A Phase 3, Open-Label, Multicenter, Randomized Study to Investigate the Efficacy and Safety of Tislelizumab, an Anti-PD-1 Antibody, Versus Docetaxel in Patients With Non-Small Cell Lung Cancer Who Have Progressed on a Prior Platinum-Containing Regimen

Background: Non-small cell lung cancer (NSCLC) accounts for 80–85% of all lung cancers and has a poor prognosis in later stages. Although lung cancers are not typically immunogenic, recent studies of immune checkpoint inhibitors have shown efficacy in patients with advanced NSCLC. 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 solid tumors, including NSCLC. A recommended phase 3 dose of 200 mg administered intravenously (IV) every 3 weeks (Q3W) has been identified for tislelizumab.

Methods: This phase 3, randomized, multicenter study (NCT03358875) was designed to evaluate the efficacy, safety, and tolerability of tislelizumab compared with docetaxel in the second- or third-line treatment of NSCLC. Adult patients aged ≥18 years with locally advanced or metastatic NSCLC (Stage IIIB or IV, squamous or non-squamous), who have progressed on ≥1 prior platinum-containing therapy, have adequate hematologic and end-organ function, and an ECOG score ≤1 are eligible to enroll. Patients with a known EGFR sensitizing/driver mutation or ALK rearrangement are excluded. Approximately 800 patients from ~100 global clinical sites will be randomized (2:1) to receive tislelizumab 200 mg IV Q3W or docetaxel 75 mg/m^2 IV Q3W. Randomization will be stratified by histology, line of therapy, and PD-1 ligand tumor cell expression (<25% vs ≥25% [PD-L1$^+$]). Co-primary endpoints are overall survival in the intent-to-treat population and in the PD-L1$^+$ population; secondary endpoints include objective response rate and health-related quality-of-life outcomes.