Phase 2 Study of Tislelizumab, an Anti-Programmed Cell Death Receptor-1 Antibody, in Patients with Unresectable Hepatocellular Carcinoma: Trial-in-Progress

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Objective Immune checkpoint inhibitors have shown antitumor activity in patients with hepatocellular carcinoma. Tislelizumab is a humanized IgG4 monoclonal antibody to PD-1 specifically engineered to minimize FcϒR binding on macrophages, possibly minimizing negative interactions with other immune cells. In a phase 1 study (NCT02407990), tislelizumab was generally well tolerated and showed antitumor activity; 200 mg IV every three weeks was established as the recommended dose.

Methods This phase 2 study (NCT03419897) is designed to evaluate the efficacy, safety/tolerability, and pharmacokinetics of tislelizumab in patients with previously treated, unresectable hepatocellular carcinoma. Patients who are ≥18 years of age with histologically confirmed, and unresectable hepatocellular carcinoma that is classified as Barcelona Clinic Liver Cancer (BCLC) Stage B or C, is not amenable to or has relapsed after locoregional therapy, and is not amenable to a curative treatment approach, are eligible. Patients must also have a Child-Pugh score A, Eastern Cooperative Oncology Group score ≤1, and must have experienced at least one line of prior systemic therapy. Patients will be excluded if they have received prior sorafenib, regorafenib, or any systemic therapy within 14 days of the first tislelizumab infusion. A total of 228 patients worldwide are planned to be treated with tislelizumab 200 mg IV every three weeks. Objective response rate, evaluated by Independent Review Committee per RECIST v1.1, is the primary endpoint; radiological assessment of tumor-response status will be performed every 6 weeks in the first 18 weeks and then every 9 weeks thereafter. Secondary endpoints include duration of response, progression-free survival, disease control rate, clinical benefit rate, overall survival, and health-related quality of life outcomes. Assessment of the pharmacokinetics and safety/tolerability profiles of tislelizumab are exploratory endpoints. Safety/tolerability assessments will include monitoring of adverse events, including immune-related adverse events.