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

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Background: Approximately 40% of patients with esophageal cancer are diagnosed with advanced unresectable or metastatic disease; the 5-year survival rate for advanced disease is <5%. Inhibition of PD-1 has demonstrated antitumor activity and was generally well tolerated in patients with advanced unresectable or metastatic ESCC. Tislelizumab is a humanized IgG4 monoclonal antibody to PD-1 specifically engineered to minimize FcγR binding on macrophages, possibly minimizing negative interactions with other immune cells. In a phase 1 study (NCT02407990), tislelizumab was generally well tolerated and showed antitumor activity; 200 mg IV every three weeks (Q3W) was established as the recommended dose.

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 patients, 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 Group score ≤1 will be enrolled. Approximately 450 patients will be randomized (1:1) to receive either tislelizumab 200 mg IV Q3W or investigator-chosen chemotherapy (paclitaxel 135–175 mg/m^2 IV on Day 1 Q3W [100 mg/m^2 IV weekly for 6 weeks with 1 week of rest in Japan only], docetaxel 75 mg/m^2 on Day 1 Q3W [70 mg/m^2 IV on Day 1 Q3W in Japan only], or irinotecan 125 mg/m^2 IV on Days 1 and 8 Q3W). Overall survival is the primary endpoint; secondary endpoints include objective response rate, progression free survival, duration of response, health-related quality-of-life outcomes, and safety. Safety/tolerability will be assessed by monitoring adverse events (AEs), including immune-related AEs, as well as physical examinations, vital signs, and electrocardiograms. Disease control rate and assessments of pharmacokinetic profile, immunogenicity, and predictive biomarkers are exploratory endpoints.