OrigAMI-5: A randomized, phase 3 study of subcutaneous amivantamab plus pembrolizumab and carboplatin vs standard of care pembrolizumab plus platinum and 5-fluorouracil as first-line treatment in recurrent/metastatic head and neck cancer

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Summary

OrigAMI-5 is a global, randomized, phase 3 study evaluating amivantamab plus pembrolizumab and carboplatin versus standard of care (pembrolizumab plus carboplatin or cisplatin and 5-FU) as first-line therapy for participants with R/M HNSCC

Current Status

OrigAMI-5 is currently enrolling, with a goal of approximately 500 participants

Registration Information

This study is registered with ClinicalTrials.gov (Identifier: NCT07276399)

Please scan the QR code

Poster

https://www.congresshub.com/Oncology/AM2026/Amivantamab/Haddad

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Disclosure

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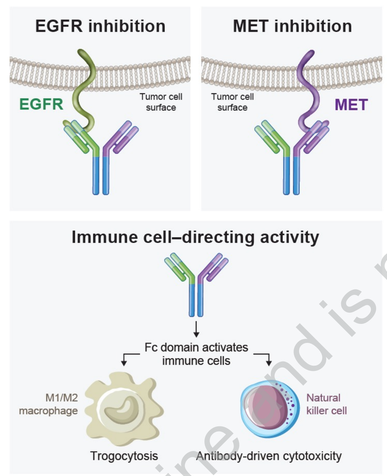
Introduction

- Recurrent and/or metastatic head and neck squamous cell cancer (R/M HNSCC) is associated with significant morbidity and mortality[1,2]
- Current first-line standard-of-care regimens, including combinations of pembrolizumab with or without platinum-based chemotherapy and 5-fluorouracil (5-FU), yield low response rates and poor long-term outcomes, with a median survival of ~1 year[3]
- Many p16-negative HNSCC tumors exhibit EGFR and MET overexpression[4,5]
- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity (**Figure 1**)[6,7] and has demonstrated meaningful activity across several solid tumor types[8–10]
- In prior reports of the phase 1b/2 OrigAMI-4 study (NCT06385080):
  - Subcutaneous amivantamab monotherapy demonstrated a confirmed investigator-assessed objective response rate (ORR) of 47% in R/M HNSCC after immune checkpoint inhibitor and platinum-based chemotherapy[8]
  - Among previously untreated R/M HNSCC, subcutaneous amivantamab plus pembrolizumab demonstrated a confirmed ORR of 56%[11]

Figure 1: Amivantamab's MoA[12]



EGFR, epidermal growth factor receptor; MoA, mechanism of action.

Objective

- This global, randomized, phase 3 study is evaluating the efficacy and safety of subcutaneous amivantamab in addition to pembrolizumab and carboplatin, as compared with the standard of care (pembrolizumab plus carboplatin or cisplatin and 5-FU), as first-line therapy for participants with R/M HNSCC

Methods

- OrigAMI-5 is a randomized, open-label, phase 3 study currently recruiting participants with R/M HNSCC (**Figure 2**)
  - Primary tumor locations of oral cavity, hypopharynx, larynx, and HPV-negative oropharyngeal cancer are eligible
  - HPV-positive oropharyngeal cancer and any known HPV positivity are excluded
- Participants will be randomized 1:1 to receive subcutaneous amivantamab with pembrolizumab and carboplatin, or 5-FU plus pembrolizumab and investigator's choice of carboplatin or cisplatin
- Key inclusion and exclusion criteria are shown in **Table 1**
- The multicenter, global OrigAMI-5 study is planned to open in approximately 205 sites across 22 countries (**Figure 3**)

Figure 2: OrigAMI-5 study design

Key eligibility criteria
- R/M HNSCC
- No prior anti-EGFR therapy
- ECOG PS score of 0 or 1
- Primary tumor locations of oral cavity, hypopharynx, larynx, or HPV-negative oropharyngeal cancer

Stratification factors
- PD-L1 CPS: <1 vs 1–19 vs ≥20
- ECOG PS: 0 vs 1

R 1:1
- **Subcutaneous amivantamab + pembrolizumab + carboplatin (n≈250)**
- **5-FU + pembrolizumab + cisplatin OR carboplatin (n≈250)**

Dosing schedule (in 21-day cycles):
- **Subcutaneous amivantamab**[a] at 2400 mg (3360 mg if ≥80 kg) weekly for the first cycle (initial dose only: 1600 mg or 2240 mg if ≥80 kg), then Q3W for up to 24 months
- **Pembrolizumab** at 200 mg IV Q3W for up to 24 months
- **Carboplatin** at AUC 5 mg/mL·min IV Q3W for up to 6 cycles
- **Cisplatin** at 100 mg/m^2 IV Q3W for up to 6 cycles
- **5-FU** at 1000 mg/m^2/day continuous IV infusion on Days 1 to 4 of each cycle for up to 6 cycles

Primary endpoints:
- Objective response rate by BICR per RECIST v1.1
- Overall survival[b]

Secondary endpoints:
- Progression-free survival by BICR per RECIST v1.1
- Duration of response by BICR
- Patient-reported outcomes
- Incidence and severity of adverse events and laboratory abnormalities

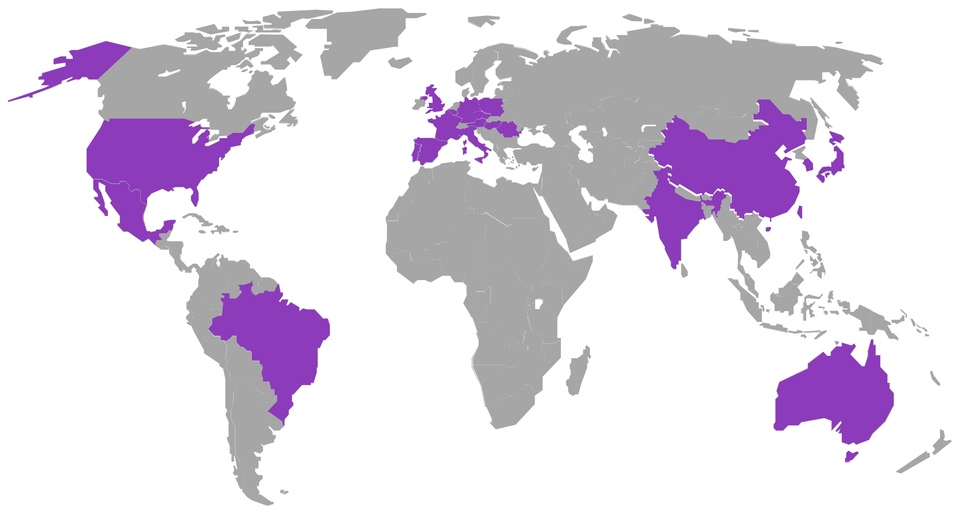
[a]Coformulated with recombinant human hyaluronidase PH20 (rHuPH20). [b]For the European Union and any applicable country/region, the primary endpoint is overall survival only.
5-FU, 5-fluorouracil; AUC, area under the curve; BICR, blinded independent central review; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HNSCC, head and neck squamous cell cancer; HPV, human papillomavirus; IV, intravenous; PD-L1, programmed death ligand 1; Q3W, every 3 weeks; R, randomized; R/M, recurrent/metastatic; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

Table 1: Key inclusion and exclusion criteria

Inclusion
• Histologically or cytologically confirmed R/M HNSCC
• Primary sites limited to oral cavity, hypopharynx, larynx, and HPV-negative oropharyngeal cancer
• No prior systemic therapy for R/M disease; prior curative-intent therapy allowed if completed >6 months prior without early progression
• ECOG PS score of 0 or 1
• PD-L1 CPS determined locally using validated testing within 6 months prior (for stratification; positivity not required for enrollment)
Exclusion
• Any prior anti-EGFR or anti-MET therapy in any setting
• Any known HPV positivity
• Untreated brain metastases or leptomeningeal disease; treated brain metastases allowed only if clinically stable and off steroids (≤10 mg prednisone or equivalent)
• Current or prior ILD, pneumonitis, or pulmonary fibrosis
• Uncontrolled illness, including (not limited to) ongoing or active infection

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HNSCC, head and neck squamous cell cancer; HPV, human papillomavirus; ILD, interstitial lung disease; PD-L1, programmed death ligand 1; R/M, recurrent/metastatic.

Figure 3: Participating countries



References

1. Faraji F, et al. *Transl Cancer Res*. 2023;12(5):1353–1358. 2. Belfiore MP, et al. *Biomedicines*. 2024;12(9):2080. 3. Burtness B, et al. *Lancet*. 2019;394(10212):1915–1928. 4. Rothenberger NJ, Stabile LP. *Cancers (Basel)*. 2017;9(4):39. 5. Hartmann S, et al. *Clin Cancer Res*. 2016;22(16):4005–4013. 6. Moores SL, et al. *Cancer Res*. 2016;76(13):3942–3953. 7. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044–2056. 8. Burtness B, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–June 2, 2026; Chicago, IL, USA. 9. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 10. Oberstein PE, et al. *J Clin Oncol*. Published online April 21, 2026. doi:10.1200/JCO-25-02187. 11. Mehra R, et al. Presented at: Multidisciplinary Head and Neck Cancers Symposium; February 19–21, 2026; Palm Desert, CA, USA. 12. Soo RA, et al. *Lung Cancer*. 2026;216:109405.

Solid Tumors

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