A Randomized, Placebo-Controlled, Phase 3 Trial-in-Progress to Evaluate the Efficacy and Safety of Tislelizumab Plus Chemotherapy as First-line Treatment for Unresectable, Locally Advanced Recurrent/Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

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Background: ESCC remains the predominant histological subtype of, and accounts for most deaths from, esophageal cancer. PD-1 inhibition has demonstrated antitumor activity and was generally well tolerated in patients (pts) with advanced unresectable or metastatic ESCC. Tislelizumab, an investigational anti-PD-1 antibody, 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. Results from early phase clinical studies suggest single-agent tislelizumab was generally well tolerated and had antitumor activity in pts with solid tumors, including ESCC.

Methods: This phase 3, randomized, placebo-controlled, double-blind study (NCT03783442) is designed to evaluate the efficacy and safety of tislelizumab plus chemotherapy as first-line treatment of unresectable, locally advanced recurrent or metastatic ESCC. Adult pts with histologically confirmed ESCC that had metastatic disease either at first diagnosis or with a ≥6 month treatment-free interval will be eligible. Additional eligibility criteria include measurable/evaluable disease, ECOG performance score ≤1, and no prior anti-PD-(L)-1, PD-L2, or other first-line therapy or palliative radiation treatment ≤4 weeks before treatment. Approximately 480 pts will be randomized 1:1 to receive investigator-chosen chemotherapy (ICC) plus tislelizumab 200 mg IV Q3W or ICC plus placebo. Chemotherapy options include: platinum (cisplatin 60–80 mg/m^2 or oxaliplatin 130 mg/m^2 IV Q3W) plus 5-FU 750–800 mg/m^2 IV daily for 5 days Q3W; or platinum plus capecitabine 1000 mg/m^2 orally BID for 14 days Q3W; or platinum + paclitaxel 175 mg/m^2 IV Q3W. Progression-free survival and overall survival are coprimary endpoints; secondary endpoints include objective response rate, duration of response, and health-related quality-of-life. Safety will be assessed by monitoring adverse events, physical examinations, vital signs, and electrocardiograms. This study is actively enrolling.