BGB-HNSCC-201 (NCT05909904): Phase 2, Open-Label, Multi-Arm, Global Study of Tislelizumab (TIS) + Investigational Agents as First-Line (1L) Treatment in Patients (Pts) with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (R/M HNSCC)

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Conclusions

- **BGB-HNSCC-201 is an ongoing phase 2 study investigating the efficacy and safety of tislelizumab in combination with BGB-A425 (anti-TIM-3 antibody) and/or LBL-007 (anti-LAG-3 antibody) as first-line treatment of PD-L1–positive patients with R/M HNSCC**
- **This study will provide insight into the clinical effect of targeting distinct and potentially synergistic immune checkpoints in R/M HNSCC**

Introduction

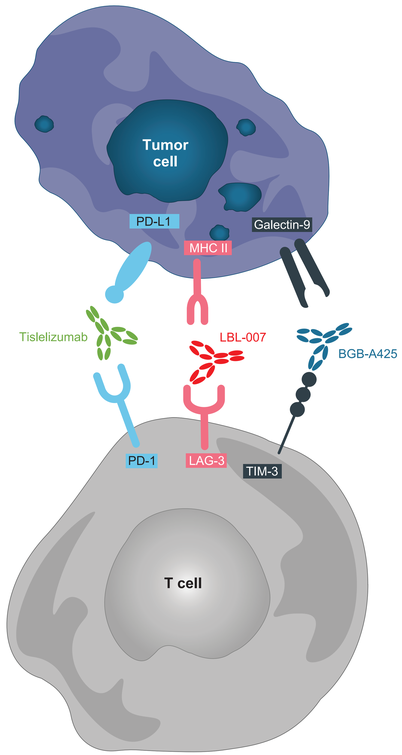
Unmet Need in HNSCC

- Head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer worldwide and its incidence is anticipated to rise by 30% by 2030[1]
- Roughly half of patients with HNSCC will develop locoregional recurrence and/or metastatic disease; historically, these patients have had a poor prognosis despite treatment, with a median survival of approximately 10 months[2]
- More recently, anti-programmed cell death-protein 1 (PD-1) therapy, either alone or in combination with chemotherapy, has extended survival and become the standard of care for first-line treatment of recurrent or metastatic (R/M) HNSCC that is not amenable to surgery or radiation[3-5]
  - In patients with a programmed death-ligand 1 (PD-L1) combined positive score (CPS) of ≥1, single-agent anti-PD-1 therapy is a treatment option, but not all patients experience durable response or prolonged survival with this approach[3]
  - The addition of chemotherapy to anti-PD-1 therapy improves survival regardless of PD-L1 status, but is associated with increased toxicity[3]
- Combining anti-PD-1 therapies with synergistic agents that target distinct biological pathways may help overcome resistance to anti-PD-1 therapy[6] and could improve anticancer activity without introducing chemotherapy-related toxicity

Introduction to Tislelizumab, Investigational Agents, and the BGB-HNSCC-201 Study

- Tislelizumab is a humanized IgG4 anti-PD-1 monoclonal antibody (mAb) engineered to minimize Fcγ receptor binding on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy[7]
  - Tislelizumab is currently approved in China and in Europe for multiple indications
- BGB-A425 is an investigational humanized IgG1 mAb directed against T-cell immunoglobulin and mucin-domain containing-3 (TIM-3)
- LBL-007 is an investigational, fully human IgG4 mAb directed against lymphocyte activation gene-3 (LAG-3)
- TIM-3 and LAG-3 are co-expressed with PD-1 on tumor-infiltrating T cells (**Figure 1**) and are upregulated in patients resistant or nonresponsive to anti-PD-1 therapy,[8-10] suggesting that co-blockade of these proteins could improve antitumor activity
- Here, we report the design of the phase 2 HNSCC-201 study, investigating the efficacy and safety of tislelizumab in combination with BGB-A425 and/or LBL-007 as first-line treatment of PD-L1–positive patients with R/M HNSCC

Figure 1. Targeting Tumor Cells with Anti-PD-1, Anti-TIM-3, and Anti-LAG-3 Antibodies



LAG-3, lymphocyte activation gene-3; MHC, major histocompatibility complex; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; TIM-3, T-cell immunoglobulin and mucin-domain containing-3.

Methods

Study Design and Treatment

- BGB-HNSCC-201(NCT05909904) is a phase 2, global, multicenter (77 sites across 14 countries), multi-arm, open-label study
- Approximately 160 patients with immunotherapy-naïve, PD-L1–positive (CPS ≥1) R/M HNSCC of the oropharynx, oral cavity, hypopharynx, or larynx who are not candidates for local/curative therapy will be enrolled in the study (**Figure 2**)
- Patients (approximately 40 per arm) will be randomly assigned (1:1:1:1) to tislelizumab monotherapy, tislelizumab in combination with BGB-A425, tislelizumab in combination with LBL-007, or tislelizumab in combination with BGB-A425 and LBL-007
  - Randomization will be stratified by PD-L1 CPS (1–19 vs ≥20)
- Tislelizumab, BGB-A425, and LBL-007 will be administered by separate intravenous infusions once every 3 weeks for up to 2 years, until disease progression, intolerable toxicity, withdrawal of informed consent, or other discontinuation event, whichever occurs first
- Study enrollment has begun and recruitment is ongoing; additional study arms may be added

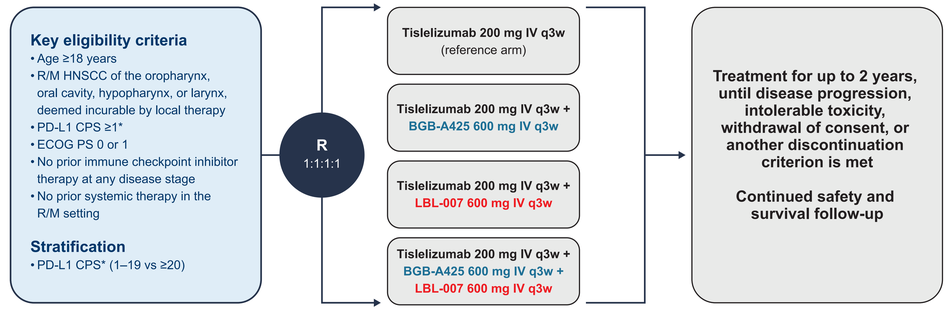
Study Population

- Eligibility criteria include the following:
  - Aged ≥18 years
  - Histologically or cytologically confirmed R/M HNSCC that is considered incurable by local therapies; eligible primary tumor locations are oropharynx, oral cavity, hypopharynx, and larynx
  - ≥1 measurable lesion, as per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)
  - No prior systemic therapy administered in the R/M setting
  - No prior therapy with an anti-PD-1, anti-PD-L1, PD-L2, TIM-3, LAG-3, or any other antibody or drug specifically targeting T-cell costimulation or immune checkpoint pathways
  - Patients must agree to provide archival tumor tissue from screening or be willing to undergo fresh tumor biopsy
  - PD-L1 CPS ≥1 in archival tumor tissue or fresh biopsy, as determined by a local or central laboratory using the 22C3 pharmDx assay
  - Eastern Cooperative Oncology Group performance status (ECOG PS) of ≤1
  - Life expectancy of ≥3 months

Endpoints and Assessments

- The primary endpoint is objective response rate (ORR), defined as the proportion of patients with a confirmed complete response or partial response, as assessed by investigators using RECIST v1.1
- Secondary and exploratory endpoints are listed in **Table 1**

Figure 2. Study Design



*Determined using the 22C3 pharmDx assay at either a local or central laboratory.
CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; HNSCC, head and neck squamous cell carcinoma; IV, intravenous; PD-L1, programmed death-ligand 1; q3w, every 3 weeks; R, randomization; R/M, recurrent or metastatic.

- Tumor imaging will be performed within 28 days before randomization/enrollment
- On-study tumor assessments will occur every 6 weeks for the first 52 weeks and then 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, vital signs, ECOG PS changes, and other examinations
  - The safety population will include all patients who receive ≥1 dose of study drug(s)
  - An independent Safety Oversight Committee will assess safety periodically throughout the study

Table 1. Study Endpoints

Primary endpoint	• Confirmed ORR (investigator-assessed per RECIST v1.1)
Secondary endpoints	• Investigator-assessed PFS, DoR, CBR, DCR • OS • Safety • Immunogenicity
Exploratory endpoints	• PK • Investigator-assessed TTR • Biomarkers

CBR, clinical benefit rate; DCR, disease control rate; DoR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic(s); RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

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Disclosures

KH: Nothing to disclose.

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