Efficacy and Safety of Tislelizumab, an Anti-PD-1 Antibody, Versus Sorafenib as First-Line Treatment in Patients With Advanced Hepatocellular Carcinoma in a Phase 3, Randomized, Open-Label, Multicenter Study

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Background: Unresectable hepatocellular carcinoma (HCC) accounts for 70% of diagnosed HCC. Tislelizumab (previously known as BGB-A317) is a humanized, IgG4 monoclonal antibody with high affinity and binding specificity for programmed cell death receptor-1 (PD-1). Furthermore, tislelizumab was specifically engineered to minimize $F_c\gamma R$ binding on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance. A first-in-human, phase 1A/1B study (NCT02407990) demonstrated that single-agent tislelizumab was generally well tolerated and showed 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 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 will be randomized (1:1) to receive tislelizumab 200 mg IV Q3W or sorafenib 400 mg orally BID. The primary outcome of this non-inferiority 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 predictive biomarkers, characterization of the tislelizumab pharmacokinetic profile in patients with HCC, and to determine host immunogenicity against tislelizumab.