BGB-LC-201 (NCT05635708): A phase 2, open-label, multi-arm study of tislelizumab (TIS; anti-PD-1) in combination with investigational agents +/- chemotherapy as first-line treatment for patients with locally advanced, unresectable, or metastatic non–small cell lung cancer (NSCLC)

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Abstract

Background: Prognosis for locally advanced, unresectable, or metastatic NSCLC remains poor despite advances in the use of immune checkpoint inhibitors (ICI) with or without histology-appropriate chemotherapy (chemo), partly due to innate or adaptive resistance to ICI. Combination therapies aim to overcome resistance to anti-programmed cell death protein-1 or programmed death-ligand-1 (PD-1/PD-L1) therapy and thus improve anticancer activity. This phase 2 study will determine whether adding investigational agents BGB-A445 (OX40 agonistic monoclonal antibody [mAb]), LBL-007 (anti-lymphocyte activation gene-3 mAb), or BGB-15025 (hematopoietic progenitor kinase 1 [HPK1] inhibitor) improves the therapeutic benefit of TIS (anti-PD-1 mAb) +/- chemo in patients with locally advanced, unresectable, or metastatic NSCLC.

Methods: The umbrella design allows for the use of multiple investigational drugs, administered alone or in combination, in patients with untreated locally advanced, unresectable, or metastatic NSCLC without actionable driver mutations. Approximately 400 patients aged ≥18 years will be enrolled in 1 of 2 Substudies based on PD-L1 expression and randomized 2:1 to either the experimental or reference arm within each Substudy. Patients in Substudy 1 (PD-L1 ≥50%) will be randomized to receive either TIS (200 mg intravenously [IV] every 3 weeks [Q3W]) in combination with BGB-A445 (2400 mg IV Q3W), LBL-007 (600 mg IV Q3W), or BGB-15025 (experimental arms) or TIS monotherapy (reference arm). Those in Substudy 2 (PD-L1 <50%) will receive TIS + chemo in combination with BGB-A445 (2400 mg IV Q3W), LBL-007 (300 mg, 600 mg, or 1200 mg IV Q3W), or BGB-15025 (experimental arms) or TIS + chemo (reference arm). Patients will receive up to 36 cycles (each cycle lasting 3 weeks) or until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint is investigator-assessed confirmed overall response rate per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; secondary endpoints include investigator-assessed progression-free survival, duration of response, clinical benefit rate, disease control rate (per RECIST v1.1), pharmacokinetics, immunogenicity, and safety. Exploratory endpoints include overall survival, time to response, and relevant biomarker associations with response or resistance to study treatments. Enrollment is ongoing at 66 sites in China, Asia-Pacific, the United States, and the European Union.