1352P

Amivantamab plus paclitaxel in recurrent/metastatic head and neck squamous cell cancer after disease progression on checkpoint inhibition: *Identification of the recommended combination dose from the phase 1b/2 OrigAMI-4 study*

Paul L Swiecicki[1], Bhumsuk Keam[2], Shau-Hsuan Li[3], Varinder Kaur[4], Hung-Ming Wang[5], Douglas Adkins[6], Myung-Ju Ahn[7], Sung-Bae Kim[8], Aarti Bhatia[9], Missak Haigentz[10], Hsiang-Fong Kao[11], Ari J Rosenberg[12], Chunying Gao[13], Joshua C Curtin[13], Xuesong Lyu[14], Kiichiro Toyoizumi[15], Aastha Kapoor[13], Emrullah Yilmaz[15], Mahadi Baig[15], Muh-Hwa Yang[16]

[1]Department of Medical Oncology, University of Michigan Rogel Cancer Center, Ann Arbor, MI, USA; [2]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [3]Division of Hematology-Oncology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; [4]Division of Hematology & Oncology, University of Virginia Health, Charlottesville, VA, USA; [5]Division of Medical Oncology, Department of Medicine Internal Medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan; [6]Division of Medical Oncology, Washington University School of Medicine, St. Louis, MO, USA; [7]Division of Haematology-Oncology, Department of Medicine, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Republic of Korea; [8]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [9]Division of Oncology, Department of Medicine, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [10]Section of Head & Neck Oncology, Rutgers Cancer Institute, Rutgers Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ, USA; [11]Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan; [12]Department of Medicine, Section of Hematology and Oncology, University of Chicago, Chicago, IL, USA; [13]Johnson & Johnson, Spring House, PA, USA; [14]Johnson & Johnson, Shanghai, China; [15]Johnson & Johnson, Raritan, NJ, USA; [16]Division of Medical Oncology, Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan.

Key Takeaway

The combination of amivantamab plus paclitaxel demonstrated durable antitumor activity among participants with 2L+ R/M HNSCC, with no new safety signals

Conclusions

Subcutaneous amivantamab plus paclitaxel demonstrated a confirmed response in 7 of 11 (64%) participants with R/M HNSCC after disease progression on checkpoint inhibitor and platinum-based chemotherapy

Safety profile was consistent with those of the individual agents; no ARRs related to amivantamab were reported

Additional cohorts from OrigAMI-4 are evaluating subcutaneous amivantamab in combination with other agents, including pembrolizumab and carboplatin

Please scan QR code

Poster

https://www.congresshub.com/Oncology/ESMO2025/Amivantamab/Swiecicki

Copies of this poster obtained through this QR code are for personal use only and may not be reproduced without written permission of the authors.

Acknowledgments

The authors would like to thank all participants who were enrolled in the study and their families and caregivers; physicians and nurses who cared for participants; staff members who supported this clinical trial, and staff members at the study sites and involved in data collection/analyses. This study was funded by Janssen Research & Development, LLC, a Johnson & Johnson company. Medical writing assistance was provided by Katharine Fang, PhD (Johnson & Johnson), with support from Lunanity Communications Inc. and funded by Johnson & Johnson.

Disclosures

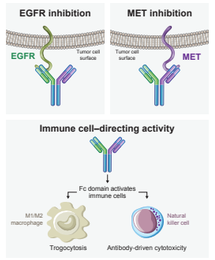
PLS received consulting fees from Astellas Pharma, CSR-Life, Elevar, EMD Serono, GenVec, Janssen, Prelude, RAPT Therapeutics, Regeneron, Remix, and Rgenta; received research funding from Ascentage Pharma and Summit Therapeutics; and holds patents/intellectual property or received royalties related to ctDNA detection technology from Bio-Rad. **BK** received honoraria from Yuhan, Lilly, AstraZeneca, Bayer, LG Chem, and MSD Oncology; served in a consulting or advisory role for Handok, Trial Informatics, NeoImmuneTech, ImmuneOncia, and TiumBio; and received research funding from Ono Pharmaceutical, MSD Oncology, and AstraZeneca. **DA** served in a consulting or advisory role for Merck, Cue Biopharma, Exelixis, Immunitas, Kura Oncology, Targimmune Therapeutics, Boehringer Ingelheim, Genmab/Seattle Genetics, Seagen, Adaz Nortye, Iribiro, Merck KGaA, Merus, Purple Biotech, Regeneron, Sanofi, and NATCO Pharma; received research funding from Pfizer, Lilly, Merck, Celgene, Novartis, AstraZeneca, Blueprint Medicines, Bristol Myers Squibb, Kura Oncology, Cue Biopharma, Cofactor Genomics, Debiopharm, ISA Pharmaceuticals, Gilead Sciences, BeiGene, Roche, Vaccinex, Immutep, Hookipa, Epizyme, Adlai Nortye, Bioatla, Boehringer Ingelheim, Calliditas Therapeutics, Genmab, NATCO Pharma, Tizona Therapeutics, Seagen, Merus, Iribiro, Eraeca, Alentis Therapeutics, Cohenus BioSciences, Takeda, Xilio Therapeutics, GSK, Johnson & Johnson/Janssen, Rgenta, AVEO, Daiichi Sankyo Europe GmbH, Exelixis, and Tempus; and received travel, accommodations, or expenses from NATCO Pharma. **M-JA** received honoraria from AstraZeneca, Takeda, Merck, MSD, Daiichi Sankyo, Amgen, and Yuhan; served in a consulting or advisory role for AstraZeneca, Takeda, Merck, Amgen, MSD, Daiichi Sankyo, BioNTech, Johnson & Johnson, Boehringer Ingelheim, Genexine, Vorcovi, Alpha Pharmaceuticals, and Yuhan; and holds patents/intellectual property or received royalties from Yuhan. **S-BK** served in a consulting or advisory role for AstraZeneca, BeiGene, Daehwa Pharmaceutical, Daiichi Sankyo/AstraZeneca, Enozi Biosciences, ISU Abxis, Lilly, and OBI Pharma; received research funding from Genzyme; received honoraria from Daehwa Pharmaceutical, Kalbe Farma, and LegoChem Biosciences; and holds stock and other ownership interests in Genospiexis. **AB** received honoraria from Clinical Care Options, Merck Serono, and Regeneron; and research funding from Boehringer Ingelheim. **MH** received consulting fees from AstraZeneca, Boehringer Ingelheim, Coherus BioSciences, Johnson & Johnson, and Takeda. **A.JR** holds stock and other ownership interests in Galectin Therapeutics and Privo Technologies; served in a consulting or advisory role for Astellas Pharma, Eisai, EMD Serono, Nanobiotix, Novartis, Regeneron, and Vaccitech; participated in a speakers bureau for Coherus BioSciences; and received research funding from AbbVie, BeiGene, Bristol Myers Squibb/Celgene, EMD Serono, Hookipa, and Purple Biotech. **CG, JCC, XL, KT, AK, EY,** and **MB** are employees of and may hold stock in Johnson & Johnson. **M-HY** received honoraria from MSD, Pfizer, Merck, and Ono Pharmaceutical; and served in a consulting or advisory role for MSD and Pfizer. **S-HL, YH, H-MW,** and **H-FK** have no conflicts of interest to report.

Background

- Outcomes among patients with previously treated recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) are poor[1–4]
  - In the 2L population, paclitaxel monotherapy resulted in low response rates
- EGFR and MET overexpression occur in 80%–90% of HNSCC tumors[5,6]
- Amivantamab is an EGFR-MET bispecific antibody with a triple mechanism of action,[7,8] including (1) EGFR inhibition, (2) MET inhibition, and (3) immune cell–directing activity (**Figure 1**)
- Subcutaneous amivantamab monotherapy has demonstrated rapid and durable activity in 2L+ HPV-unrelated R/M HNSCC[9]

We evaluated subcutaneous amivantamab plus paclitaxel in R/M HNSCC after disease progression on checkpoint inhibitor

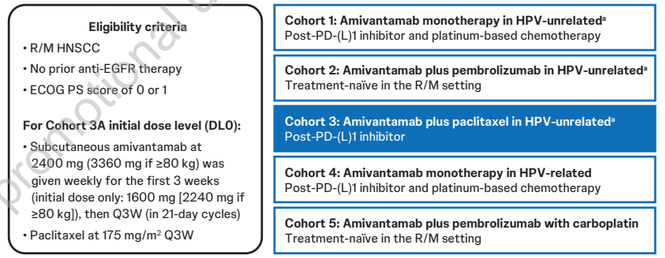
Figure 1: Amivantamab's triple action mechanism



Methods

- OrigAMI-4 (ClinicalTrials.gov Identifier: NCT06385080) is assessing subcutaneous amivantamab in R/M HNSCC (**Figure 2**)
- Cohort 3A planned to enroll 6–12 participants to evaluate the combination dose of amivantamab and paclitaxel
  - Prior anti-EGFR and taxane therapy were exclusionary
- Primary endpoints were dose-limiting toxicity (DLT) and safety
- Responses were assessed by the investigator per RECIST v1.1

Figure 2: OrigAMI-4 study design



Note: All cohorts of OrigAMI-4 will utilize the subcutaneous formulation of amivantamab, which is coformulated with recombinant human hyaluronidase PH20 and manually injected in the abdomen.
[a]Participants with HPV+ oropharyngeal cancer were excluded.
ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks.

Results

Demographic and baseline disease characteristics

- As of August 6, 2025, 11 participants were dosed (**Table 1**), with a median follow-up of 9.8 months (range, 0.4–12.5)
- All participants had at least 1 prior line of treatment, previously receiving a checkpoint inhibitor as well as platinum-based chemotherapy

Table 1: Demographic and baseline disease characteristics

Characteristic, n (%)	N=11
Median age (range), years	58 (39–69)
Male / female	9 (82) / 2 (18)
Race: Asian / White / Unknown	7 (64) / 3 (27) / 1 (9)
Primary tumor location	
Hypopharynx	1 (9)
Larynx	1 (9)
Oral cavity	8 (73)
Oropharynx	1 (9)

Dose-limiting toxicity and safety

- DLO was identified as the phase 2 combination dose
  - Among those DLT-evaluable (n=7), 1 participant experienced DLTs (grade 3 mucositis and fatigue, both resolved)
- Adverse events were mostly grades 1–2 and related to EGFR and MET inhibition (**Table 2**)
- No administration-related reactions (ARRs) related to amivantamab were reported

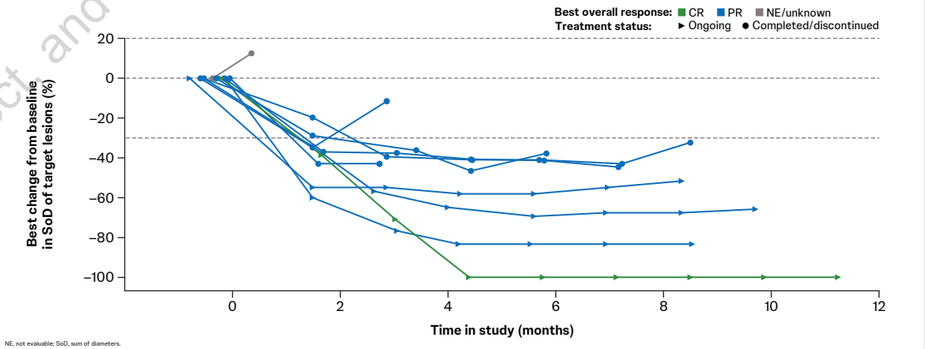
Table 2: Safety profile

Treatment-emergent adverse events (≥20%) by preferred term, n (%)	N=11	
	All grades	Grade ≥3
Related to EGFR inhibition		
Dermatitis acneiform	5 (45)	1 (9)
Paronychia	5 (45)	0
Stomatitis	5 (45)	2 (18)
Rash	4 (36)	0
Diarrhea	3 (27)	1 (9)
Related to MET inhibition		
Hypoalbuminemia	3 (27)	0
Other		
Fatigue	5 (45)	1 (9)
Hypophosphatemia	4 (36)	0
Neutropenia	3 (27)	2 (18)
Pneumonia	3 (27)	2 (18)
Leukopenia	3 (27)	1 (9)
Myalgia	3 (27)	1 (9)
Alanine aminotransferase increased	3 (27)	0
Anemia	3 (27)	0
Back pain	3 (27)	0
Constipation	3 (27)	0
Hypokalemia	3 (27)	0
Nausea	3 (27)	0
Pyrexia	3 (27)	0

Efficacy

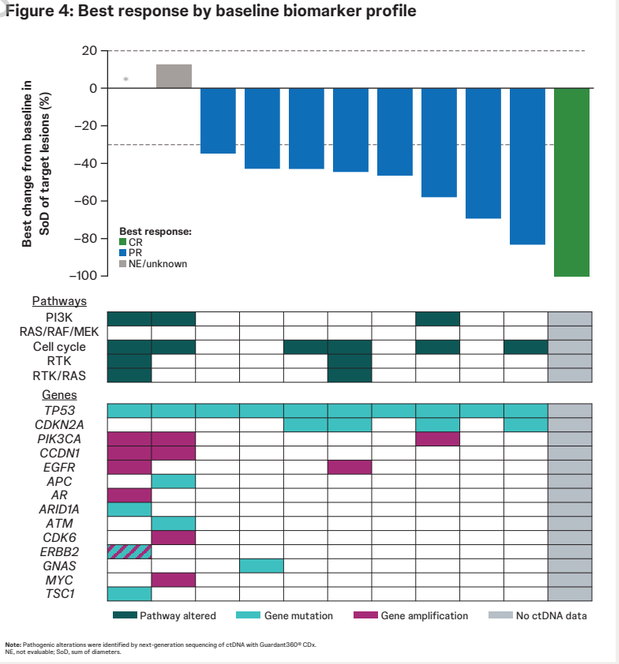
- Objective response rate was 64% (95% CI, 31–89)
  - As of data cutoff, median response duration was not reached
  - Among confirmed responders, 4 of 7 remained on treatment
  - 1 participant achieved a complete response and is ongoing (**Figure 3**)
- Tumor shrinkage of target lesions was seen in 9 of 11 participants
- Median time to first response was 6.6 weeks (range, 6.1–14.6)
- Median progression-free survival and overall survival were not estimable

Figure 3: Antitumor activity over time



NE, not evaluable; SoD, sum of diameters.

Figure 4: Best response by baseline biomarker profile



Note: Pathogenic alterations were identified by next-generation sequencing of ctDNA with Guardant360® CDx.
NE, not evaluable; SoD, sum of diameters.

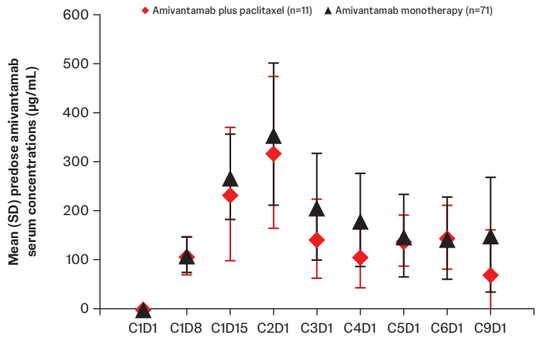
Biomarker analysis

- Antitumor activity among responders was observed regardless of baseline alterations; the 2 participants who were not evaluable had more mutations, but due to small numbers, the high response rate, and limited data on non-responders, the significance of this is unclear (**Figure 4**)

Pharmacokinetics

- Predose concentrations of amivantamab were measured for a pharmacokinetics (PK) analysis
- Observed amivantamab serum concentrations were consistent between the amivantamab plus paclitaxel and amivantamab monotherapy cohorts, suggesting amivantamab PK exposure was not impacted by paclitaxel (**Figure 5**)

Figure 5: Observed trough amivantamab concentrations from the amivantamab plus paclitaxel and amivantamab monotherapy cohorts



References

1. Ferris RL, et al. *N Engl J Med*. 2016;375(19):1856–1867. 2. Soulières D, et al. *Lancet Oncol*. 2017;18(3):323–335. 3. Cohen EEW, et al. *Lancet*. 2019;393(10167):156–167. 4. Fayette J, et al. *Clin Cancer Res*. 2025;31(13):2617–2627. 5. Rothenberger NJ, Stabile LP. *Cancers (Basel)*. 2017;9(4):39. 6. Hartmann S, et al. *Clin Cancer Res*. 2016;22(16):4005–4013. 7. Moores SL, et al. *Cancer Res*. 2016;76(13):3942–3953. 8. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044–2056. 9. Harrington K, et al. Presented at: European Society for Medical Oncology (ESMO) Congress; October 17–21, 2025; Berlin, Germany. Poster 1327MO.

Solid Tumors

Presented by PL Swiecicki at the European Society for Medical Oncology (ESMO) Congress; October 17–21, 2025; Berlin, Germany.

This material is distributed by J&J Medical Connect and is for promotional use for scientific purposes only.