BGB-LC-201 (NCT05635708) is a phase 2 umbrella study investigating the efficacy and safety of tislelizumab in combination with BGB-A445, BGB-15025, or LBL-007 with or without histology-appropriate chemotherapy as first-line treatment of patients with NSCLC without actionable driver mutations.

The study is currently enrolling patients at 61 sites across the Asia-Pacific (Australia, China, Malaysia, Singapore, South Korea, Thailand), Brazil, Canada, the European Union (France, Georgia, Italy, Moldova, Romania, Spain), and the United States.

**Background**

Unmet Need in NSCLC

- Lung cancer is the second most common cancer worldwide, with an estimated 2.2 million new cases and 1.8 million deaths in 2020.
- Non–small cell lung cancer (NSCLC) accounts for 80%–85% of all lung cancer cases, with approximately 35% of patients diagnosed with metastatic disease.
- Immune checkpoint inhibitor-based therapeutic strategies have significantly improved clinical outcomes for patients with advanced or metastatic NSCLC; however, prognosis remains poor, partly due to innate or adaptive resistance to immune checkpoint inhibitors.
- Single-agent programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors are the preferred first-line therapy for patients with advanced or metastatic NSCLC with PD-L1 expression of ≥50% (PD-L1–high) without targetable genetic alterations, irrespective of histology.
- Anti-PD-1/PD-L1 combination therapy, as monotherapy or in combination with chemotherapy, has shown enhanced antitumor activity in NSCLC.
- However, only a small proportion of patients develop long-term responses.
- Combination therapies targeting different biological pathways aim to overcome resistance to PD-1/PD-L1 therapy and thus improve antitumor activity.

**Introduction to Tislelizumab (TIS) and Investigational Agents (Figure 1)**

- TIS is a humanized IgG4 anti-PD-1 monoclonal antibody (mAb) engineered to minimize Fc receptor (FcγR) binding on macrophages to abrogate antibody-dependent cellular cytotoxicity (ADCC), a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy.
- TIS, as monotherapy or in combination with chemotherapy, is currently being evaluated in first-line treatment of patients with NSCLC without actionable driver mutations.
- Approximately 40% patients with previously untreated, locally advanced, or metastatic NSCLC with TIS in combination with BGB-A445, LBL-007, or BGB-15025 with or without histology-appropriate chemotherapy as first-line treatment of patients with NSCLC without actionable driver mutations.
- The randomized ratio is 2:1 between the experimental arms and the reference arm within each substudy.
- Additional study arms, with other investigational drugs, may be added in the future.

**Study Design and Treatment**

- **Figure 1: Targeting Tumor Cells With BGB-15025, BGB-A445, LBL-007, and TIS**

**Methods**

**Study Population**

- Key eligibility criteria are summarized in Figure 2. Other key criteria include:
  - Histologically confirmed locally advanced or metastatic NSCLC (non-squamous or squamous)
  - ≥1 measurable lesion, as per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)^5^
  - No prior therapy with anti-TGFβ antibody or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways.
  - Patients must agree to provide archival tumor tissue from screening or be willing to undergo fresh tumor biopsy to evaluate tumor PD-L1 expression, either by a local laboratory (using 22C3, SP263, or 28–E1; LIN [using patients only], or by a central laboratory (using SP263 Ventana assay).
  - Patients with unknown PD-L1 expression will not be eligible for this study.
  - No known actionable mutations (including, but not limited to, EGFR, ALK, BRAF, RET, and ROS1 mutations).

**Endpoints and Assessments**

- The primary endpoint is objective response rate, defined as the proportion of patients with a complete response or partial response, as assessed by the investigator using RECIST v1.1.
- Select secondary endpoints include progression-free survival, disease-control rate, safety, and pharmacokinetics (Figure 2).
- Tumor imaging will be performed within 28 days before randomization/enrollment.
- Objective tumor assessments will occur at the first 52 weeks and every 12 weeks thereafter.
- Safety will be assessed through monitoring of the incidence and severity of adverse events (graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0), laboratory results, and clinical symptoms and signs.
- The safety population will include all patients who receive ≥1 dose of study drug.
- An independent Safety Oversight Committee will periodically assess safety throughout the study.

**Enrollment Status**

- Enrollment is ongoing at 61 sites (Figure 3).