A Phase 3 Trial in Progress Comparing Tislelizumab Plus Chemotherapy With Placebo Plus Chemotherapy in Chinese Patients With Recurrent or Metastatic Nasopharyngeal Cancer

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Background Nasopharyngeal cancer (NPC) is characterized by a unique geographic distribution, with southern China having one of the highest incidence rates worldwide. Patients (pts) with stage IV disease have a poor prognosis with a 5-year survival rate <10%. In the majority of NPC tumors, PD-L1 is overexpressed, potentially contributing to immune evasion. Tislelizumab is an investigational monoclonal antibody with high affinity and specificity for PD-1 that 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. A phase 1/2 study (CTR20160872) showed tislelizumab was generally well tolerated and demonstrated preliminary antitumor activity in Chinese pts with advanced solid tumors, including NPC. The recommended dose was established as 200 mg IV Q3W.

Methods This double-blind, randomized, phase 3 study (NCT03924986) is designed to compare the efficacy of tislelizumab in combination with gemcitabine and cisplatin vs placebo with gemcitabine and cisplatin as first-line treatment for recurrent or metastatic NPC. Chinese pts (n≈256) from 30 sites will be enrolled. 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 adverse events are also secondary endpoints; biomarker evaluation is an exploratory endpoint.