AdvanTIG-203: A randomized Phase 2 study comparing anti-TIGIT ociperlimab plus tislelizumab vs tislelizumab plus placebo as second-line treatment in patients with advanced or recurrent esophageal squamous cell carcinoma (ESCC) expressing programmed death-ligand 1 (PD-L1).

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Background:

The programmed death-1 (PD-1)/PD-L1 pathway plays an important role in tumor induced immunosuppression. PD-L1 overexpression is observed in approximately 30–60% of esophageal cancers and is associated with poor prognosis. Anti-PD-1 agents demonstrate moderate efficacy in PD-L1-positive esophageal cancer in terms of response rate and overall survival, however, long-term outcomes remain poor due to primary and secondary resistance driven by tumor immune escape. The T-cell immunoglobulin and immunoreceptor tyrosine-based inhibition motif domain (TIGIT) is upregulated on T-cells and natural killer cells in multiple solid tumors, which can inhibit anticancer immune responses. Ociperlimab (BGB-A1217) is a novel, humanized, monoclonal antibody that binds TIGIT with high specificity and affinity, blocking the interaction with its ligands on tumor cells. Preclinical and clinical studies suggest that dual targeting with anti-TIGIT and anti-PD-1 antibodies produces synergistic immune cell activation and enhanced antitumor activity.

Methods:

AdvanTIG-203 is a Phase 2, global, randomized, double-blind, placebo-controlled study (NCT04732494) of patients with unresectable, locally advanced, recurrent or metastatic ESCC, who progressed on or after 1st line systemic therapy and whose tumors express PD-L1 (visually estimated combined positive score ≥10%). After stratification by Eastern Cooperative Oncology Group performance status (0 or 1), number of metastatic sites (≤1 or ≥2) and region (Asian or non-Asian), 280 patients will be randomized (1:1) to either ociperlimab 900 mg intravenous (IV) plus tislelizumab 200 mg IV every 3 weeks (Q3W), or tislelizumab plus placebo Q3W, until disease progression (per RECIST v1.1), unacceptable toxicity, death or withdrawal of consent. Co-primary endpoints are investigator-assessed overall response rate (ORR) and overall survival (OS) in the intention-to-treat population. A sample size of 280 patients was estimated to provide approximately 94.8% power to detect a 20% difference in ORR at a one-sided significance level of 0.025. With 198 deaths, the study was estimated to provide approximately 86% power to detect a hazard ratio of 0.65 for OS. Secondary endpoints are ORR by independent review, progression-free survival, duration of response, disease control rate, and clinical benefit rate per investigator and independent assessment, cancer-specific health-related quality of life (HRQoL), and safety. Exploratory endpoints include but are not limited to expression of TIGIT, CD226, CD155, CD112, and PD-L1, pharmacokinetics, immunogenicity, and generic HRQoL measures.