Tislelizumab + Chemotherapy Versus Placebo + Chemotherapy in Chinese Patients With Recurrent or Metastatic Nasopharyngeal Cancer: A Phase 3 Trial-in-Progress

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Background Nasopharyngeal cancer (NPC) is characterized by a unique geographic distribution, with southern China and Southeast Asia having some of the highest incidence rates worldwide. In most NPC tumors, PD-L1 is overexpressed, potentially contributing to immune evasion. Tislelizumab, a monoclonal antibody with high affinity and specificity for PD-1, 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. Tislelizumab, alone and in combination with chemotherapy, has shown a manageable tolerability profile and has demonstrated antitumor activity in patients (pts) with advanced solid tumors regardless of PD-L1 status. Tislelizumab was recently approved in China for the treatment of relapsed/refractory classical Hodgkin lymphoma and for pts with PD-L1-high urothelial carcinoma who have progressed during/after platinum chemotherapy.

Methods This double-blind, randomized, phase 3 study (NCT03924986) is designed to compare the efficacy of tislelizumab plus gemcitabine and cisplatin vs placebo plus gemcitabine and cisplatin as first-line treatment for recurrent or metastatic NPC in ~256 pts. Patients will be randomized 1:1 to receive either tislelizumab (200 mg IV Q3W) or placebo (IV Q3W) plus chemotherapy. Chemotherapy will consist of gemcitabine (1 g/m² IV D1 and D8 of 21-day cycle) and cisplatin (80 mg/m² IV Q3W) for 4 to 6 cycles at the investigator's discretion, unless unacceptable toxicity or disease progression occurs. Upon central confirmation of disease progression by the Independent Review Committee (IRC), pts on placebo may cross over to receive tislelizumab. The primary endpoint is progression-free survival (PFS), assessed by the IRC, in the intent-to-treat population. Secondary efficacy endpoints include overall survival, objective response rate, and duration of response assessed by the IRC as well as investigator-assessed PFS after next line of treatment. Patient-reported outcomes and incidence and severity of AEs are also secondary endpoints; biomarker evaluation is an exploratory endpoint.