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

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Background/Aim: Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1. Tislelizumab was specifically engineered to minimize $F_c\gamma R$ binding on macrophages that, based on preclinical evidence, is believed to minimize potentially negative interactions with other immune cells. A first-in-human, phase 1A/1B study (NCT02407990) demonstrated that single-agent tislelizumab was generally well tolerated and showed preliminary evidence of antitumor activity in patients with advanced solid tumors, including HCC. A recommended dose of tislelizumab administered at 200mg intravenously (IV) every 3 weeks (Q3W) has been established.

Trial Design: This phase 2 study (NCT03419897) is designed to evaluate the efficacy, safety/tolerability, and pharmacokinetics of tislelizumab in patients with previously treated, unresectable HCC. Patients who are ≥18 years of age with histologically confirmed, locally advanced or unresectable HCC, including patients who are not amenable to, or who have relapsed after, a curative treatment approach or locoregional therapy, are eligible. Patients must also have a Child-Pugh score A, ECOG performance status ≤1, and must have experienced ≤2 lines of prior systemic therapy. Patients will be excluded if they have received prior PD-1 or PD-L1 treatment or have received 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 200mg IV Q3W. 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, quality-of-life outcomes, and assessment of the pharmacokinetic and safety/tolerability profiles of tislelizumab. Safety/tolerability assessments will include monitoring of adverse events (AEs), including immune-related AEs.