A Phase 3, Randomized, Open-Label Study to Compare the Efficacy of Tislelizumab (BGB-A317) Versus Chemotherapy as Second-Line Therapy for Advanced Unresectable/Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

Background: Approximately 40% of patients (pts) with esophageal cancer are diagnosed with advanced unresectable or metastatic disease; the 5-year survival rate for advanced disease is <5%. Inhibition of programmed cell death protein-1 (PD-1) has demonstrated promising antitumor activity and manageable safety in pts with advanced unresectable or metastatic ESCC. Tislelizumab (also known as BGB-A317), a humanized IgG4 monoclonal antibody, has high affinity and specificity for PD-1. Tislelizumab was specifically engineered to minimize $F_c\gamma R$ binding on macrophages, thus abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance. A first-in-human study (NCT02407990) demonstrated that single-agent tislelizumab was generally well tolerated and had preliminary antitumor effects in pts with solid tumors, including ESCC. A recommended phase 2 dose of 200 mg administered IV every 3 weeks (Q3W) has been established for tislelizumab.

Methods: This phase 3, randomized study (NCT03430843) was designed to evaluate the efficacy, safety, and tolerability of tislelizumab compared with chemotherapy for second-line treatment of advanced unresectable/metastatic ESCC. Adult pts, aged ≥18 years, with histologically or cytologically confirmed ESCC that has progressed with first-line therapy, have ≥1 measurable/evaluable lesion, and have an Eastern Cooperative Oncology score ≤1 will be enrolled. Approximately 450 pts will be randomized (1:1) to receive either tislelizumab 200 mg IV Q3W or investigator-chosen chemotherapy (paclitaxel 135–175 mg/m^2 IV Q3W or 100 mg/m^2 IV weekly for 6 weeks with 1 week of rest [Japan only], docetaxel 75 mg/m^2 or 70 mg/m^2 IV Q3W, or irinotecan 125 mg/m^2 IV Q3W). Overall survival is the primary endpoint; secondary endpoints include objective response rate, progression free survival, duration of response, and health-related quality-of-life outcomes. Safety/tolerability will be assessed by monitoring adverse events (AEs), including immune-related AEs, as well as physical examinations, vital signs, and electrocardiograms.