Phase 3 Study Comparing Tislelizumab in Combination With Cisplatin/Carboplatin + Gemcitabine With Placebo in Combination With Cisplatin/Carboplatin + Gemcitabine as Treatment for Chinese Patients With Advanced Urothelial Carcinoma: A Trial in Progress

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Background: Cisplatin-based chemotherapy is standard first-line treatment for patients with advanced urothelial carcinoma (UC). However, many patients are unable to receive cisplatin due to medical frailty or comorbidities; for these patients, a carboplatin-based regimen is an option. 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. Previous reports showed tislelizumab, as a single agent or in combination with chemotherapy, was generally well tolerated and had antitumor activity in patients with advanced solid tumors, including UC.

Methods: This phase 3, randomized, double-blind, placebo-controlled study (NCT03967977) is designed to compare the efficacy and safety/tolerability of tislelizumab vs placebo in combination with cisplatin/carboplatin + gemcitabine. Adult patients (18-75 yrs) with histologically confirmed, inoperable, locally advanced/metastatic UC, who are eligible for, but have not received, prior systemic therapy are being enrolled. Approximately 420 patients from 25 to 36 centers across China will be randomized 1:1 to receive tislelizumab (200 mg Q3W) or placebo (Q3W) in combination with gemcitabine (1000 mg/m^2 administered on Day 1 and 8 of each 3-wk cycle) and cisplatin (70 mg/m^2) or carboplatin (AUC 4.5) administered on Day 1 or 2 of each 3-wk cycle. Overall survival (OS) is the primary endpoint. Investigator-assessed overall response rate (RECIST V1.1), duration of response, progression-free survival, and OS rates at Year 1 and 2 are secondary efficacy endpoints. Safety/tolerability, assessed by monitoring incidence and severity of adverse events, and health-related quality-of-life measures are also secondary endpoints.