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

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Background Unresectable hepatocellular carcinoma accounts for 70% of diagnosed 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 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 hepatocellular carcinoma. Adult patients, aged ≥18 years, with unresectable, histologically confirmed hepatocellular carcinoma, an Eastern Cooperative Oncology Group score ≤1, Child-Pugh A classification, Barcelona Clinic Liver Cancer Stage C disease or Stage B disease that has relapsed after loco-regional therapy, and who have not received prior systemic therapy, are being enrolled. Approximately 640 patients are planned to be randomized (1:1) to receive tislelizumab 200 mg IV every three weeks or sorafenib 400 mg orally twice daily. The primary outcome of this study is overall survival of patients treated with tislelizumab compared with overall survival 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, including immune-related adverse events, 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 hepatocellular carcinoma, and assessment of host immunogenicity to tislelizumab. Radiological assessment of tumor response status will be performed every 9 weeks in Year 1 and every 12 weeks from Year 2 onwards.