

Neoadjuvant and adjuvant amivantamab plus pembrolizumab in resectable, locally advanced HPV-unrelated head and neck squamous cell cancer: Cohort 6 of the phase 1b/2 OrigAMI-4 study

Douglas Adkins,¹ Robert I Haddad,² Paul Swiecicki,³ Ari Rosenberg,⁴ Jessica McDermott,⁵ Jessica Geiger,⁶ Siddharth Sheth,⁷ Kevin Harrington,⁸ Ravindra Uppaluri,² Robert L Ferris,⁹ Nishant Agrawal,¹⁰ Shlomo Koymfman,¹¹ Ken Tian,¹² Joshua C Curtin,¹² Kiichiro Toyozumi,¹³ Isabelle Leconte,¹⁴ Emrullah Yilmaz,¹⁵ Sujay Shah,¹⁵ Barbara Burtness¹⁶

¹Robert Ebert and Greg Stubblefield Head and Neck Tumor Center at Washington University School of Medicine, Alvin J Siteman Cancer Center, Barnes-Jewish Hospital, St Louis, MO, USA; ²Dana-Farber Cancer Institute, Boston, MA, USA; Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ³Department of Medical Oncology, University of Michigan, Ann Arbor, MI, USA; ⁴Department of Hematology and Oncology, University of Chicago, Chicago, IL, USA; ⁵Department of Medical Oncology, University of Colorado Anschutz School of Medicine, Aurora, CO, USA; ⁶Department of Hematology and Medical Oncology, Taussig Cancer Center, Cleveland Clinic, Cleveland, OH, USA; ⁷Division of Oncology, Department of Medicine, University of North Carolina, Chapel Hill, NC, USA; ⁸The Institute of Cancer Research/Royal Marsden Hospital, London, UK; ⁹Department of Otolaryngology/Head and Neck Surgery, UNC Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; ¹⁰Section of Otolaryngology-Head and Neck Surgery, University of Chicago, Chicago, IL, USA; ¹¹Department of Radiation Oncology, Cleveland Clinic Taussig Cancer Center, Cleveland, OH, USA; ¹²Johnson & Johnson, Spring House, PA, USA; ¹³Johnson & Johnson, Tokyo, Japan; ¹⁴Johnson & Johnson, Allschwil, Switzerland; ¹⁵Johnson & Johnson, Raritan, NJ, USA; ¹⁶Yale School of Medicine, New Haven, CT, USA.

Summary
Cohort 6 of the OrigAMI-4 study is evaluating perioperative amivantamab plus pembrolizumab among participants with previously untreated resectable locally advanced HPV-unrelated HNSCC

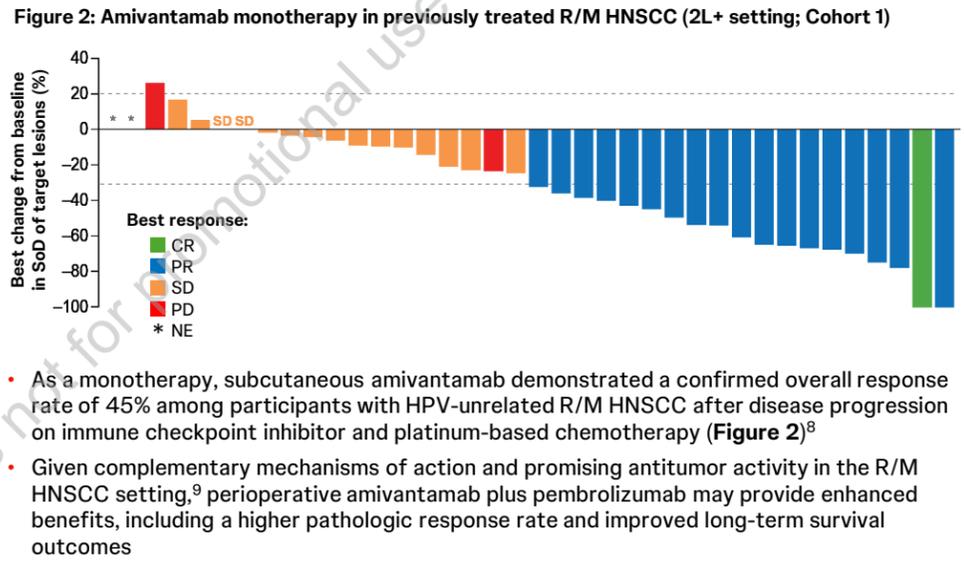
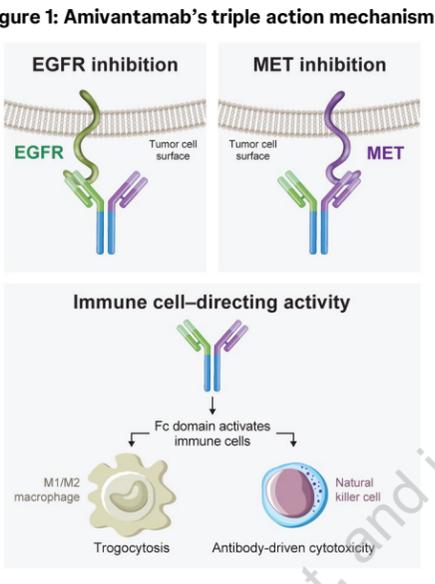
Current Status
OrigAMI-4 is currently enrolling
For more information on OrigAMI-4, please scan this QR code.

Registrational Information
This study is registered with ClinicalTrials.gov (Identifier: NCT06385080)

Acknowledgments
This study was funded by Janssen Research & Development, LLC, a Johnson & Johnson company. Medical writing assistance was provided by Katherine Fang, PhD (Johnson & Johnson), with editorial and graphical support from Lamantia Communications Inc., and funded by Johnson & Johnson.

Disclosures
DA served in a consulting or advisory role for Adco, AstraZeneca, Boehringer Ingelheim, Cue Biopharma, GSK, Immunata, Inhibrx, Sanofi, Janssen, Johnson & Johnson, Kura Oncology, Merck, Merus, Purple Biotech, Pyxis Oncology, Regeneron, and Tobin; and received research funding to the institution from AstraZeneca, Auro Oncology, Bicara, Celgene, Cohrus, Cue Biopharma, Daiichi Sankyo, Eli Lilly, Exelixis, Genmab, Gilead Sciences, GSK, Inhibrx, Sanofi, Janux, Johnson & Johnson, Kura Oncology, Merck, Merus, Novartis, Pfizer, Regeneron, Takeda, Tempus, and Xilio. RIH received research funding to the institution from Merck and GSK; received honoraria from Bristol Myers Squibb, Johnson & Johnson, AstraZeneca, Boehringer Ingelheim, Genmab, Takeda, AbbVie, and Astellas; and is the Chair of the Thyroid panel and a member of the Head and Neck panel for National Comprehensive Cancer Network. PS received honoraria from Eisai Therapeutics, CDRI Life, Praludis Therapeutics, Remo Therapeutics, Astellas, and Regeneron; received grants or research funding from Ascentage Pharma and Summit Therapeutics; and has a patent for HPV cDNA assay. AR served in an advisory board for Astellas, Eisai, EMD Serono, Nambiotix, Novartis, Regeneron, and Vaccitech; served on a Speaker's Bureau for Cohrus Biosciences; and received research funding to the institution from AbbVie, BeiGene, Bristol Myers Squibb/Celgene, EMD Serono, Hookipa Biotech, and Purple Biotech. JM has no conflicts of interest to report. JG received honoraria from Astellas and AVEA Pharmaceuticals. Sibeth received research funding to the institution from Merck, Regeneron, and Exelixis; and served on an advisory board for Eisai. KH received honoraria from ALX Oncology; received grant or research funding from AstraZeneca; and served on the scientific advisory board for Bicara. RU served on a scientific board for Merck, Daiichi Sankyo, and Regeneron; and received royalties from Washington University in St Louis. RLF received research funding from AstraZeneca/MedImmune, Merck, and Merus NV; received honoraria from Nambiotix, Novartis, and Novotect; served on a data safety monitoring board for Bicara Therapeutics, Inc, Merck, and Merus NV; served on an advisory board for Bristol Myers Squibb, Boehringer Ingelheim, Johnson & Johnson, and Johnson & Johnson; served on an independent data monitoring committee for Cohrus Biosciences, Corvus Therapeutics, CareViv, and Fortvita Biologics, Inc; and owns stock in Novartis. NA received grants from NCI/NCI, University of Chicago Comprehensive Cancer Center, and Cancer Research Foundation; served on a speakers bureau for Merck; has patents with OncoX; and has stock with Privo Technologies and OncoX. SK served in a consulting role for Merck, Bristol Myers Squibb, Regeneron, Galera Therapeutics, and Castle Biosciences; received research funding from Merck and Castle Biosciences; and reported other financial relationships with UpToDate, KT Tunstall, KT Tunstall, IL, EV, and SShah are employees of and may hold stock in Johnson & Johnson. BB received honoraria from Johnson & Johnson, Merck, IO Biotech, Pfizer, Rakuten, GSK, Takeda, and MSD; served in a consulting role for Genentech and Rakuten; served on an advisory board for Merus NV and ALX Oncology; and reported other nonfinancial relationships with Zentaris, AstraZeneca, and VITAC.

- Background**
- The addition of neoadjuvant and adjuvant pembrolizumab to standard of care surgery and adjuvant (chemo)radiation significantly improved event-free survival among participants with resectable, locally advanced head and neck squamous cell carcinoma (HNSCC) with PD-L1 combined positive score (CPS) ≥1 (KEYNOTE-689)¹
 - However, there is a need to further improve response rates and reduce the proportion of patients with disease progression during neoadjuvant treatment
 - Of note, >95% of participants in the KEYNOTE-689 trial had human papillomavirus (HPV)-negative disease
 - Epidermal growth factor receptor (EGFR) and MET are overexpressed in HNSCC tumors^{2,3}
 - Amivantamab, an EGFR-MET bispecific antibody with immune cell-directing activity (Figure 1),^{4,5} is approved for 4 indications in advanced non-small cell lung cancer and has demonstrated promising and meaningful antitumor activity in metastatic colorectal cancer^{6,7} and recurrent/metastatic (R/M) HNSCC⁸



- Methods**
- The multicenter, global, phase 1b/2 OrigAMI-4 study (ClinicalTrials.gov Identifier: NCT06385080) is assessing subcutaneous amivantamab as monotherapy or in combination with other agents in HNSCC (Figure 3)
 - Cohorts 1 to 5 have enrolled participants with R/M HNSCC
 - Cohort 6 is evaluating perioperative amivantamab plus pembrolizumab in participants with resectable, locally advanced HPV-unrelated HNSCC
 - Key inclusion criteria are presented in Table 1
 - Up to approximately 40 participants will be enrolled into Cohort 6 from 9 sites (Figure 4)
 - All enrolled participants will receive neoadjuvant amivantamab plus pembrolizumab prior to surgery
 - Following surgery, participants will receive adjuvant radiation (with or without cisplatin) plus pembrolizumab, followed by adjuvant amivantamab plus pembrolizumab
 - The primary endpoint will be major pathologic response
 - Secondary endpoints include event-free survival and overall survival
 - Safety assessments will include monitoring adverse events and laboratory abnormalities

Figure 3: OrigAMI-4 study design

Eligibility criteria for Cohort 6

- Locally advanced HNSCC
- No prior anti-EGFR therapy
- ECOG PS 0 or 1
- PD-L1 CPS ≥1
- HPV-unrelated: primary tumor locations of oral cavity, hypopharynx, larynx and HPV-negative oropharyngeal cancer

Dosing schedule

- Subcutaneous amivantamab at 2400 mg (3360 mg if ≥80 kg) is given weekly for the first 3 weeks (initial dose only: 1600 mg or 2240 mg if ≥80 kg), then Q3W (in 21-day cycles)
- IV pembrolizumab is administered at 200 mg Q3W

- Cohort 1: amivantamab monotherapy in HPV-unrelated** Post-PD-(L)1 inhibitor and platinum-based chemotherapy
- Cohort 2: amivantamab plus pembrolizumab in HPV-unrelated** Treatment-naïve in the R/M setting
- Cohort 3: amivantamab plus paclitaxel in HPV-unrelated** Post-PD-(L)1 inhibitor
- Cohort 4: amivantamab monotherapy in HPV-related** Post-PD-(L)1 inhibitor and platinum-based chemotherapy
- Cohort 5: amivantamab plus pembrolizumab with carboplatin** Treatment-naïve in the R/M setting
- Cohort 6: amivantamab plus pembrolizumab in HPV-unrelated** Treatment-naïve in the locally advanced setting

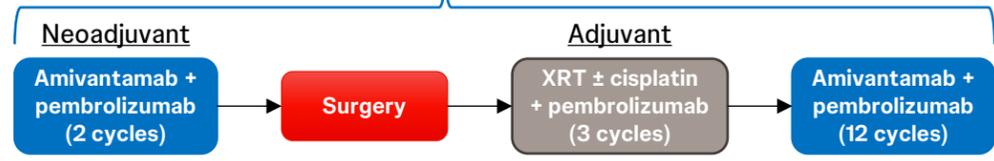
Presented at ESMO 2025 by Dr Harrington (Preliminary results shown in Figure 2)

Presented at MHNCS 2026 by Dr Mehra

Presented at ESMO 2025 by Dr Swiecicki

Endpoints for Cohort 6

- Major pathologic response (primary)
- Event-free survival
- Overall survival
- Safety



ECOG PS, Eastern Cooperative Oncology Group performance score; Q3W, every 3 weeks; XRT, radiation therapy.

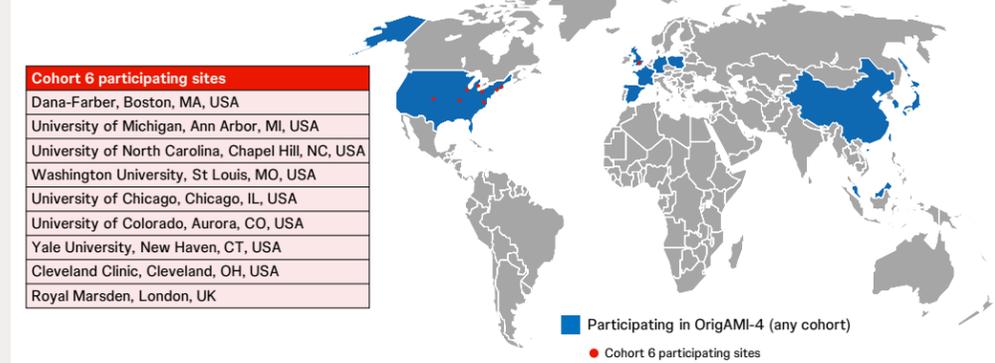
Table 1: Key inclusion/exclusion criteria

Inclusion	Exclusion
<ul style="list-style-type: none"> ≥18 years Resectable Stage III or IVa disease Primary location(s) in the oropharynx (HPV-negative), oral cavity, hypopharynx, or larynx Tumor CPS ≥1 by local testing Participant must provide a baseline biopsy sample (can be newly performed during screening or be tissue obtained prior to locally advanced diagnosis and within 3 months prior to the start of neoadjuvant therapy) 	<ul style="list-style-type: none"> HPV-positive oropharyngeal cancer Prior use of an EGFR- or MET-targeting agent Autoimmune disease that has required systemic therapy within the past 2 years Known allergies, hypersensitivity, intolerance, or contraindication to excipients of pembrolizumab Untreated brain metastases
<ul style="list-style-type: none"> Treatment-naïve 	

References

1. Uppaluri R, et al. *N Engl J Med*. 2025;393(1):37–50. 2. Rothenberger NJ, Stabile LP. *Cancers (Basel)*. 2017;9(4):39. 3. Hartmann S, et al. *Clin Cancer Res*. 2016;22(16):4005–4013. 4. Moores SL, et al. *Cancer Res*. 2016;76(13):3942–3953. 5. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044–2056. 6. Oberstein P, et al. Presented at: American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium; January 18–20, 2024; San Francisco, CA, USA. 7. Chen EX, et al. Presented at: American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium; January 8–10, 2026; San Francisco, CA, USA. 8. Harrington K, et al. *Oral Oncol*. 2025;171:107791. 9. Mehra R, et al. Presented at: Multidisciplinary Head and Neck Cancers Symposium; February 19–21, 2026; Palm Desert, CA, USA.

Figure 4: OrigAMI-4 study map



Solid Tumors