A Phase 3 Trial-in-Progress Comparing Tislelizumab Plus Chemotherapy With Placebo Plus Chemotherapy as First-line Therapy in Patients With Locally Advanced Unresectable or Metastatic Gastric or Gastroesophageal Junction (G/GEJ) Adenocarcinoma

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Background: In patients (pts) with locally advanced or metastatic G/GEJ cancer, fluoropyrimidine- and platinum (plt)-based combination chemotherapy is first-line standard of care. Despite improvement in chemotherapy regimens, outcomes are poor and survival remains low. Tislelizumab, an investigational anti-PD-1 antibody, was engineered to minimize binding of FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous reports suggested tislelizumab, as a single agent and in combination with chemotherapy, was generally well tolerated and had antitumor activity in pts with advanced solid tumors, including G/GEJ cancer.

Methods: This global, double-blind, randomized, phase 3 study (NCT03777657) is designed to compare plt/fluoropyrimidine + tislelizumab versus plt/fluoropyrimidine + placebo as first-line therapy for pts with locally advanced or metastatic G/GEJ cancer. Approximately 720 pts from 160 centers will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo (IV Q3W) in combination with chemotherapy. Oxaliplatin (130 mg/m² IV Q3W) plus capecitabine (1000 mg/m^2 orally twice daily for 2 weeks) or cisplatin (80 mg/m² IV Q3W) plus 5-fluorouracil (800 mg/m^2/day IV on Days 1–5 Q3W) will be used as backbone chemotherapy on an individual basis. Chemotherapy will be administered for up to 6 cycles; capecitabine maintenance therapy is optional for pts who received capecitabine and oxaliplatin. PD-L1 expression will be assessed using the VENTANA PD-L1 (SP263) assay. Progression-free survival and overall survival are primary endpoints in the intent-to-treat and PD-L1-positive analysis sets of the study. Secondary endpoints include overall response rate, duration of response, quality-of-life outcomes, and the safety/tolerability profile of combination therapy. Exploratory endpoints include disease control rate, time to response, and an analysis of potential predictive biomarkers including, but not limited to, PD-L1 expression.