Efficacy, Safety, and Pharmacokinetics of the Anti-Programmed Cell Death Receptor-1 (PD-1) Monoclonal Antibody, Tislelizumab (BGB-A317) in a Phase 2, Open-label, Multicenter Study to Investigate in Patients with Unresectable Hepatocellular Carcinoma

Ann-Lii Cheng[1], Ghassan K. Abou-Alfa[2], Zhenggang Ren[3], Eric Assenat[4], Antonio Cubillo[5], Stefan Pluntke[6], Lorenza Rimassa[7], Paul J. Ross[8], Lucjan Wyrwicz[9], Jeannie Hou[10], Cindy Li[11], John Wu[12], Michel Ducreux[13]

[1]National Taiwan University Hospital, Taipei, Taiwan; [2]Memorial Sloan Kettering Cancer Center, New York, NY; [3]Zhongshan Hospital, Fudan University, Shanghai, China; [4]CHRU Saint Eloi, Montpellier, France; [5]HM Universitario Sanchinarro, Centro Integral Oncológico Clara Campal (CIOCC), Madrid, Spain; [6]Kliniken Essen-Mitte, Essen, Germany; [7]Humanitas Clinical and Research Center, Rozzano, Italy; [8]Guy's and StThomas' NHS Foundation Trust, London, United Kingdom; [9]Centrum Onkologii-Instytut im. M. Sklodowskiej Curie, Warszawa, Poland; [10]BeiGene USA, Inc., Emeryville, CA; [11]BeiGene (Beijing) Co., Ltd., Beijing, CN; [12]BeiGene USA, Inc., Fort Lee, NJ; [13]Gustave Roussy, Villejuif, France

Background: Tislelizumab (BGB-A317) is a humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1 that 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 had preliminary antitumor effects in patients with solid tumors, including HCC. A recommended dose of tislelizumab administered at 200 mg intravenously (IV) every 3 weeks (Q3W) has been established.

Methods: This phase 2, multicenter study (NCT03419897) was designed to evaluate the efficacy, safety, tolerability, and pharmacokinetics of tislelizumab in patients with previously treated, unresectable HCC. This study will enroll patients who are ≥18 years of age with histologically confirmed locally advanced or unresectable HCC. This includes patients who are not amenable to, or who have relapsed after, locoregional therapy and are not amenable to a curative treatment approach. To be enrolled, patients must also have a Child-Pugh classification Grade A, ECOG performance status ≤1 and must have experienced sorafenib, regorafenib, or chemotherapy in 1−2 lines of prior systemic therapy.

Radiological assessment of tumor-response status will be performed every 6 weeks in the first 18 weeks then every 9 weeks thereafter. Patients with prior PD-1 or PD-L1 treatment or who received sorafenib or regorafenib within 14 days of the first study drug administration will be excluded. A total of 228 patients worldwide will be treated with tislelizumab 200 mg IV Q3W. The primary endpoint of this study is objective response rate assessed by Independent Review Committee per RECISIT v1.1; 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 tislelizumab pharmacokinetic and safety/tolerability profiles. Exploratory endpoints include assessment of potential biomarkers, assessment of host immunogenicity to tislelizumab. Safety/tolerability assessments will include monitoring of adverse events (AEs), including immune-related AEs, as well as physical examinations, vital signs, and electrocardiograms.