenter, dose-escalation study (NCT04047862) that assessed the safety and preliminary antitumor activity of OCI plus TIS in pts with advanced, metastatic, unresectable solid tumors, for which standard therapy was ineffective or unavailable. Eligible pts had an Eastern Cooperative Oncology Group performance score ≤1 and no prior therapy targeting TIGIT. Pts received OCI intravenously (IV) on Day 1 of Cycle 1 and TIS 200 mg IV on Day 8. Pts were monitored for dose-limiting toxicities (DLTs) until Day 28. If tolerated, OCI and TIS were administered sequentially on Day 29 and every 3 weeks (Q3W) thereafter. Pts received escalating doses of OCI (50-900 mg) plus TIS 200 mg. The study objective was determination of recommended Phase 2 dose (RP2D) of OCI plus TIS. Study endpoints included assessment of adverse events (AEs), pharmacokinetics and antitumor activity. Data cut-off was October 12 2020.

Results:

24 pts with various advanced solid tumors received OCI plus TIS. At baseline, pts had undergone a median of 2 prior treatment regimens; 9/24 (37.5%) pts had received prior immunotherapy. Median follow-up time was 17 weeks. No DLTs were observed. 20 pts had ≥1 treatment emergent AE (TEAE) and most TEAEs were Grade ≤2; fatigue (6 pts) and diarrhea (4 pts) were most commonly reported. No pts had Grade ≥4 TEAEs or TEAEs leading to death. There were 2 Grade 3 immune related AEs (colitis and low cortisol). One pt on OCI 450 mg achieved partial response and 9 pts had stable disease. The longest duration of stable disease was 36 weeks (1 pt on OCI 150 mg). After administration, serum concentration of OCI decreased in a biphasic manner. Exposure to OCI increased proportionally with dose, and TIGIT receptor occupancy was sustained at ≥50 mg doses.

Conclusions:

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