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Amivantamab in recurrent/metastatic head & neck squamous cell cancer (HNSCC) after disease progression on checkpoint inhibition and chemotherapy: Results from the phase Ib/II OrigAMI-4 study

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Background

EGFR and MET overexpression occur in 80%–90% of HNSCC tumors. Amivantamab (ami) is an EGFR-MET bispecific antibody with immune cell-directing activity. We evaluated ami monotherapy in previously treated HPV-unrelated recurrent/metastatic (R/M) HNSCC.

Methods

OrigAMI-4 (NCT06385080) is assessing subcutaneous (SC) ami as monotherapy and in combination with other agents in participants (pts) with R/M HNSCC. Cohort 1 is evaluating ami monotherapy in HPV-unrelated R/M HNSCC previously treated with platinum-based chemotherapy and a PD-1/PD-L1 inhibitor. Prior anti-EGFR therapy is exclusionary. Primary endpoint is objective response rate (ORR) per RECIST v1.1.

Results

As of 6 May 2025 (median follow-up: 3.4 months [mo]; range, 0–11.8), 67 pts have received ami monotherapy. Median age was 66 years, 76% were male, 64% had ECOG performance status score of 1, and the most common site of metastasis was lung (62%). The efficacy-evaluable population consisted of 32 pts with ≥2 disease evaluations (or discontinued for any reason before any disease evaluation) with a median follow-up of 5.7 mo. Confirmed ORR was 41% (13/32); 1 complete response (CR), 12 partial responses (PR), 15 stable diseases (SD). Among pts with confirmed response, 85% (11/13) have ongoing responses and remain on treatment. Median duration of response was 7.2 mo (95% CI, 7.2–not estimable). Median time to initial response was 6.4 weeks (range, 5.7–18.3). Clinical benefit rate (CR + PR + durable SD) was 88% (28/32). Most common treatment-emergent AEs (TEAE; >25%) were rash, fatigue, and hypoalbuminemia. Administration-related reactions were seen in 7% of pts (0 grade ≥3). In total, 7% discontinued ami due to TEAEs. Updated results with additional pts, longer follow-up, and biomarker analyses will be presented at the meeting.

Conclusions

Amivantamab demonstrated rapid and meaningful antitumor activity in pts with HPV-unrelated, previously treated R/M HNSCC after disease progression on checkpoint inhibition and chemotherapy. The early safety profile was consistent with prior studies, with no new safety signals identified.

Clinical trial identification

NCT06385080.

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Legal entity responsible for the study

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Disclosure

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