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Evaluation of the Safety and Efficacy of Ivonescimab in Combination With Ligufalimab as First-Line Treatment for PD-L1–Positive Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

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BACKGROUND

- Although programmed cell death protein 1 (PD-1) inhibitors combined with chemotherapy are approved as first-line treatment for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC), some patients respond poorly to this treatment, warranting the need for new treatment strategies[1-2]
- Cluster of differentiation 47 (CD47) is a macrophage immune checkpoint protein that is overexpressed in HNSCC; overexpression of CD47 may correlate with elevated tumor programmed death-ligand 1 (PD-L1) levels and other markers of immunosuppression[3,4]
- Ivonescimab is a novel, investigational bispecific antibody against PD-1 and vascular endothelial growth factor (VEGF) that has exhibited cooperative binding in vitro and could produce complementary and synergistic antitumor effects through both the PD-1 and the VEGF pathways[5-7]
- Ligufalimab is a novel humanized immunoglobulin G4 monoclonal antibody to target CD47 that was designed to avoid hemagglutination, which adversely affected the safety profile of previous CD47-blocking antibodies[8,9]
  - Ligufalimab may enhance antitumor activity when combined with ivonescimab, as demonstrated in xenograft models[8]
- Here, we present data on the efficacy and safety of ivonescimab, both with and without ligufalimab, in patients with PD-L1–positive R/M HNSCC who have not received systemic anticancer therapy for recurrent or metastatic disease

OBJECTIVE

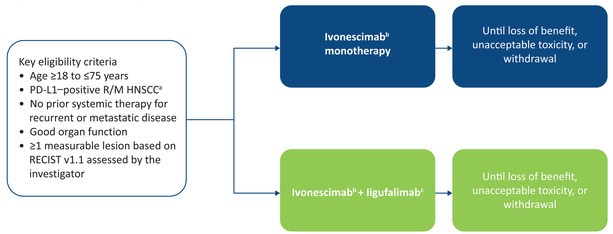
- To assess the safety and efficacy of ivonescimab as monotherapy or in combination with ligufalimab in patients 18-75 years of age with PD-L1–positive R/M HNSCC

METHODS

Study Design

- In this open-label, multicenter phase 2 trial (NCT05229497), patients in China with R/M HNSCC were assigned to receive ivonescimab monotherapy or ivonescimab in combination with ligufalimab (**Figure 1**)

Figure 1. Study Design



HNSCC, head and neck squamous cell carcinoma; Q3W, once every 3 weeks; PD-L1, programmed death-ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; R/M, recurrent/metastatic.

[a]Histologically or cytologically confirmed R/M HNSCC with a PD-L1 combined positive score of ≥1.

[b]Ivonescimab 10 mg/kg Q3W.

[c]Ligufalimab 45 mg/kg Q3W.

Outcomes

- The primary safety end points were incidence and severity of adverse events (AEs), and clinically significant abnormal laboratory findings
- The primary efficacy end point was investigator-assessed objective response rate (ORR) based on Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1)
- Key secondary end points were disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS) based on RECIST v1.1

RESULTS

Participants

- As of March 19, 2024, a total of 30 patients (10 in the ivonescimab monotherapy group; 20 in the ivonescimab + ligufalimab group) with R/M HNSCC were enrolled in the study
- Most enrolled patients were male (86.7%), with a median age of 60 years (range, 34-75 years; **Table 1**)
- All enrolled patients (100%) had an Eastern Cooperative Oncology Group performance status score of 1 and 17 (57%) had a PD-L1 combined positive score of ≥20 at baseline
- The median duration of follow-up was 3.3 months (95% CI, 0.9-6.4) for the ivonescimab monotherapy group and 4.1 months (95% CI, 2.8-4.8) for the ivonescimab + ligufalimab group
- The median duration of exposure to study treatment was 1.9 months (range, 0.7-6.4) in the ivonescimab monotherapy group and 3.9 months (range, 1.4-10.1) in the ivonescimab + ligufalimab group

Table 1. Baseline Characteristics

Characteristic	Ivonescimab n = 10	Ivonescimab + ligufalimab n = 20
Age, median (range), years	59.2 (34.3-67.2)	60.8 (41.8-75.2)
Sex, n (%)		
Male	8 (80.0)	18 (90.0)
Female	2 (20.0)	2 (10.0)
ECOG PS score, n (%)		
1	10 (100)	20 (100)
Smoking status, n (%)		
Current	3 (30.0)	2 (10.0)
Former	2 (20.0)	10 (50.0)
Never	5 (50.0)	8 (40.0)
Primary tumor location, n (%)		
Hypopharynx	0	3 (15.0)
Larynx	2 (20.0)	6 (30.0)
Oral cavity	7 (70.0)	4 (20.0)
Oropharynx	1 (10.0)	7 (35.0)
Disease status, n (%)		
Metastatic	2 (20.0)	9 (45.0)
Recurrent only	8 (80.0)	10 (50.0)
Newly diagnosed, nonmetastatic	0	1 (5.0)
PD-L1 CPS, n (%)		
CPS ≥1 and <20	4 (40.0)	9 (45.0)
CPS ≥20	6 (60.0)	11 (55.0)

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1.
Race/ethnicity demographics data were not collected.

Safety

- Treatment-related adverse events (TRAEs) were reported in 20 patients (66.6%); 1 was grade ≥3 (3.3%), and none led to discontinuation of treatment or death (**Table 2**)
- The most common TRAEs across both treatment groups were proteinuria (16.7%) and hypothyroidism (13.3%; **Figure 2**)

Table 2. Summary of Safety Results

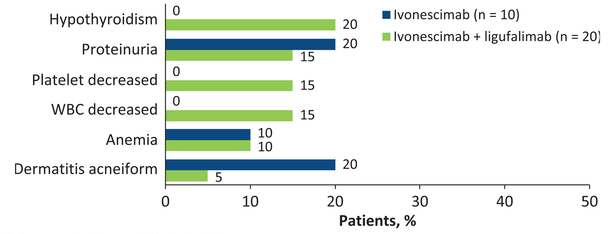
Adverse event	Ivonescimab n = 10	Ivonescimab + ligufalimab n = 20
TEAEs, n (%)		
Grade ≥3	1 (10.0)	5 (25.0)
Leading to discontinuation	0	1 (5.0)
Serious TEAE	1 (10.0)	4 (20.0)
Leading to death	1 (10.0)	3 (15.0)
TRAEs, n (%)		
Grade ≥3	0	1 (5.0)[a]
Leading to discontinuation	0	0
Serious TRAE	0	1 (5.0)
Leading to death	0	0

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

[a]1 patient reported grade ≥3 TRAEs in the ivonescimab + ligufalimab group (decreased appetite and tumor hemorrhage).

RESULTS (CONTINUED)

Figure 2. Most Common TRAEs (≥10% overall)[a]



TRAE, treatment-related adverse event; WBC, white blood cell.

[a]All of the most common TRAEs ≥10% were grades 1 to 2.

Efficacy

- At the time of data cutoff, ORR by investigator assessment was 30% (3/10) in the ivonescimab monotherapy group and 60% (12/20) in the ivonescimab + ligufalimab group (**Table 3**)
- DCR was 80% (8/10) in the ivonescimab monotherapy group and 90% (18/20) in the ivonescimab + ligufalimab group
- Median DOR was not reached in either treatment group
- Individual patient-level responses at the time of data cutoff are shown in **Figures 3 and 4**

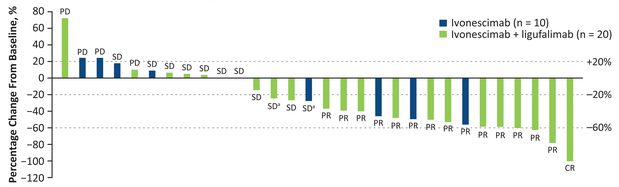
Table 3. Overview of Objective Response Rate

Response	Ivonescimab n = 10	Ivonescimab + ligufalimab n = 20
ORR %, (95% CI)		
Overall	30.0 (6.7-65.2)[a]	60.0 (36.1-80.9)[a]
PD-L1 CPS ≥1 and <20	75.0 (19.4-99.4)[a]	44.4 (13.7-78.8)[a]
PD-L1 CPS ≥20	0	72.7 (39.0-94.0)
BOR, n (%)		
CR	0	1 (5.0)
PR	3 (30.0)	11 (55.0)
SD	5 (50.0)	6 (30.0)
PD	2 (20.0)	2 (10.0)

BOR, best overall response; CPS, combined positive score; CR, complete response; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.

[a]2 patients (n = 1 in each treatment group) with SD subsequently had PR after data cutoff. This resulted in an ORR of 40.0% and 65.0%, respectively, in the ivonescimab group and ivonescimab + ligufalimab groups overall and 80.0% and 55.5% in the PD-L1 CPS≥1 and <20 subgroup.

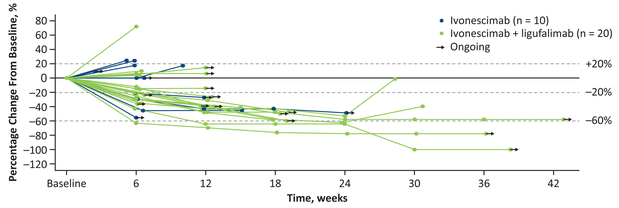
Figure 3. Best Percentage Change From Baseline in Sum of Tumor Diameters



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

[a]Patient subsequently had PR after data cutoff.

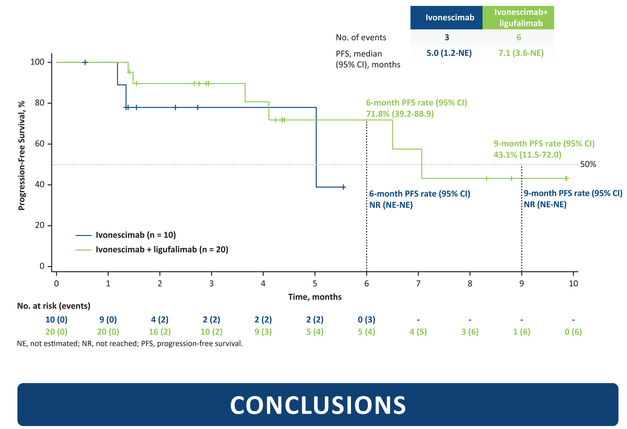
Figure 4. Percentage Change From Baseline in Sum of Diameters Over Time



RESULTS (CONTINUED)

- Median PFS was 5.0 months (95% CI, 1.2-NE) for the ivonescimab monotherapy group; the 6-month PFS rate was not reached
- Median PFS in the ivonescimab + ligufalimab group was 7.1 months (95% CI, 3.6-NE), with a 6-month PFS rate of 71.8% (**Figure 5**)

Figure 5. Kaplan Meier Curve of Progression-Free Survival



NE, not estimated; NR, not reached; PFS, progression-free survival.

CONCLUSIONS

- Ivonescimab as monotherapy or in combination with ligufalimab showed promising antitumor activity and an acceptable safety profile in patients with PD-L1–positive R/M HNSCC
- Results of this analysis support further evaluation of ivonescimab as monotherapy or in combination with ligufalimab in the treatment of patients with R/M HNSCC

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DISCLOSURES

W.L., Z.M.W., B.L., and M.X. are employees of Akeso Biopharma, Inc. All other authors have no conflicts of interest to disclose.

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