

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

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 FcγR 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, non-inferiority 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.