Phase 3 Trial in Progress: Tislelizumab vs Placebo in Combination With Concurrent Chemoradiotherapy (cCRT) in Patients With Localized Esophageal Squamous Cell Carcinoma (ESCC)

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Objective In China, esophageal cancer ranks as the eighth most common cancer and sixth most common cause of cancer-related death; ESCC is the predominant histological subtype. At initial diagnosis, ≥50% of patients (pts) with ESCC are unfit for surgery. A surgical alternative is cCRT, but many pts experience local failure or distant metastasis after cCRT. As such, innovative therapies are needed. Tislelizumab, a monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. In previous studies, tislelizumab, alone and in combination with chemotherapy, was generally well tolerated and had antitumor activity in pts with ESCC. Recommended dosing of tislelizumab was established as 200 mg IV Q3W.

Methods This phase 3, randomized, double-blind, placebo-controlled study (NCT03957590) compares the efficacy of tislelizumab vs placebo in combination with cCRT. Eligible pts have histologically confirmed localized ESCC for which cCRT is suitable and surgery is unsuitable/declined; prior chemotherapy (<3 cycles) without radiotherapy is allowed. Chinese pts (n≈316) will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo (IV Q3W) in combination with cisplatin (25 mg/m^2 IV, D1-3 of each 3-wk cycle) plus paclitaxel (135 mg/m^2 IV Q3W) and radiotherapy (total dose, 50.4 Gy). An Independent Data Monitoring Committee will assess the safety/tolerability in the first 20 enrolled pts; monitoring across the study will occur at regular intervals thereafter. Progression-free survival (PFS), assessed by a Blinded Independent Review Committee per RECIST v1.1, is the primary endpoint. Secondary efficacy endpoints include overall response rate, duration of response, and overall survival. Incidence and severity of adverse events (CTCAE V5.0) and health-related QoL are additional secondary endpoints. Exploratory endpoints include PFS rate at Yrs 1 and 2, pharmacokinetic profile, and predictive biomarker analyses. This trial is currently enrolling.