A phase 2 study of tislelizumab (TIS) + investigational agents as first-line (1L) treatment in recurrent and/or metastatic head and neck squamous cell carcinoma (R/M HNSCC)

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ABSTRACT

Background: Despite the use of anti-programmed cell death protein-1 (PD-1)/programmed cell death protein ligand-1 (PD-L1) monotherapy in HNSCC, not all patients (pts) experience a durable response or prolonged survival; thus, there is an unmet need for novel treatment combinations. TIS is an anti-PD-1 monoclonal antibody (mAb) that blocks the PD-1/PD-L1 immune checkpoint. Here, we present results from a phase 2, open-label, international study of TIS with or without the anti–TIM-3 mAb surzebiclimab (SUR) and/or the anti–LAG-3 mAb alcestobart (LBL-007 hereafter) as 1L treatment in pts with R/M HNSCC (NCT05909904).

Methods: Eligible pts were ≥18 years with histologically/cytologically confirmed R/M HNSCC and positive PD-L1 expression CPS ≥1. Pts were randomized to receive TIS monotherapy (Arm A), TIS plus SUR (Arm B), TIS plus LBL-007 (Arm C), or TIS plus SUR and LBL-007 (Arm D). The primary endpoint was investigator-assessed objective response rate (ORR) per RECIST v1.1; secondary endpoints included clinical benefit rate (CBR), disease control rate (DCR), and safety/tolerability.

Results: As of June 17, 2025, 160 pts were enrolled (40 in each arm). In the overall cohort, the median (range) age was 64.0 (22-84) years; most pts were male (84.4%), Asian (70.6%), with ECOG PS of 1 (52.5%), had the oral cavity as the primary disease location (42.5%), and had received prior platinum-based chemotherapy (60.0%). Median study follow-up time was 13.1 (range: 0.1-21.2) months.

Similar ORRs were observed across treatment arms, with confirmed ORRs (95% CI) of 27.5% (14.6-43.9) in Arms A, B, and D, and 25.0% (12.7-41.2) in Arm C; complete responses occurred in 3 pts in Arm C and 2 pts in Arm D. CBR (95% CI) was 32.5% (18.6-49.1) in Arm A, 37.5% (22.7-54.2) in Arms B and D, and 35.0% (20.6-51.7) in Arm C. DCR (95% CI) was 55.0% (38.5-70.7), 67.5% (50.9-81.4), 62.5 (45.8-77.3), and 65.0 (48.3-79.4) in Arms A, B, C, and D, respectively.

The treatment in each arm was well tolerated and toxicities were manageable. The most common TEAEs were anemia (23.3%), hypothyroidism (18.9%), and increased aspartate aminotransferase (15.1%) in the overall cohort. Treatment-related TEAEs occurred in 67.5%, 61.5%, 77.5%, and 67.5% of pts in Arms A, B, C, and D, respectively. Fatal TEAEs occurred in 5.7% of pts in the overall cohort, of which none were treatment related. Immune-mediated adverse events occurred in 35.2% of pts in the overall cohort; most were grade 1 or 2 and non-serious. Infusion-related reactions occurred in 6.9% of pts in the overall cohort, with only a single grade ≥3 event reported in Arm A.

Conclusion: Overall, efficacy was comparable between treatment arms. Safety profiles were consistent with previous reports. No additional benefit accrued from adding SUR, LBL-007, or SUR and LBL-007 to TIS as 1L treatment in pts with R/M HNSCC.