

Global Phase 3 Study of Tislelizumab Versus Sorafenib as First-Line Treatment in Patients with Advanced Hepatocellular Carcinoma (HCC): A Trial-in-Progress

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Background: Unresectable HCC accounts for 70% of diagnosed HCC. Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity and specificity for programmed cell death receptor-1 (PD-1). Tislelizumab was specifically engineered to minimize Fc γ R binding on macrophages that, based on preclinical evidence, is believed to minimize potentially negative interactions with other immune cells. A 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 phase 3 dose of 200 mg administered intravenously (IV) every 3 weeks (Q3W) has been established for tislelizumab.

Methods: This global, phase 3, randomized, multicenter study (NCT03412773) was designed to evaluate the efficacy and safety of tislelizumab compared with sorafenib as a potential first-line treatment of unresectable HCC. Adult patients, aged ≥ 18 years, with unresectable, histologically confirmed HCC, an ECOG score ≤ 1 , Child-Pugh A classification, BCLC Stage C disease or BCLC Stage B disease that has relapsed after loco-regional therapy, and who have not received prior systemic therapy, are being enrolled. Approximately 640 patients from 100 international centers are planned to be randomized (1:1) to receive tislelizumab 200 mg IV Q3W or sorafenib 400 mg orally BID. The primary outcome of this study is overall survival (OS) of patients treated with tislelizumab compared with OS of patients treated with sorafenib; secondary outcomes include objective response rate, progression-free survival, duration of response, time to progression, and quality-of-life outcomes. Safety/tolerability assessments include monitoring adverse events (AEs), including immune-related AEs, as well as physical examinations, vital signs, and electrocardiograms. Exploratory endpoints include assessment of potential biomarkers, characterization of the tislelizumab pharmacokinetic profile in patients with HCC, and assessment of host immunogenicity to tislelizumab. As of 11 April 2018, 11 patients have been enrolled.