A Phase 3 Trial in Progress Comparing Tislelizumab Plus Concurrent Chemoradiotherapy (cCRT) With Placebo Plus cCRT in Patients With Localized Esophageal Squamous Cell Carcinoma (ESCC)

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Background In China, esophageal cancer (EC) ranks as the eighth most common cancer and the sixth most common cause of cancer related death. The predominant histological subtype of EC is ESCC. At first diagnosis, more than half of patients (pts) with ESCC are unfit for surgery. An alternative to surgery is cCRT; however, many pts experience local failure or distant metastasis after cCRT. As such, innovative therapies are needed. Tislelizumab, an investigational humanized monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. In previous studies, tislelizumab, as a monotherapy and in combination with chemotherapy, was generally well tolerated and had antitumor activity in pts with ESCC.

Methods This phase 3, randomized, double-blind, placebo-controlled study (NCT03957590) is designed to compare the efficacy of tislelizumab versus placebo in combination with cCRT. Patients with histologically confirmed localized ESCC for whom cCRT is suitable and surgery is unsuitable/declined are being enrolled. Approximately 316 Chinese pts 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 on Days 1-3 of each 3-week cycle) plus paclitaxel (135 mg/m^2 IV Q3W) and radiotherapy at a total dose of 50.4 Gy. An Independent Data Monitoring Committee will be established to assess the safety/tolerability of tislelizumab plus cCRT 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 HRQoL are additional secondary endpoints. Exploratory endpoints include PFS rate at Years 1 and 2, pharmacokinetic profile, and predictive biomarker analyses.