AdvanTIG-302: Anti-TIGIT monoclonal antibody (mAb) ociperlimab (OCI) plus tislelizumab (TIS) vs pembrolizumab (PEM) in programmed death ligand 1 (PD-L1) selected, previously untreated, locally advanced, unresectable or metastatic non-small cell lung cancer (NSCLC).

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Background:

Monotherapy with programmed death 1 (PD-1)/PD-L1 antibodies has improved clinical outcomes for patients (pts) with non-oncogenic driven NSCLC but clinical responses are limited by primary and secondary resistance, and improvements in durability of response are required. T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domain (TIGIT) is a co-inhibitory, immune checkpoint receptor upregulated on T-cells and natural killer cells in multiple solid tumors, which can inhibit anticancer immune responses. OCI (BGB-A1217) is a novel, humanized mAb that binds to TIGIT with high affinity and specificity, which has demonstrated competent binding with C1q and all Fcγ receptors while inducing antibody-dependent cellular cytotoxicity. 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-302 is a Phase 3, multicenter, international, randomized, double-blind study (NCT04746924) investigating OCI in combination with TIS compared with PEM in adult pts (≥ 18 years of age) with PD-L1 selected, previously untreated, locally advanced, unresectable or metastatic NSCLC without oncogenic *EGFR* or *ALK* mutation. Approximately 605 pts will be randomized 5:5:1 to receive: OCI 900 mg intravenously (IV) plus TIS 200 mg IV every three weeks (Q3W; Arm A), PEM 200 mg IV plus placebo IV Q3W (Arm B) or TIS 200 mg IV plus placebo IV Q3W (Arm C). Pts will be treated until disease progression, loss of clinical benefit, intolerable toxicity or withdrawal of consent. Stratification factors include histology (squamous vs non-squamous) and region (Asian vs non-Asian). Cross-over is not permitted. Key eligibility criteria include histologically confirmed disease, PD-L1 expression ≥ 50%, no known *EGFR* or *ALK* mutations and no prior checkpoint inhibitor therapy. Dual primary endpoints are investigator-assessed progression-free survival (PFS; RECIST v1.1) and overall survival (Arms A and B) in the Intention-to-Treat population. Secondary endpoints include PFS (assessed by Blinded Independent Review Committee), investigator-assessed overall response rate and duration of response, safety and tolerability, and patient-reported health-related quality of life (EORTC-QLQ-C30, QLQ-LC13 and EQ-5D-5L; Arms A and B). Exploratory endpoints include disease control rate, clinical benefit rate and time to response. This study will also evaluate the association between biomarkers and response or resistance. Study enrollment has begun and recruitment is ongoing.