A Phase 2 Study of Tislelizumab + Investigational Agents as First-line Treatment in Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma

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Disclosure Information

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I have the following relevant financial relationships to disclose:

Speaker's Bureau for: AstraZeneca, Takeda, and MSD

- and -

My additional financial relationship disclosures are:

Advisory board participant: Bayer, AstraZeneca, Bristol Myers Squibb, Takeda, Daiichi Sankyo, and Yuhan

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Background

- HNSCC accounted for 890,000 new cancer cases and 450,000 deaths worldwide in 2018[1]
- Despite the use of anti-PD-1/PD-L1 monotherapy, such as pembrolizumab and nivolumab in HNSCC,[2,3] not all patients experience a durable response or prolonged survival; thus, there is an unmet need for novel treatment combinations
- Tislelizumab is an anti-PD-1 mAb that blocks the PD-1/PD-L1 immune checkpoint, resulting in T-cell activation
- Surzebiclimab is an anti-TIM-3 mAb that blocks the binding of phosphatidylserine to TIM-3 while concomitantly inducing TIM-3 internalization
- Alcestobart (LBL-007 hereafter) is an anti-LAG-3 mAb that effectively blocks the binding of LAG-3 to its ligands such as MHC II molecules and others, to prevent the inhibitory signaling by LAG-3 on T cells

Abbreviations: HNSCC, head and neck squamous cell carcinoma; LAG-3, lymphocyte activation gene-3; mAb, monoclonal antibody; MHC, major histocompatibility complex; PD-1, programmed cell death protein-1; PD-L1, programmed cell death protein ligand-1; TIM-3, T-cell immunoglobulin and mucin-domain containing-3.

1. Johnson DE, et al. *Nat Rev Dis Primers*. 2020;6:92. 2. Merck. KEYTRUDA prescribing information. Available at: https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf. Accessed February 23, 2026. 3. Bristol Myers Squibb. OPDIVO prescribing information. Available at: https://packageinserts.bms.com/pi/pi_opdivo.pdf. Accessed February 23, 2026.

Methods

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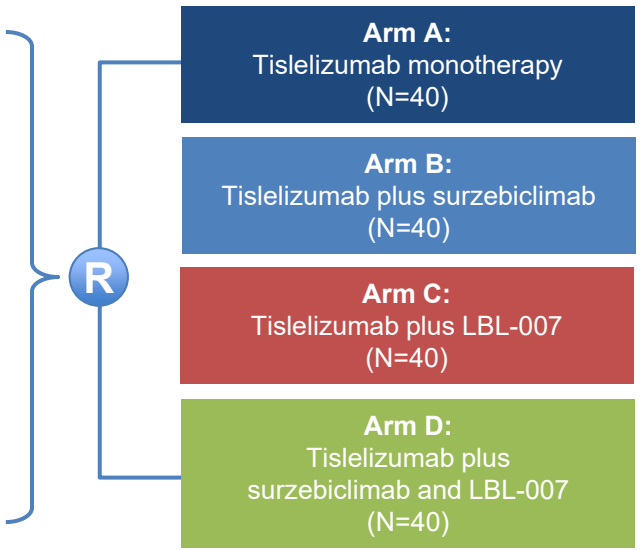
- This was a phase 2, randomized open-label, international study of tislelizumab with or without surzebiclimab and/or LBL-007 as 1L treatment in patients with R/M HNSCC (NCT05909904)

Key eligibility criteria

- Patients with squamous cell carcinoma of oropharynx, oral cavity, hypopharynx or larynx
- R/M disease incurable by local therapy
- PD-L1 expression CPS≥1
- No prior checkpoint inhibitor treatment
- ECOG PS 0 or 1
- Provide fresh or archival tumor tissue for PD-L1 status

Stratification

- PD-L1 (1-19 vs ≥20)



Endpoints

Primary endpoint

- Confirmed ORR by the investigator per RECIST v1.1

Select secondary endpoints

- PFS, DoR, CBR, and DCR
- Safety

Data cutoff date: June 17, 2025
Median (range) study follow up time: 13.1 (0.1-21.2) months overall

Abbreviations: 1L, first line; CBR, clinical benefit rate; CPS, combined positive score; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; ORR, overall response ratel PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; R/M, recurrent/metastatic.

Results: Baseline Characteristics

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- Baseline demographics were similar across all treatment arms and were representative of the target population

	Arm A TIS mono (N=40)	Arm B TIS + SUR (N=40)	Arm C TIS + LBL-007 (N=40)	Arm D TIS + SUR + LBL-007 (N=40)	Total (N=160)
Median (range), age, years	63.5 (41-81)	62.5 (35-83)	65.5 (22-82)	65.5 (35-84)	64.0 (22-84)
Sex, %					
Male	82.5	87.5	85.0	82.5	84.4
Female	17.5	12.5	15.0	17.5	15.6
ECOG PS, %					
0	52.5	45.0	50.0	42.5	47.5
1	47.5	55.0	50.0	57.5	52.5
Primary disease location, %					
Hypopharynx	15.0	5.0	5.0	15.0	10.0
Larynx	15.0	22.5	22.5	12.5	18.1
Oral cavity	35.0	47.5	45.0	42.5	42.5
Oropharynx	35.0	25.0	27.5	30.0	29.4
HPV, %					
Positive	15.0	12.5	22.5	27.5	19.4
Negative	40.0	37.5	37.5	30.0	36.3
Unknown	45.0	50.0	40.0	42.5	44.4
Prior platinum, %					
Yes	65.0	50.0	62.5	62.5	60.0
No	35.0	50.0	37.5	37.5	40.0
PD-L1 expression (CPS), %					
1-19	55.0	52.5	52.5	55.0	53.8
≥20	45.0	47.5	47.5	45.0	46.3

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; HPV, human papillomavirus; SUR, surzebiclimab; TIS, tislelizumab.

Results: Efficacy

- Similar confirmed ORRs were observed across all treatment arms

Analysis of Confirmed Disease Response by Investigator Assessment per RECIST v 1.1 (ITT Analysis Set)

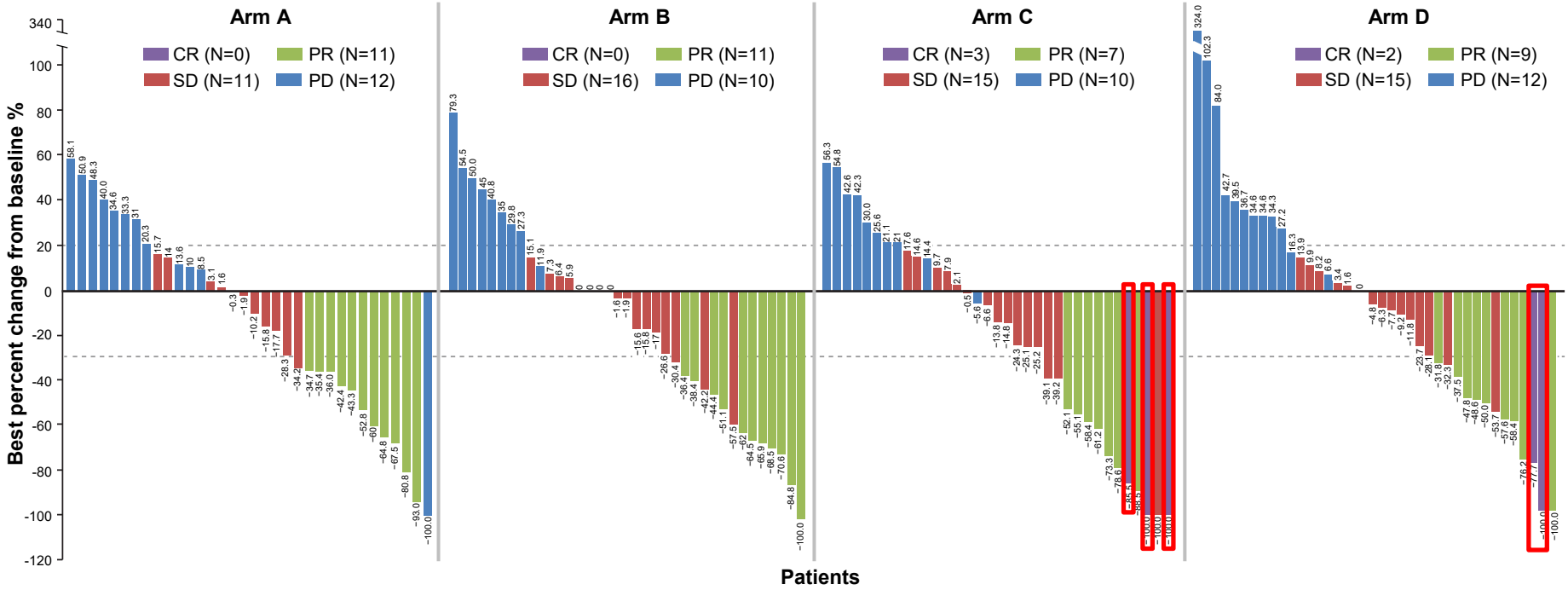
	Arm A TIS mono (N=40)	Arm B TIS + SUR (N=40)	Arm C TIS + LBL-007 (N=40)	Arm D TIS + SUR + LBL-007 (N=40)
ORR, % (95% CI)[a]	27.5 (14.6-43.9)	27.5 (14.6-43.9)	25.0 (12.7-41.2)	27.5 (14.6-43.9)
BOR, %				
CR	0	0	7.5	5.0
PR	27.5	27.5	17.5	22.5
SD	27.5	40.0	37.5	37.5
PD	40.0	25.0	27.5	30.0
Not evaluable/not assessed	5.0	7.5	10.0	5.0
Median DoR, months (95% CI)[b]	8.2 (3.9-NE)	NE (2.6-NE)	NE (8.4-NE)	NE (3.4-NE)
CBR, % (95% CI) [a,c]	32.5 (18.6-49.1)	37.5 (22.7-54.2)	35.0 (20.6-51.7)	37.5 (22.7-54.2)
DCR, % (95% CI) [a,d]	55.0 (38.5-70.7)	67.5 (50.9-81.4)	62.5 (45.8-77.3)	65.0 (48.3-79.4)

[a]The 95% CI was estimated using the Clopper–Pearson method. [b]Medians and other quartiles were estimated using the Kaplan–Meier method with 95% CIs estimated using the Brookmeyer and Crowley method with log-log transformation. [c]CBR defined as the proportion of patients who have confirmed CR, confirmed PR, or durable SD of ≥24 weeks in duration. [d]DCR defined as the proportion of patients who have confirmed CR, confirmed PR, or SD.
Abbreviations: BOR, best overall response; CI, confidence interval; CR, complete response; ITT, intent-to-treat; NE, not estimable; PD, progressive disease; PR, partial response; SD, stable disease.

Results: Efficacy

- Three patients in Arm C and two patients in Arm D achieved CRs

Best Percent Change from Baseline in Target Lesion Sum of Diameters by Confirmed BOR per Investigator (ITT Analysis Set)

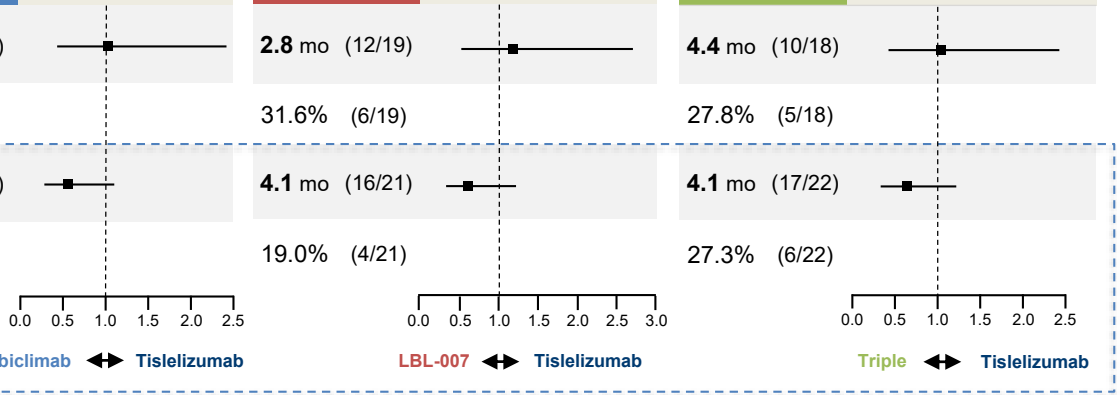


Results: Biomarkers

- In patients with **PD-L1 CPS 1-19**, tislelizumab with surzebiclimab and/or LBL-007 showed numerically longer median PFS (4.1-5.4 months vs 1.4 months) and higher ORR (19.0-27.3% vs 13.6%) compared with tislelizumab monotherapy

Median PFS and ORR in PD-L1 CPS ≥20 and 1-19 Subgroups (ITT Analysis Set)

		Tislelizumab	+ Surzebiclimab	PFS HR (95%CI)	+ LBL-007	PFS HR (95%CI)	Triple	PFS HR (95%CI)
PD-L1 CPS ≥20	mPFS (events)	**8.1** mo (11/18)	**5.6** mo (10/19)		**2.8** mo (12/19)		**4.4** mo (10/18)	
	ORR (n)	44.4% (8/18)	36.8% (7/19)		31.6% (6/19)		27.8% (5/18)	
PD-L1 CPS 1-19	mPFS (events)	**1.4** mo (19/22)	**5.4** mo (14/21)		**4.1** mo (16/21)		**4.1** mo (17/22)	
	ORR (n)	13.6% (3/22)	19.0% (4/21)		19.0% (4/21)		27.3% (6/22)	



Abbreviations: HR, hazard ratio.

Results: Safety

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Overall Safety Summary (Safety Analysis Set)

	Arm A TIS mono (N=40)	Arm B TIS + SUR (N=39)	Arm C TIS + LBL-007 (N=40)	Arm D TIS + SUR + LBL-007 (N=40)
Any TEAE, %	92.5	87.2	97.5	100.0
Grade ≥3	52.5	38.5	35.0	57.5
Serious	42.5	35.9	27.5	40.0
Leading to death	10.0	2.6	5.0	5.0
Any treatment-related TEAE, %	67.5	61.5	77.5	67.5
Grade ≥3	17.5	10.3	10.0	12.5
Serious	7.5	7.7	7.5	10.0
Leading to death	0	0	0	0
imAEs, %	32.5	33.3	47.5	27.5
IRRs, %	15.0	2.6	2.5	7.5

TEAEs in ≥15% of Patients in Any Arm (Safety Analysis Set)

	Arm A TIS mono (N=40)	Arm B TIS + SUR (N=39)	Arm C TIS + LBL-007 (N=40)	Arm D TIS + SUR + LBL-007 (N=40)
Any TEAE, %	92.5	87.2	97.5	100.0
Anemia	20.0	20.5	15.0	37.5
Hypothyroidism	5.0	15.4	35.0	20.0
AST increased	15.0	15.4	12.5	17.5
Pneumonia	12.5	17.9	15.0	10.0
Pruritus	10.0	7.7	22.5	15.0
Diarrhea	12.5	12.8	7.5	20.0
Fatigue	12.5	10.3	10.0	20.0
Constipation	12.5	10.3	17.5	7.5
Decreased appetite	17.5	12.8	2.5	15.0
Nausea	10.0	7.7	7.5	15.0
Hyponatraemia	5.0	15.4	10.0	10.0
Hypoalbuminaemia	5.0	15.4	7.5	10.0

A TEAE is defined as an AE that had onset or increase in severity level date on or after the date of the first dose of study drug and up to 30 days after the last dose of study drug(s) or the initiation of new anticancer therapy, whichever is earlier. Treatment-related TEAEs include those events considered by the investigator to be related or with missing assessment of the causal relationship. IRRs were identified any adverse event with the checkbox of IRR ticked by the investigator. Patients with multiple events for a given preferred term were counted once at the preferred term level.
Abbreviations: AST, aspartate aminotransferase; imAE, immune-mediated adverse event; IRR, infusion-related reaction.

Conclusions

- In patients with R/M HNSCC, efficacy was comparable between treatment arms, with no additional benefit accrued from adding surzebiclimab and/or LBL-007 to tislelizumab as 1L treatment
- The safety profile for tislelizumab, whether used as monotherapy or in doublet or triplet combination therapies, was generally well-tolerated and consistent with previous reports on immune checkpoint inhibitor therapies

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