Tislelizumab plus cisplatin/carboplatin and gemcitabine versus placebo plus cisplatin/carboplatin and gemcitabine in Chinese patients with advanced urothelial carcinoma: A phase III trial in progress.

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Background: Platinum-based chemotherapy is standard first-line treatment for patients with advanced urothelial carcinoma (UC). Checkpoint inhibitors (ie, anti-PD-1 antibodies) are first-line treatment options for cisplatin-ineligible patients. Combining anti-PD-1 treatment with chemotherapy may have synergistic effects and has demonstrated antitumor activity in a variety of tumor types. Tislelizumab, an investigational 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 combined with chemotherapy, was generally well tolerated and had antitumor activity in patients with advanced UC.**Methods:**This phase 3, randomized, double-blind, placebo-controlled study (NCT03967977) will compare the efficacy and safety/tolerability of tislelizumab vs placebo, both in combination with cisplatin/carboplatin and gemcitabine. Adult Chinese patients (n≈420) with histologically confirmed, inoperable, locally advanced/metastatic UC who are eligible for (but have not received) systemic anticancer therapy for advanced UC, therapies targeting PD-1/L1, or other antibody/drug targeting T-cell costimulation or checkpoint pathways, will be randomized 1:1 to receive tislelizumab (200 mg Q3W) or placebo (Q3W) plus gemcitabine (1000 mg/m^2 administered on Day 1 and 8 of each 3-week cycle) and cisplatin (70 mg/m^2) or carboplatin (AUC 4.5) administered on Day 1 or 2 of each 3-week cycle. Patients must provide a fresh biopsy or archival tissue for central assessment of PD-L1 expression. 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 endpoints. Safety/tolerability, assessed by monitoring incidence and severity of adverse events, and health-related quality-of-life measures will also be evaluated. Clinical trial information: NCT03967977